UNITED STATES NUCLEAR REGULATORY COMMISSION

MEETING WITH ADVISORY COMMITTEE ON

MEDICAL USES OF ISOTOPES

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THURSDAY

JUNE 25, 2009

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The Commission met at 1:30 p.m., the Honorable Gregory B. Jaczko, Chairman, presiding.

COMMISSIONERS PRESENT:

GREGORY B. JACZKO, Chairman

PETER B. LYONS, Commissioner

DALE E. KLEIN, Commissioner

KRISTINE L. SVINICKI, Commissioner

ACMUI PANEL

LEON MALMUD, M.D., Chairman

WILLIAM VAN DECKER, M.D., Nuclear Cardiologist

STEVEN R. MATIMULLER, Nuclear Pharmacist Representative

BRUCE R. THOMADSEN, Ph.D., Medical Physicist, Radiation Therapy

DARRELL FISHER, PhD, Patients Rights Advocate

JAMES S. WELSH, M.D., Radiation Oncologist

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

CHAIRMAN JACZKO: Well, today is one of the good opportunities we have to get a perspective on the effects of the regulatory actions we take from the medical community. As I was going through the slides, I was certainly reminded, I think, of the breath of issues that you as a committee deal with and of the importance of these issues have, both, I think, certainly from a regulatory perspective as well as in the practice of medicine and other activities.

And it is certainly one of the things I'm always reminded of in these particular areas is that this is an area in which individuals are getting often times inadvertent doses. We have a lot focus and attention, I think, as a regulatory agency on the power reactors.

And for the most part, those issues there are really about hypothetical scenarios and potential doses. This is an area in which we are actually dealing with, on a periodic basis, unattended doses to patients, to individuals. So, it's certainly a very important program, a very important issue.

One of the issues I know the committee will talk about today are the events that happened at the Department of Veterans Affairs, and I think this is certainly a very important issue. Making sure we have the right regulatory program in place to oversee the VA program is extremely important.

And we do have an ongoing investigation right now in this area and we are continuing to get information. And it certainly will, I think, be a priority of mine and I suspect of the Commission as well to make sure that we process that properly

and promptly to make sure we keep the focus on protecting public health and safety.

So this is -- certainly the number of incidents in this areas that we deal with and all medical events is a small percentage of, I think, all the activity that goes on in the medical arena, but they certainly are important issues and ones where we want to continue to see how we can improve our programs and make them better to ensure that we bring those numbers down as small as possible.

So I look forward to hearing from you with your particular expertise and your experience in the field and how that can better inform our decision-making process with our regulations. So, I ask if any of my fellow Commissioners have any comments they would like to make?

COMMISSIONER KLEIN: I would just like to thank you for what you do on behalf of the Commission. As Greg indicated, we spend a lot of time on power reactors, but I think meetings like this remind us that there is a lot of other activities that we are involved in, that you all are involved in. So I would like to thank you for your activities for the beneficial uses of radiation that so many people depend on. So thanks for your contributions.

CHAIRMAN JACZKO: Dr. Malmud, I think we will begin with you.

DR. MALMUD: Thank you. Good afternoon Chairman Jaczko and Commissioners Svinicki, Lyons and Klein. I'm Leon Malmud. I'm professor of radiology and medicine and dean emeritus, Temple University School of Medicine. My role here is as chairman of the ACMUI. And we are pleased to have this

opportunity to report to you and share our thoughts on five subjects today.

The five include the following, which will be presented in order by Dr. William Van Decker, who is the director of nuclear cardiology and associate professor of medicine at Temple University School of Medicine, and that topic is perspectives on the clinical benefit of diagnostic nuclear medicine.

The second will be Mr. Steve Mattmuller who is the chief of nuclear pharmacist at Kettering Medical Center in Dayton, Ohio.

The third is the cesium-137 chloride irradiator subject, and Dr. Bruce Thomadsen will be presenting that. He is a medical physicist and professor at the University of Wisconsin, in Madison. And Dr. Thomadsen is the incoming ACMUI vice chairman, who will take office in that role on October 1st.

The next topic will be presented by Dr. Darrell Fisher, who is a senior scientist at Pacific Northwest National Laboratory in Richland, Washington. And he will address the availability of cobalt-60 for gamma stereotactic radiosurgery.

And the last subject will be presented by Dr. James Walsh, who is medical director at the University of Wisconsin Cancer Center Riverview in Wisconsin Rapids and he is clinical professor of human oncology at the University of Wisconsin School of Medicine and Public Health in Madison. He will address the medical events involving permanent prostate brachytherapy.

Each of these subjects has been discussed with the full ACMUI in preparation for presentation to you today. And if I may, I will pass this on to Dr. Van Decker.

DR. VAN DECKER: Thank you, Dr. Malmud. I'm Bill Van Decker. Good afternoon, all. I'm a physician practitioner in the field of diagnostic nuclear cardiology, which is a subset of the universe of nuclear medicine testing in this nation. And it's my pleasure to speak a little bit this afternoon about the perspectives of clinical benefits of diagnostic nuclear medicine, especially in light of the recent timely report of NCRP Report 160.

NCRP Report 160 is actually a statistical compilation of the ionizing radiation exposure of the U.S. population in 2006. It is actually compared by the NCRP group to their last report in this arena, which is actually now about 30 years old, and quite a bit has obviously happened over that period of time.

It averages out ionizing radiation exposure over the entire population and points out that over the 30 years there has been about a 1.7 times increase. It points it out that on average right now average exposure is about 50 percent from ubiquitous environmental background, which obviously can vary from site to site and altitude to altitude throughout the United States, and that there is a portion of it for medical diagnostics.

The medical diagnostics dose has increased over 30 years about five to six times, which is a total absolute value of about 3 millisieverts, which is about the amount a commercial airline crew would get flying continental in the U.S. in a year's worth of work.

The increase has been shown to be due mostly to increased care utilization of CT scanning and diagnostic nuclear medicine as these technologies have

become more mature and useful in our patient care. I would point out that in the world of general nuclear medicine, some of those numbers have actually flattened to be decreasing somewhat over the past three or four years.

I would also point out that these technologies are not general screening technologies like colonoscopy or mammography. They are essentially modalities used for people with signs or symptoms of significant disease. And so, it is a subset of population that we are really testing.

The report does attribute the average over the entire population, and it does not take into account that this may by correctly and disproportionately performed on the elderly and those with more serious medical problems. The report does not attempt to qualify any associated health risks or specify the actions that should be taken in light of this statistical data.

The report also does not have time to really go into the enormous benefit of medical imaging on patient care and the intense efforts of the provider community to keep radiation dosing as low as reasonable in achieving good diagnosis and good patient care.

I think that, you know, if one were to say what is true healthcare outcome data on what you're doing with patients, both diagnostically and therapeutically, the real answer is how is our population doing over the past 30 years. And I would just point out that, obviously, the life expectancy over the period of time we are talking about has actually increased, which is quite good obviously.

And I would also point out that death rates, especially in my own field of

cardiovascular diseases, have actually decreased, and decreased significantly in cardiovascular diseases. And the data you seen on this slide is from the CDC and their national vital statistics publication.

Interestingly, deaths from neoplasms have also declined slightly and cancer incidences have taken a slight dip possibly because of some of our better screening issues, but also recognizing that we are not having increases by the modalities we are using to find these very significant issues in patients right now.

Just to look at an example of the clinical benefits of diagnostic nuclear medicine and using my own field of nuclear cardiology as an example, the ability to detect flow to the heart muscle is a very reliable way of trying to figure out whether blockages are present in arteries. The only real FDA way approved to do this right now is through the use of radioisotopes, although there are competitors trying to gather this data in other modalities.

The images are obtained both at rest flow to the heart and then after a stress test to look for differences in flow patterns in the pipes. On a risk management basis, I would point out that the patient already has a risk in being put under stress for the stress test to find the blockage. So on a clinical management basis, we are dealing with trading off risks at all points in time here to find people who are sick enough to benefit from the therapies we can of offer.

The test itself serves as a gatekeeper for higher clinical tests downstream such as clinical angiography and catheter replace.

The test helps stratify for revascularization and appropriate use of stenting

in bypass surgery, so there is a lot of utilization issues here that this is extremely helpful for in choosing the right therapy, right patient, right time.

We have come to learn over the years that regardless of the amount of blockage in any artery in the heart, those people whose flow is relatively okay to the muscle, usually do relatively well with simple medical therapy.

We have learned that people who we can find that there are flow perturbations that are indirect evidences of their blockages, these people do worse and worse the worse that their flow to their heart muscle is, and we know we need to be more aggressive with them before naturals history takes its course and reverses some of the fine work of the cardiovascular community over the last 30 years.

This is just an example to give you a sense for things. These are three different patient scenarios. The far left is tomographic images of the heart in three planes. The top set of image in each one is under flow stress. The bottom one is under rest. The left set is equal flow throughout.

This is a patient that even if they had 30, 40 percent blockages in their arteries, they are going to do relatively well and can get medically managed.

The middle set shows unequal flow patterns, and this is indirect markers of blockages in the pipes, and we know we need to be more aggressive with.

And the one on the third is obviously a situation where the top set of images show very little flow to large pieces of muscle that improve at rest. This is a person who we know on a risk adjusted basis is going do very poorly without more

aggressive therapies. You know, this allows us to target some of these pipe fixing type therapies.

In the first set of images above, you can see an old bypass graph which now has a stenosis in it and fixed by stenting.

The second set of images on the right is a closed artery with flow down the pipe restored after stenting.

The bottom two sets of images is the medical student image. This is what's called the widow maker's lesion. It's a very, very tight blockage in a big major vessel on top of the heart. These are the ones we want to be finding and being able to reestablish flow before myocardial infarction loses large pieces of muscle.

Having said all of that, I would point out that there is -- we have from the provider community, a strong interest in making sure that we are using ionizing radiation appropriately for the appropriate patients at the highest risks. And that we are getting the quality type of tests to make good decisions.

Certainly there are appropriateness criteria out there in the medical community of who should be tested and what might be the best things to do with testing results. The medical provider community has multiple sets of imaging acquisition guidelines with the help of health physicists and medical physicists in trying to fine-tune these protocols to the best possible.

There are new hardware on the horizon that may allow to us to use less dose and still get the same quality picture, which would obviously be a win in all worlds. But we do need good pictures to make good diagnoses. And then there

are lab accreditation opportunities throughout the nation in trying to help all providers improve the quality of their care in delivering quality services.

In conclusion for this end, I would say that NCRP Report 160 is greatly appreciated and fully noted by the full medical community, of which I'm only a small representative. We actually would prefer seeing it more than every 30 years. It's a helpful reminder to relooking at things.

I would point out that the clinical benefits of imaging in the room with patients are incredibly great and they are driven by physician-patient discussions of what the risks of not knowing versus what the risks of knowing are and where you go from there. That is the basis of our healthcare system, that relationship and that open discussion.

The broad medical community across multiple subspecialties are greatly involved in assessing their use of ionizing radiation and how to use it in the smallest, most appropriate amounts.

And in that regard, and after discussion, the advisory committee recommends that the NRC retain its current policy where we are considering the current review.

And I thank you for your time.

DR. MALMUD: Thank you, Dr. Van Decker. We're now open to questions if you wish.

CHAIRMAN JACZKO: We will go through all the presentations and do questions at the end.

DR. MALMUD: Thank you.

Next presentation.

MR. MATTMULLER: Good afternoon, I'm Steve Mattmuller, chief pharmacist at Kettering Medical Center in Kettering, Ohio. I'll be discussing today the medical isotopes shortages, specifically Mo-99 that we are facing in our field today.

The four areas we will be touching on are why we need Mo-99, the causes of the shortage that we are enduring right now, the effects of the shortage on your patients, and possible solutions.

Very simply, we need Mo-99 for good patient care. More than 34,000 nuclear medicine procedures each day in the United States depend on a reliable supply of Mo-99 for our patients. Nuclear medicine procedures are some of the most accurate methods and essential tools used by physicians to provide optimal patient care to their patients.

Our Technetium radiopharmaceuticals have two components: The Technetium atom and a chemical component that attaches to it. And it's the differences in the chemical component that -- based on its structure that determines where it goes into the body and how the same radionuclide with different chemical components can be used for multiple different tests.

For example, we can use Technetium with sestamibi for myocardial perfusion imaging much like Dr. Decker just demonstrated, or we can use Technetium with MDP for diagnostic metastatic bone disease.

This shows why we need Mo-99 every week. This is a graph of elusion characteristics from a generator. It shows the decay of Mo-99 over time and decreasing yields of Technetium over time also. And you can see the activity of the Technetium rise and then it drops to zero. And that's when we elute the generator, when we remove the Technetium off of the generator to use with our Technetium kits to prepare for the different procedures.

And then, as you can see over time, in about 24 hours, the Technetium builds back up to its maximum level of Mo-99 for that day.

So through the week, you can see it's somewhat of a race against time where our Mo-99 is decaying and producing smaller and smaller levels of Technetium.

This is actually a real demo generator without the lead. This is the column that the Mo-99 would be loaded on. It would sit in it like this. Sadly today, this represents the typical generator with no Mo-99 because of the shortages.

This is just an example of nuclear medicine procedures. On the left shows a heart study for myocardial perfusion imaging. Approximately, 50 percent of all doses used with Technetium in nuclear medicine are for heart myocardial perfusion studies.

On the right is a bone study used to diagnose metastatic bone disease. This category of test represents about 30 percent of all Technetium used in the U.S. And, again, nuclear medicine images are based on the physiology of the disease versus the anatomy of disease. And CT and MRI do a terrific job of

creating anatomical images of the disease process, whereas nuclear medicine is complementary information based on the physiology of the disease.

The causes of our problem: It is due to a fragile supply chain. Uranium-235 targets have to first be irradiated in a reactor. Then the targets are processed to purify Mo-99. The purified Mo-99 goes to the generator manufacturers. And those are then shipped to centralized pharmacies or to individual hospital departments, where the individual doses of Technetium can be prepared for the various studies.

By far and way, the weakest link in this whole chain is the small number of reactors that produce Mo-99 for us. There are four in the world that produce about 90 to 95 percent of all Mo-99 in the world. The U.S. gets 100 percent of its supply from just two reactors.

The National Research Universal Reactor at Chalk River, Canada, produces about 60 percent of our needs. And that Mo-99 typically goes to Lantheus in the production of their generators.

The other reactors, the High Flux Reactor in Petten, the Netherlands, which produces about 40 percent of our needs, and that Mo-99 goes to Covidien for the production of their generators.

Talk about the fragility here. Our biggest problem is that our reactors are old. The NRU reactor is 52 years hold and it's responsible for the current shortage that we are enduring right now that started in May of this year.

The High Flux Reactor in the Netherlands is 47 years old, and it was

responsible for a shortage that started in August of last year and that continued on to January of this year. And both of them are due to corrosion issues with various subsystems in their reactors.

Our current shortage is from the Canadian reactor is now inoperable. And the current estimate is three months of time that it needs to unload the fuel, complete the repairs and to reload. But that's a best-case scenario for us, and we certainly hope it turns out that way, but there is no guarantee that in three months the Canadian reactor will be back on line.

It's going to get worse for us very shortly. The Dutch reactor is scheduled to shut down for maintenance for a month in mid-July, which coincides at the same time that the Canadian reactor will still be down. So our two biggest reactors that we are dependent on for Mo-99 will both be down.

That bad outlook continues for 2010. In the beginning of next year, the Dutch reactor is scheduled for repairs, in which they estimate will take six months. So we are in the very precarious position right now.

So the effects of the shortages are diminished patient care. These are survey numbers collected by the Society of Nuclear Medicine. The 2008 column represents the shortage that started last year and ended the beginning of this year. The 2009 figures are very preliminary figures. This only represents about two or three weeks of actual shortages. And as you know, it continues today.

The shortage now is actually much more severe and probably, the worse statistic here is cancellation of a procedure. It is now almost a third are being

cancelled due to the lack of Mo-99.

The differences in these two shortages reflect which reactor is down. Last year it was the Dutch reactor, which provides Mo-99 to Covidien, but the Canadian reactor was still operable. And the Canadian reactor also has extra capacity, so they were able to ramp up their production to help cover the shortages that we were experiencing last year and into this year.

Sadly now that the Canadian reactor is down, there is no other reactor in the world that has extra capacity to sort of make up for the full amount that we are missing from Chalk River.

The diminished patient care. Referring physicians who refer to us to provide these tests are frustrated, in that they are trying to take care of their patients; that's their primary focus. And when we can't provide these procedures to them, they have to choose something else.

Typically, because of the nature of a nuclear medicine procedure, these other tests can be inferior in accuracy. They might be more expensive, or in some cases, the alternate procedure may actually have a higher radiation dose to the patient than our procedure. And again, this is because nuclear medicine procedures are based on physiology as opposed to anatomy, and so, it is unique information that is difficult to provide from alternate testing methods.

So our hope, the solutions are new Mo-99 suppliers. At Missouri University their research reactor, they are undergoing studies now on plans to produce, Mo-99. They have produced medical isotopes in other areas, and they have a

successful track record in that regard. But, at this point right now, they need 40 to $50 million to build and construct a processing facility to handle the Mo-99 targets that they would irradiate in the reactor.

Our second best hope is with Babcock & Wilcox. They are partnering with Covidien. They are using a different reactor design, an Aqueous Homogenous Reactor. These are much -- and you are probably more familiar with these than I am, but this a modular reactor design. A modular unit,200 kilowatts. Their facility would probably have four or five of these individual reactors.

But also, they have -- instead of having separate solid fuel rods and targets, it is a liquid slurry of the target fuel and the reactor fuel that then has to be -- where the Mo-99 has to be separated from. So they have some technological challenges ahead of them as this type of reactor has never been used before for medical isotope production.

Both of these plants have some regulatory issues facing them. And flexibility is going to be needed during the licensing process in regards to construction plans, environmental issues and radioactive waste stream issues, if these time lines of five to seven years are going to be met.

And finally, I wanted to finish with two of our patients for Kettering to remind us why we are here and why this is so important to us. One of these -- the lady on the left had heart disease, and the gentleman on the right had metastatic bone disease. And they are just part or two of the 34,000 people a day who rely on nuclear medicine.

We are in a pickle now. There are plans to get us out of it. But the next five to seven years will be very challenging for us, and we hope we can rely on the assistance from the NRC to help get us there in time. Thank you.

DR. MALMUD: Thank you, Mr. Mattmuller.

The next presentation will be made by Dr. Bruce Thomadsen, and the subject is the cesium-137 chloride Irradiators. Dr. Thomadsen.

DR. THOMADSEN: Thank you and good afternoon.

The National Research Council issued a report that suggested that Cesium-137 Chloride irradiators be eliminated. These are necessary in medicine, and the ACMUI when learning about this, looked into the issue and questioned some of the facets of that recommendation and established a subcommittee of the six people listed on the slide to look into three particular aspects of these irradiators, the need for the sources, alternatives and security of the sources.

Under need of the irradiators, the first and most well-known use is as blood irradiators. Around 15 to 40 percent of patients receive irradiated blood, mostly these are oncology and hematology patients who are very immune compromised. The reason for the radiation is to kill the host white blood cells that are in the blood. Otherwise they can react with the patient, and these patients can die.

The original report assumed about 10 percent of patients receive irradiated blood. This is probably because in their survey, the weighting that they had might have been more heavily towards trauma center, where the irradiation is not necessary.

Without access to the irradiated blood, the patients who do need it would either die or have very severe consequences.

The other use in medicine is for animal irradiation. This is for research to bring new types of therapy to light. There are two particular uses that are very dominant in this field.

First is to suppress the immune system of animals who are being used to test stem cell work and other types of treatments where the bone marrow needs to be suppressed.

The other main use is for cancer research, particularly in radiotherapy where the irradiators are necessary.

There are alternatives to the Cesium Chloride irradiator. Usually the most common alternatives would be x-ray units or linear accelerators. Both have been used and are used for animal irradiation, blood irradiation and material irradiation.

For x-ray units with blood irradiation, the FDA has only approved one unit for this use, at a cost of $250,000 with a $33,000 a year service contract. This is different from in the report, which specified it was $180,000 for the machine and $10,000 a year for the service contract. This is a lot of money for these facilities, most of whom do not operate with a large fund to replace their units.

Extra expenses for these x-ray machines include replacement of tubes, calibration and quality management. The calibration has to be done periodically with x-ray machines. They are not stable like the cesium machine, which is can be calibrated once and run very reliably for years. It requires some intervention on

the operator's part for quality management, and as I mentioned replacement of tubes.

With 48,000 blood units irradiated each year, a tube would have to be replaced in about 3.7 years. This is adding tremendous costs on top of the initial cost of the machine to the operators.

In addition, the throughput is much lower than for a Cesium machine, because the x-ray machines do not have as high of a dose rate, limiting how many units of blood a machine can process.

For animal irradiation, there are several machines on the market, but unfortunately, very few that operate above 200kV. The energy is very important for two reasons. One is you have to have adequate penetration to irradiate all of the bone marrow in the animals. Operating below 200 means that the skin dose is going to be very high and the penetration is not usually adequate to give good irradiation to the bone marrow.

The second is that radiation of different energies have different relative biological effectiveness, that is, how much damage the radiation does to different types of cells per unit dose. This varies not only with the energy but with the species and with the biological end point, which makes a very complicated matrix if you're trying to replace the historic Cesium with any of the x-ray machines.

The prices for these range between $146,000 and $250,000, with a service contract of 10 percent per year.

The low dose rate makes it difficult when you have an animal under

anesthesia, because you have to keep the animal anesthetized for a longer time than you would with a Cesium machine. All together, this is a lot of expense and trouble for institutions who usually don't have, once again, a source of revenue to replace and maintain these expensive machines.

For a medical linear accelerator, the price tag goes up even higher, with a typical linear accelerator, a stripped down model, costing around $150 million a year, plus $150,000 per year for the service contract.

One could use radiotherapy department's linear accelerator for the irradiations. This is done sometimes for animal irradiation. It has to be done after hours, of course, limiting the access to the machine. For blood irradiation, it would probably have to fit in between the patients during the day, causing a disruption both to the radiotherapy facility and to the blood bank.

Moving on to the security issue. The security of the machines has changed remarkably, since the report was issued. There are security enhancements for the users. Now, all the users for these machines have to go through background checks with fingerprints, and this has tightened the security for the users.

The facilities have been tightened through the directives of the NRC. The rooms in which the machines are located have to be very secure. Typically, at the University of Wisconsin where we have about five of these machines, the security enhancements cost a little bit more than $15,000 for a typical machine, some of them a lot more. But this has greatly improved the security for those rooms.

And finally through a program with the Department of Energy and the

Department of Homeland Security, the units themselves are being hardened. With three thrusts, these have become much more secure.

This slide illustrates a typical machine, the Cesium sits in the middle of this machine, immobile. The sample is put in a tube on the top that slides down into the source configuration during the irradiation.

In order to get at the Cesium, one would need a cutting torch and a lot of tools. In order to get the machine off its pedestal, you would need also these tools, a lot of others. You also have the problem that the machine itself is on a reinforced floor, and as soon as you took it off that floor, it would be too heavy for regular floor to support. Stealing this machine would be very difficult.

The source material possibly could be made to a form that would be less attractive to people who might want to steal it possibly as fused glass. Unfortunately, right now, the manufacturers have no interest in making changes in the chemical form because this would be very expensive for them. We can't direct them what to do, because at the time no American manufacturer makes these sources. We import them from other countries not always who are very friendly to this country.

In summary, the irradiator facilities are essential for irradiating blood and for medical research. Forced replacement of the Cesium-137 Chloride units would result in great expenses to the facilities and possibly lead to facilities stopping their irradiation programs.

There are problems or large expenses with changing for animal irradiation

to x-rays. The enhanced securities for these units has mitigated much of what would have concerned people with these machines just a couple of years ago.

And finally, without a source, a domestic source for Cesium-137, newer and possibly safer forms of the radionuclide are not very likely. Thank you.

DR. MALMUD: Thank you, Dr. Thomadsen.

If we may, we will move on the next subject, and that will be presented by Dr. Darrell Fisher. The subject is cobalt-60 for stereotactic Gamma Knife radiosurgery systems.

DR. FISHER: Distinguished Commissioners, I represent patients' rights and their healthcare concerns on the committee.

Cobalt-60 is a critically important medical isotope, and its continued availability is a quality of healthcare issue. Today I will briefly discuss the medical need for Cbalt-60, supply and availability, transportation of sources, source security, and state fee regulation.

The use of Cobalt-60 in the U.S. for external beam radiation therapy has declined substantially; however, it is still used worldwide in large amounts. Today, Cobalt-60 is a highly effective isotope for radiation therapy in the newest and most advanced computer-driven stereotactic systems for treating brain tumors. These are collectively referred to as stereotactic radiosurgery or Gamma Knifes.

The major regulatory issues impacts supply and costs of the isotopes. Most of the world supply of Cobalt-60 is produced in Canada and is distributed by MDS Nordion. It is produced in the CANDU Reactors Bruce B, Pickering A and B,

Gentilly and in the NRU reactor previously mentioned today.

High specific-activity Cobalt-60 for the Elekta Gamma Knife are produced in the U.S. by Isotopes International at the Advanced Test Reactor near Idaho Falls. High specific-activity Cobalt-60 sources are used for medical therapy and cargo imaging. Two to three-year production cycles are required to produce a source.

Low specific-activity Cobalt-60 sources are used to in radiation sterilizers. The supply and availability are currently adequate to meet international needs, as long as the ATR continues to operate and the ability to transport sources is not impeded.

According to industry representatives, the major Cobalt-60 supply issues are availability of approved transport containers and casks, source security, the costly import/export licensing requirements for U.S. licensees, and excessive state transportation permit fees. These issues impact availability and the ability to move Cobalt-60 from the reactor to the cancer treatment systems.

When we increase the difficulty of transporting sources, we also decrease availability and increase the ultimate cost of cancer treatment to patients.

Shipping containers is the next subject. The U.S. Department of Transportation withdrew approval of all specification packages in October 2008 after a four-year transition period.

The availability of replacement package designs has not kept up with the need to make shipments.

Approval of new replacement package designs can take 18 to 24 months

and can cost up to $750,000 per design.

The NRC, in the interim, is working with industry and has approved the use of discontinued packages on a case-by-case basis. This is a appreciated by industry.

However, the major issue seems to be that packages approved by foreign regulators are not equally recognized by U.S. regulators. This situation makes it more difficult to transport category one sources inside the United States. Some strategies have involved exporting sources, and then reimporting them to make deliveries within the United States.

The container revalidation process is burdensome to industry. Industry recommends a process to improve the approval of shipping containers already approved by foreign regulators according to well-defined international standards.

In the area of source security, industry supports the concept of increased source security. Fundamentally source tracking is a very good idea, but industry reports that the current NRC system is not working well in practice.

For example, under current requirements, the 200 sources shipped to replace aging Cobalt-60 sources for a single Gamma Knife unit have to be tracked individually rather than as a unit. This has required, for example, the transmitting of 200 individual faxes to track those sources for a single shipment.

If Category 3 sources are also tracked, the current system will not be able to handle the large number of individual sources.

Import authorization should be included in the possession and use license

to reduce the financial burden on industry.

Export license fees and expirations should be based on the U.S. licensee and not on the importing country, which is a fee uniformity issue.

U.S. companies should not be required to list all possible customers on the import/export license. These are recommendations from industry representatives.

Also for your information there are two other issues that may be mentioned. Under state fee regulation, some states require excessive fees to transport Cobalt-60 within state boundaries. Therefore, shippers and carriers often bypass these states whenever it is possible which increases transportation costs and in-route times. One example is the high fees charged in the State of Iowa.

The NRC does not have preemptive authority over the states for transportation to help make fees uniform from one state to another.

On the positive side, there is the good news that the recovery and recycling program is working very well.

In summary, Cobalt-60 availability is very good but always subject to ongoing reactor operations.

Approved container shortages, the complex transportation regulations, and costly import/export licensing requirements have made it extremely difficult and costly to supply cancer therapy devices with Cobalt-60. These costs are eventually borne by our healthcare system. Further efforts are needed to streamline the approval of shipping containers. And I thank you.

DR. MALMUD: Thank you. And we will move on to our next presentation,

which will be made by James Welsh, who is a physician and a radiation oncologist, and who will present the ACMUI's observations regarding multiple medical events involving permanent prostate brachytherapy within the Department of Veterans Affairs Medical System.

Dr. Welsh.

DR. WELSH: Distinguished Commissioners, good afternoon, and thank you for the opportunity to speak before you today.

There has been a good deal of publicity surrounding this sensitive matter recently, and thus, I have prepared this introductory statement.

ACMUI joins with the Commissioners and the NRC staff in our concern regarding the reported number of incidents at the VA Philadelphia. Due to recent public awareness, I have refocused my presentation slightly. NRC has confirmed that there is an ongoing inspection and has committed to keeping the ACMUI informed of its progress. The ACMUI remains intensely interested in this issue and will offer advice, as requested.

I have followed the recent coverage closely, and I would like to offer today the perspective of a radiation oncologist who is concerned with patient outcomes. If the ongoing inspection by the NRC should conclude that there has been substandard patient care, I would join with my colleagues in encouraging appropriate corrective action. We acknowledge that the VA understands the gravity of the situation and is moving on this matter.

Some of the reported events may prove to be clinically significant, others

may not. For example, there have been criticisms that post-implant dosimetry was not uniformly performed. Is post-implant dosimetry strongly recommended? Is it considered by many to be standard of care? Yes. But is it mandatory? No. However, even a single event which does not comply with radiation and patient standards of care, is of great concern to me, as well as to all members of the ACMUI.

I hope that in this brief presentation today, we can maintain objectivity in what appears to be a very serious situation. We look forward to hearing more of the results from the NRC, and, in the interim, we should not rush to judgment. At the end of the day, we must ensure that our veterans and all patients, receive what they deserve, that is, the very finest in medical care.

So with that introduction, I move to the first slide, which is simply a synopsis of the events.

The NRC received reports from VA Medical Center, Philadelphia of multiple medical events involving prostate brachytherapy.

NRC inspected 13 medical facilities of the same permittee. Numerous medical events were identified at multiple locations.

Prostate brachytherapy at the VA Philadelphia has been suspended along with three other programs.

Corrective actions have been taken, which I will describe a little bit today.

The VA will not start its suspended cancer programs until these commitments have been met. Several have appropriately asked where our

veterans will be going to receive their prostate brachytherapy should they so desire it, and this is an important question.

So before I talk about additional actions taken beyond the corrective actions, I want to make a brief comment about the corrective actions themselves.

One of them, which I wouldn't detail here explicitly, mentions the ordering of an external review of the prostate brachytherapy program by an Administrative Board of Investigation or ABI. One would hope and expect that this ABI includes some of the true experts in our field.

Additional actions taken are on the slide here for patients care concerns at one facility, the licensee performed verification CT scans on all patients, reevaluated the dose, and reimplanted some patients at a different facility.

The question that arises immediately is can one really trust these verification CTs if they were done long after the fact, which appears to have been the case in some situations?

This is a schematic diagram of what is considered to be a good implant. Note the dose of 144 Gray and note also that the bladder in this case is partially anterior to the prostate; in other words, at the top of the screen here.

Among the caveats and pitfalls of this matter is the question about whether our criteria for medical events could possibly be too low? In other words, are our criteria too sensitive but not specific enough? Perhaps not,, based on the statistics, which there were approximately 100 medical events out of 50,000 procedures, suggesting that that large denominator -- that large denominator

suggesting that this is not a huge pervasive problem in the United States.

But, one has to ask if there are too many medical events being reported that are not truly of a clinical significance? This is a general question, but may be of great relevance here as we attempt to answer the important question of whether there were many bad implants conducted, or are they so labeled because of our current definitions?

Let's look at the definitions, or the definitions that were used in the VA medical events. Twenty percent -- greater than 20 percent of the prescribed dose. No one can fault someone for using this, because it comes straight from 10 CFR 35.3045. But one does have to ask how is the dose actually determined?

If we say that not all the patients underwent post-implant dosimetry, where is the data coming from? Get this from a CT scan that was done a year later? That is an important question that remains to be answered. Or the D90s and B100s calculated, these are parameters that are used to define a quality implant and assess the technical quality event procedure. We don't have any information on that yet.

One important topic that I would like to touch on in this slide here is regarding the external tissue. In the analysis, five or more seeds located beyond 1 centimeter exterior and inferior to the surface of the prostate was one of the criteria for a medical event.

Recall that one of the treatment planning goals in prostate brachytherapy is to cover the prostate, the prostate gross target volume or GTV, the prostate itself,

plus a margin of 3 to 5 millimeters to cover potential extra capsular extension of disease; in other words, the clinical target volume or the CTV.

In order do to achieve this, one must frequently implant seeds intentionally beyond the prostate capsule. Thus, some might contend that the definition used in this context was a bit too strict.

This brings up the other important point, which is that there is a new rule being contemplated regarding medical events for prostate brachytherapy. The current criteria of determining medical events was used in this analysis.

But the proposed criteria put forth by experts from national organizations such as ASTRO and ACRO and discussed by the ACMUI is 20 percent or more of the seeds implanted beyond 3 centimeters from the boundary of the treatment site. Treatment site could be a planning target volume or PTV.

This is significantly different from the criteria used in the analysis, and one has to wonder whether the medical events in question would still be so classified if one used the proposed new rule that was proposed by some of the experts.

Normal practice is to have a post-implant CT scan to determine seed placement. We know that this was not done routinely because of the faulty software. Comparisons, therefore, could not uniformly be made.

One of the corrective actions was instruction to the Radiation Safety Officer and quality management staff to immediately report all deviations that exceed 10 percent of the prescribed dose or dose fraction. This raises the question about whether an RS0 or medical physicist or any nonphysician member of the quality

management staff can make this call. Some might, some certainly could not.

I would submit that only a trained specialist M.D. who is fluent in male urogenital anatomy can really make this call reliably.

I would like you to take a look at this particular slide and I call to your attention first that this schematic is based on a CT that was done after the fact and the prostate is in red. But as I said, the prostate is very difficult to define at its inferior most border. Thus, the seeds in green here in this diagram to be well below the inferior border.

But what if the inferior border is not correctly contoured here? You can't tell from this diagram if the physician who put those green seeds way down towards the right side inferiorly in this patient was making the right call or if the person who created this diagram for us today made the correct call and has the prostate in red significantly in a different location. It is not very easy to reconstruct this afterwards.

So can we determine this late if a medical event has truly happened? For patient care, the licensee performed verification CTs on all patients between 2002 and 2008, re-evaluated the dose and re-implanted some of these patients.

I personally have a little problem with this. First of all, I, as you can sense, I'm not convinced that one can use a CT scan done months or years after the fact to ascertain where the seeds were originally placed when the seeds were first put in there. Seeds can migrate, the prostate can enlarge, the prostate can shrink, the prostate can change shape. So I do not believe that one can reliably determine

medical event using this methodology.

Secondly, I would not recommend reimplantation solely based on late after the fact CT data. Other clinical data such as the PSA and digital rectal exam would be far more important, and I suspect that they were used in the cases that were reimplanted.

I have already mentioned that it is known that the prostate may shrink following prostate brachytherapy, but long after the fact, the prostate can grow, seeds can migrate, the prostate can change shape, leading one to question the reliability of post-implant dosimetry that is done long after the implant.

ACMUI is concerned about determination of medical events based on CTs that were done a year after implantation, and in some cases perhaps longer.

So, of course, the goal is to prevent such events from ever happening again.

The licensee instituted a medical center peer-review system for radiation oncology services and post-treatment evaluations. ACMUI fully supports the idea of performing peer reviews for permanent prostate brachytherapy procedures.

Another question on the table is, should an authorized medical physicist participate in the procedure?

A third question is, should post-implant dosimetry recommended move from strongly recommended and endorsed by professional societies to become mandated? I have my opinion on that.

The answers to these questions by the ACMUI formally awaits further

information from NRC before any definite recommendations are made.

So I would like to thank the following individuals for allowing me to use some of their slides and for their presentation at the recent ACMUI meeting.

Thank you very much again for my opportunity to speak with you today.

DR. MALMUD: Thank you, Dr. Welsh.

CHAIRMAN JACZKO: Thank you. Appreciate the presentations. We will start our questions with Commissioner Lyons?

COMMISSIONER LYONS: Well, first I would like to thank all of you for a really very informative presentations, and each one of you spoke to an area that I think is of very substantial interest to the agency and to the Commission.

Dr. Malmud, I have appreciated a number of opportunities to work with you and other members of ACMUI. Over my tenure here, I have just greatly appreciated the opportunity that I have had to interact with you and your team and contributions of ACMUI going well beyond the discussions that are ongoing today. You certainly have my great appreciation, all of you.

DR. MALMUD: Thank you.

COMMISSIONER LYONS: I could start with questions, I think, for almost any one of you where I have a very strong interest. But, perhaps starting with Dr. Welsh first.

Certainly very much appreciated your comments on the current concerns at the Philadelphia VA, and those are concerns that I know are shared throughout the agency. And I also appreciated your discussion of possible reevaluation of the

criteria for reporting of medical events.

But even with the uncertainty that you expressed in whether we have the best definitions, I guess every morning as I come in and review the incident reports and see the types of medical events that are reported, I keep wishing that we could find better ways of encouraging far fewer such events.

We have talked at the Commission and staff level about trying to instill a greater safety culture, more attention to the different attributes of safety culture within the medical community, but in general among material licensees. I just would be curious in any thoughts you might have or any other members of your team here today on actions that the Commission and the agency might take to try to reduce events in the future, including specifically, whether you see any potential for trying to instill a greater focus on safety culture.

DR. WELSH: Well, I did briefly mention that I think that in general within the radiation oncology community, the safety culture is there. The reason I can say that is because even including the events at the VA Medical Center, there were approximately 100 out of 50,000 medical events in 2008, which amounts to 0.2 percent. Meaning that, in general, it appears that most radiation oncology programs and practitioners do have a safety culture already in place.

However, it is alarming whenever you see 92 or more medical events from a single institution, and therefore, one does have to really wonder if that particular institution was lacking in safety culture. The analysis thus far appears that safety culture may have been lacking.

But I have to say that I and ACMUI have relatively limited data on this, and that therefore, I cannot make a definitive statement on how lacking the safety culture might have been, nor can I make a statement on just how severe the medical events truly were, based on the limited data that I have before me.

Thus, my discussion today did seem to focus a bit on the question of whether these events which are labeled as medical events and do meet the criteria as defined, are they of clinical significance. They may very well be, but I do not have that detailed information.

So, our recommendations such as making sure that all prostate brachytherapy programs have a peer review done on a regular basis, that this peer review is mandatory might be one suggestion to make sure that medical events do not happen in such large succession at another facility ever again.

Post-implant dosimetry was done in some cases here but not all cases. Perhaps it's time that we make that mandatory, and this would improve the quality assurance. And if after one or two cases we see that the post-implant dosimetry is indicating that the implants were suboptimal, corrective actions can be taken there and then before you have something like 90 in a row.

COMMISSIONER LYONS: Would any other of you like to comment on safety culture and medical event frequency in general?

DR. MALMUD: Dr. Fisher.

DR. FISHER: I agree with Dr. Welsh, improved quality assurance, quality control is important. Second person checks, particularly in dosimetry, but also in

the surgical placement of seeds and improve training, and as Dr. Welsh mentioned, better peer oversight all could have really helped in this case.

DR. MALMUD: Other members of the committee?

I think that the concept of peer review is critical. The physician is the individual who identifies the anatomy prior to the treatment. The dose calculation is done jointly by the physician and the physicist.

Then, when the procedure is ongoing, the anatomy of the prostate changes. As it is injected with the seeds, it swells, becomes distorted slightly until the process is completed.

So at the end of the procedure, the organ is larger than it was before the installation of the seeds, and not necessarily in the same location. So that a second calculation is performed at the time of the procedure.

And then my understanding is that it is routine to do a post therapy recalculation after it is known to where the seeds migrate. And the seeds do migrate because of the swelling and shrinking of the prostate.

Also, my understanding, though I'm not a radiotherapist, is that it is within the range of normal procedure for a certain number of these seeds to be misplaced at the time of the installation of the seeds. And perhaps the term "misplaced" is incorrect, but to be a placed outside of the gland for several reasons.

One is that if we think of the prostate as being a lemon-sized organ through which a sipping straw runs right through the center of it, when the seeds are

placed in, they are placed so that they emit the radioactivity to the tissue of the lemon. That means that they have to be scattered about. Some of that tissue is at the edge of the lemon, and therefore, some of the radiation will penetrate and go to the adjacent organ. That's calculated by the radiotherapist and physicist together.

But occasionally, in trying to achieve closeness to the edge of lemon, it will go into the adjacent organs. The two adjacent organs are the rectum and the bladder. So a certain number of these will migrate or may by placed at the periphery or may be actually outside.

And my understanding is, having learned a lot about this recently, but still not being an expert in the area, that a one-centimeter perimeter was considered a reasonable margin, because within the centimeter, that seed would still be treating some of the tissue at the margin of the prostate.

It is essential, though, in whatever we do in medicine that there be some peer review, particularly when it's an invasive procedure or therapeutic procedure. And it's common in radiology for us to reread each other's scans and X-rays.

And the ACR has a program in which after a study has been read by one of my colleagues, a certain number of those are randomly accessed by myself, and then I check and see whether I agree or disagree and grade these, and these are then scored. And if there is a significant discrepancy, we review the individual case.

And that helps to prevent the same error from recurring, if perhaps I had

read something incorrectly, and my colleague points it out to me or vice versa.

So that the peer review process that Dr. Welsh addressed is a critical process and should be performed by another expert in the area. In this case it would be a physician, because it is the physician who has the anatomy. The physicist has the skill with the calculation. It is the physician who would identify the anatomy.

COMMISSIONER LYONS: You used the word "mandatory peer review." Are you suggesting that NRC should mandate, or that that should be mandated through -- I don't know all the right words here -- the procedures at the hospital, different clinical boards who should do this mandating?

DR. MALMUD: That is an excellent question because as you know, we try to not become involved in the practice of medicine and leave that, in this case, to ASTRO, the professional society for radiation oncology. But it is reasonable to review the dosimetry in the peer review process.

And if the feeling at the end of this investigation is that the current system is not sufficient, it may be sufficient. This may just be a lapse at one institution. But if it is felt that it is not sufficient, then, it may be that the -- may have to be a requirement of the NRC as well.

We need to see the database first, though. And that database is still being aggressively collected by NRC investigators staff.

COMMISSIONER LYONS: Darrell and James, I'm well over my time, but would you concur with that statement that perhaps NRC should be the one

mandating? Which probably is not what I would have first suggested, but it very much appreciate that point of view. But would you share that view?

DR. FISHER: I think that it's more important for the individual scientist physician involved to oversee the quality assurance and make sure that it is practice -- it's part of common practice, at least for the treatment plans that I'm responsible for, I always involve a second medical physicist as part of the check. And in brachytherapy, I do review seed orders and find mistakes, and I think that a voluntary QA/QC program might be more effective than one that is mandated by regulation.

COMMISSIONER LYONS: I'm done -- I'll stop now, but I don't know if Dr. Welsh wanted to respond too.

CHAIRMAN JACZKO: Did you want to add any additional information, Dr. Welsh?

DR. WELSH: I could just say that I concur that this is a challenging question, challenging situation about who can impose this regulation. It is a recommendation already, but it is not enforceable. Only if it becomes enforceable would all conform to this recommendation.

I also like Dr. Malmud's lemon and straw analogy, although it has ruined forever my taste for lemonade, but I would like to point out that the rind is also part of a treatment target. And in order to treat that rind, seeds will occasionally have to be placed outside there. And when you are withdrawing that straw, inevitably in some cases, that straw will suck out a seed or two as part of the process. And this

is something that is acknowledged to happen in the process.

CHAIRMAN JACZKO: We will turn to Dr. Klein next for questions.

COMMISSIONER KLEIN: Thanks. Again, thank all of you for a very informative presentation, and I think we oftentimes forget the value of the medical applications of radiation and the positive effects that it has, and it is a good reminder when we have these kind of presentations.

Let me start with the order -- my questions usually go by the presentations, and so, I get to start with Dr. Van Decker first.

On your slide six, you showed some healthcare outcomes. And I think when we looked at the increased medical exposures, we tend not to hear the decreased death rates. You know, we only hear one side of that. We don't hear the positive aspects.

I guess, is there any cause/effect relationship that you all can show to the fact that while the average exposures are going up, that this directly correlates to these decreased death rates?

DR. VAN DECKER: I think that, obviously, this is a multi-factorial thing, and there are certain testing and therapeutic paradigms in place now that utilize this on an everyday basis. And so, I think we have to say that the process of our current thought process in therapeutics has made a difference here.

And obviously, you know, on non-population studies if you looked at -- supplied some literature on outcomes data for following individual patient populations in different risk groups, how they did with intervening or not

intervening, that certainly made a difference in those smaller populations as opposed the population in general.

So, I think we have data on select populations that shows that appropriate testing utility leading to appropriate therapeutics is helpful. And I think that, you know, we certainly can say that if the concern was, is there an underlying negative effect for the positive effect we are following in those studies, we don't see dramatic negative effect here from what we are doing and we are doing on a fairly widespread basis right now on the realm of, you know, diagnostics, obviously, though, targeted to appropriate patients at appropriate times who are mostly older and mostly having symptoms and getting sicker.

DR. MALMUD: Mr. Klein, Dr. Van Decker is much too modest being a cardiologist.

Fifty years ago, if a man had a heart attack and made it by ambulance to the hospital before dying of an arrhythmia, the treatment was oxygen, bed rest, something for pain, a primitive pill to remove water and mercurial diuretic and prayer. If the man recovered from myocardial infarction after a six or eight-week period of bed rest, he was a cardiac cripple from that point on and did not return to gainful employment in many situations.

Today, the same man, with the same degree of heart disease is seen in the emergency -- is first of all, maintained in the emergency vehicle with cardiac monitoring, if necessary, gets to the emergency department, is whisked into a cardiac cath lab, has a catheter inserted in the groin up into the heart. The blood

vessel that is affected is opened -- reopened. That man is healthier 48 hours later than he had been for months before the heart attack and returns to work within a matter of two weeks.

The price of that man's altered lifestyle and productivity following myocardial infarction is way beyond the extremely high cost of having treated him that way.

Now, what techniques were used in being able to do this? Not a chest X-ray, which only gave 30 millirem, and that was done 50 years ago, but an intensive radiologic procedure in which the patient is under a fluoroscopy unit while the vessel is opened up or a stent placed in. So the radiation burden is much higher, but the man is now alive and back to work and back with his family, or a woman, because women now have increasing incidents of heart disease, thanks to their larger use of tobacco.

It is very difficult -- and I agree with Dr. Van Decker, it is very difficult to attribute the greater longevity and survivability to one particular technique. It may be the statin drugs. It may be the reduced use of tobacco. It may be our greater awareness of lifestyle, though, our body habitus does not say that that's true. But at any rate, it may be any of those.

But the contribution of radiologic techniques in the hands of cardiologists and radiologists has been enormous and has revolutionized the healthcare of heart disease. So that when we look at the long-term effects of the slight increase in radiation exposure and compare it with flying a jet plane for a year as a pilot or

living in Denver at mile high with a greater exposure, it becomes the risk is much less than the gain, as far as we can measure it today.

COMMISSIONER KLEIN: Thank you very much. That is a good analogy. Certainly the risk benefit for that person to survive was very high.

Steve, I have got a question for you. We met yesterday with the head regulator from Canada, Mr. Michael Binder, and he made an interesting comment, and I'd like your thoughts on this as well. He says when you look at the shortage of medical isotopes, that you are really impacting people's lives, you know, it's cancer, cancer treatment, and so forth.

And so, he asked a question, where is outrage, where is the incentive from Congress, where is the incentive from the medical community? In other words, you don't pick up a newspaper and read about this. It is only those of us that are sort of in the business that really are aware of this.

Can you comment on why there is no outreach?

MR. MATTMULLER: Perhaps that would be a better question for the media who is in this room. I'm certainly frustrated by that, and even within our own community for those who -- and for example, at this point, we have a Covidien generator at our facility, so we're relatively, unaffected for the moment. But in a month or so, we are going to be in significant trouble.

In talking with other colleagues we struggle with that, too. We don't quite understand how this has remained under the radar, so-to-speak, and more people are not concerned about it.

DR. VAN DECKER: You know, we have gone through these bumps over the last couple of years, and it has always bounced back so far, so I think that there is a lot of belief in the trenches that this is maybe a short-term thing and it will go away. You know, this is a type of that is going to take several months to really begin to go to enough people that they are buying dramatically, disadvantaged – to learn more about it, that's for sure.

COMMISSIONER KLEIN: It certainly puts us as a regulator in a unique position because we are not really the advocate for the production. You know, we into protecting people and the environment. But, yet, the NRC and our fellow regulators have been raising this issue for quite a while and it has not really gotten a lot of attention. And it really does need, I think, more emphasize.

And it was a good question that he brought up, because he feels in a difficult position as the Canadian regulator of having to make some difficult choices of people's lives versus operating a very old facility that has need of repair. So I'm sure -- hopefully, we will get on to some paths for long-term sustainability.

Well, I had a question for you on your -- I was enlightened at your comments about some of the assumptions that the national academy made in their Cesium activities. Some of those were pretty dramatic in terms of missing some data. I guess the questions is, how did that happen and is there any corrective actions that we can take to get the better assumptions out there?

DR. THOMADSEN: If you're asking me how could the committee that wrote the initial recommendations miss that, I can't address that, and it would be best to

talk with them directly. How to get the information out there is a much more difficult question, and it is very related to the one you had just asked.

There is a lot of things that are going on under the radar in the medical radiation community mostly because the population does not know much about radiation. They don't understand much about it and how it factors into their health and well-being.

The professional organizations bring up that issue frequently, how can we make this more appealing for the general population to look into and to understand? So far, it does not seem to have been an initiative that brings such things to the general population's light. I'm sorry I can't be of more help.

COMMISSIONER KLEIN: That is helpful.

Well, Dr. Fisher, I had a question for you in terms of you look at some of the issues that you brought up, are there any actions that you think the NRC should by taking that we're not taking?

DR. FISHER: Well, I did mention that NRC is doing some good things with industry. I think the main thing I have heard in my survey with industry is that some of their concerns are not being heard adequately. In particular, the issue on recognizing foreign approved containers. I think that was the main issue.

One thing to keep in mind, this is a relatively safe industry. The Cobalt-60 industry have produced over a billion curries of Cobalt-60 since 1950. Hundreds of thousands of high-level sources have been produced, shipped safely with relatively few incidents over many, many years.

The difficult part today is transporting sources according to regulation. And I think from what I have heard from -- and I have talked to many industry representatives, some of the regulations are very, very burdensome and make the transportation of these sources maybe more difficult than they need to be.

COMMISSIONER KLEIN: Thank you.

CHAIRMAN JACZKO: Commissioner Svinicki.

COMMISSIONER SVINICKI: Thank you all. I would like to add my voice to the commendation and thanks that you have received from my colleagues. I don't think I can adequately convey how important and beneficial I think it is to sit here as an individual Commissioner and hear your perspectives, and I have heard the NRC staff also compliment your work.

And, Dr. Malmud, thank you for your willingness to serve as chairman which is an added service that you take on. I think it is important.

We have gotten a bit off cycle, as I understand it. We used to convene with you when eight more of your members might be here in town. And my hope is that we can rejoin the schedule so that we will -- and I appreciate your willingness to support this meeting on a schedule off of your normal cycle where more of your member might be able to attend.

And again, as was noted, your contributions go well beyond the topics that we have addressed today.

I want to start with something that I did not want to interrupt my colleagues question, but I want to turn to the lemon. But it is important, because Dr. Welsh

had talked about these imaging diagrams and they been in the newspapers as well. So I want to be certain of my understanding of what we are seeing there.

Dr. Welsh, you had a diagram of a successful placement of the seeds, and then you also had a diagram where the seeds appeared to not be placed in the prostate. And Dr. Malmud was explaining the physiological response of swelling of the prostate as the seeds are in place.

So if I understand correctly, after the seed placement if that swelling diminishes, would the prostate eject seeds, or would the seeds move with the -- as the prostate got smaller so that that image then, I guess -- and I'm not speaking to the specifics of the incident under investigation.

I'm trying to understand the phenomenology generally, so I'm not taking your statement to specifically go to any of the incidents in Philadelphia. But just generally as it reduced in size, would the seeds be carried along with it?

DR. MALMUD: Dr. Welsh.

DR. WELSH: In general, the prostate may expand or shrink and the seeds will go along with that expansion or shrinkage. They will not stay in place and so migrate. They generally maintain their relative positions.

But if edema occurs or swelling occurs, although their relative positions may remain stable, their absolute difference in distances between each other may increase. Therefore, the dose between seeds can be slightly lower if edema is pronounced and prolonged, which happens to be one of the reasons why I like the longer half life isotopes but not all my colleagues are in full agreement with that.

But the prostate does expands, and if it expands and the seeds remain separated from each other, there could be areas of under dosing. More of a concern with the short half life isotope than a long half life isotope.

COMMISSIONER SVINICKI: The reason I'm pursuing this and want to be certain of my understanding is that one of the themes that I took from your presentation is it is very hard a year later to have great clarity on exactly what kind of dose would have been delivered where. And I'm taking from the discussion about the edema and then its duration, which again, you couldn't establish a year later, I'm assuming. So it becomes very difficult to reconstruct exactly what occurred.

Is that accurate?

DR. WELSH: I should point out that what I just stated is relative to what happens within the first month or so. That expansion through edema and that subsequent contraction is well known, well studied.

What happens, months, years -- several years later is not as well characterized and there could be changes, asymmetrical changes in the prostate shape or size as opposed to the generally symmetrical changes that occur acutely. So, try to ascertain what happened years later can be far more challenging because of this asymmetrical change in shape and size.

COMMISSIONER SVINICKI: Okay. And again, without the specific expertise, what I'm drawing from this is that these are the types of complications again which as we think about any particular medical event, there are all these

layers of complexity in terms of the medical significance that are -- can be difficult to establish patient by patient, particularly if a number -- a certain amount of time has passed.

So, I appreciate you bringing that forward. Again, it does not speak to any of these specific incidents, but just I think it helps me to understand the complexity of what we are talking about when you see one image and it looks like none of the seeds were placed where they should have been. It is not quite as simple as just that one image. Thank you for that. I appreciate that.

Dr. Fisher, I would ask, could you address -- you talked lot about the transportation issues, and beyond the case-by-case exception for expired packaging, would you assess generally that progress is being made on the development of new packages to be certified?

I didn't take a sense that there was a lot of focus in your presentation on dealing with the day-to-day, but as you look out over longer time periods, do you see that transportation package manufacturers are in development in licensing of new packages? Are you encouraged or discouraged?

DR. FISHER: Personally I don't qualify as an expert in the package design area. That's not what I do. But it has been my perception that finding qualified packages is very difficult. And, having previously qualified package disqualified exacerbates the situation. Trying to find good packaging is extremely difficult in today's world, and I'm not encouraged that the process is moving along very quickly.

COMMISSIONER SVINICKI: Thank you. And, again, I realize you don't speak for that segment. But just generally as you canvas for availability, it sounds like at least you're not aware of groundswell of development of new packages to be available. So, it is something to keep our eye on, I think.

And Dr. Thomadsen, you were asked question about the report and why were estimates in the report different. I might come at it a little differently and ask you for the cost estimates that you provided, and you had some specific costs, I think, for x-ray units. Where did you derive those? I'm assuming when I read that, that that's perhaps a manufacturer's price or something, that that number that you used in your presentation was derived from manufacturer's literature or list price for a device?

DR. FISHER: Not necessarily. List price, that is the prices that people have received on quotes very recently.

COMMISSIONER SVINICKI: Would that also be true when you gave cost for annual service contract, is that bid prices --

DR. FISHER: That is correct.

COMMISSIONER SVINICKI: -- that various facilities have received?

DR. FISHER: That is correct.

COMMISSIONER SVINICKI: So, that's the source for your estimates, and I won't question any of the estimates that were used by others.

Mr. Mattmuller, I wanted to be certain I understood on slide number 21, where you talked about diminished patient care and you talked about preliminary

survey results for 2009. This has to do with postponed procedures or canceled or changed procedures. And I'm trying to project forward in an answer, I think, to Dr. Klein, you talked about facilities that were not yet feeling the full effect of the NRU shutdown.

And so, drawing from that, that the 2009 numbers as the effect is felt more fully would be even more pronounced than is listed here, up to and including -- if Chalk River were in a position never to restart, would we reach a point on this statistics that are listed here for postponing and canceling procedures, would we reach a kind of steady state if we only had Petten available and then obviously, it would be altered during the time period when Petten would not be available for four or five years? I guess I'm asking us to think about a worst case scenario there.

MR. MATTMULLER: Well, I think the worst case scenario would be upon us in about a month when the Petten reactor does go down. And then the typical suppliers that supply 100 percent of Mo-99 to the US will both be down.

COMMISSIONER SVINICKI: Okay. Because at that point in terms of availability, it is just we are at the lowest availability, we just don't know the duration, because if NRU comes up in three or four months, it is a different circumstance than if they don't?

MR. MATTMULLER: Right. And that's a big wildcard as far as how long the NRU at Chalk River is going to be down. Hopefully, no more than three months, but there is no guarantee on that.

I mean, at this point there is still -- it's my understanding from a recent visit up there that they are still evaluating the reactor. So they don't -- at this point, they are making their predictions based on what they know is wrong and what they anticipate would be wrong, but they are there is still more discovery -- the discovery process has not been completed yet.

COMMISSIONER SVINICKI: And I'm aware of the significant uncertainty around that three-month estimate, as you are mentioning here. The statistics as they are, even the preliminary results are obviously very sobering, and I'm speaking only to my own reaction here, and I'm no fan of melodrama and hyperbole. But I think this is a factual based conclusion that I'm drawing, given the number of procedures that are done, and you have mentioned a figure. And we're talking a very large patient population.

And I know that the substitutes have their drawbacks, so if we look at postponing and cancellation and those statistics become more pronounced. Even in changing a procedure, I guess there is an alteration of the potential medical outcome there.

So given the patient population affected, I think it is safe to conclude that in a prolonged unavailability, there are patients who will die as a result because of -- and it's hard to know exactly who they are. But I think it's merely factual to conclude that given a large number of procedures that might be postponed or cancelled, that there will be patients who will suffer a horrible outcome as a result of that.

And so, I appreciate that you're frustrated. I might use a stronger word than that, but it's obviously, a national -- and you did use the term "crisis," I appreciate that. I do think it is a national crisis.

I know I'm over my time. Thank you.

CHAIRMAN JACZKO: Thank you, Commissioner Svinicki.

I wanted to -- I don't want to go into too much depth, we have talked a lot about the VA issue. But I didn't want to leave, I think, the impression, that the NRC doesn't view this as a very serious incident. I just wanted to read from the -- I think, Dr. Welsh, you talked a little bit about the lack of the CT scan, I guess, to do the dose assessment post incident --

DR. WELSH: Post implant.

CHAIRMAN JACZKO: Post implant. And I think that certainly is an important factor. As the NRC developed -- as we developed this, we did a inspection. And I just wanted to read from this again.

The NRC is finishing up an investigation on this, and so I don't want to get into too much detail beyond this. But I thought it was useful just to read the assessment from that inspection report and -- which, I think, puts a slightly different character, perhaps, on this incident than maybe has been conveyed to this point.

And that says that, “The NRC contracted a medical consultant to review a selected number of medical events and determine if any health consequences to the patients were expected” -- and I think this is the important sentence. “The

consultant noted that the seed placement in the cases reviewed was quite erratic and not consistent with current medical standards."

So again, I think we are not necessarily talking here about a disagreement in terms of very vagaries of a difficult procedure, which I think every since I come to the Commission I have learned about brachytherapy, and in particular, in prostate seed implantation. And it is difficult because the -- as I understand it, the prostate is not a well defined -- and when you're injecting straws into the lemon, that is not a precision process. There is a lot of vagaries here.

But I just wanted to put that statement on the record, because again, that was one of the findings of the contractor that we had contracted with in order to do the inspection. And it certainly does indicate some challenges. As I understand it the inability to have the CT scans was the inability, I guess, of the dose reconstruction software to read the CT images, but they, in fact, took the CT scans, had the information.

So it was not that they were not taking the -- they were not doing the CT scan the following day, they were do the CT scans, however, they never corrected the software errors to allow them to then use those CT scans to do dose reconstruction the day following.

So, I just wanted to make sure we have factually a lot of the information correct on this particular issue, because I think it certainly is an issue that I think we take very seriously as an agency, and I think one that we will continue to pursue the investigation.

Dr. Fisher, you raised an issue on the Cobalt-60, which I think is an interesting one and I recall -- I don't think Mike Webber is here. I wish he were here. I asked him a question about the transportation issue a while ago, and perhaps you can answer this question as well for me.

The issue with transportation packages is an issue that goes back, I think, to 2004. That is when the NRC initially implemented the new regulations to conform ultimately with international standards. The whole purpose of our change to the package designs was really to conform with the new International Atomic Energy Agency standard PSR, whichever it was, 1 -- I get the cues from the back.

We did a variety of communication tools to let people know that they had four years to get new packages in place. In August of last year, we put in place -- we made another announcement, sent it out to the industry explaining that these packages were going to expire in October of 2008, that there was -- we outlined, I think, five criteria that they needed to come in and satisfy for an exemption request. The agency has approved number of exemption requests for certain packages to be used beyond their expiration date.

What do you think we could do beyond that, because it seems that for some reason, we have not communicated in that four-year time, well, our expectations -- or maybe we did communicate and the industry just ignored it. I don't know if you can shed some light on what you think happened with that?

DR. FISHER: Each of the things that you have mentioned are correct, and industry has had time to respond. But I think there's -- there is a disconnect

between the manufacturers of these casks and the suppliers of isotopes. They are not always the same organizations.

And what happens is, if progress is slow in cask design and approval, that does impact on the manufacturers of the isotopes, and they are kind of caught without a package.

I know that, at least back at the laboratory where I work, the containers that we have been relying on for a number of years are no longer available to us to use, and we don't have a replacement. There are some new containers available that are very, very expensive to lease -- impossible to purchase but expensive to lease. And finding the packages for specific applications is still very difficult.

What the NRC can do, I think, number one, listen to the industry concerns. Hear what they are saying. They met before the Commission in the past.

CHAIRMAN JACZKO: To some extent, that was 2004. We made the rule change. And I think we had a good process. That largely -- again, part of the reason we did this -- is it interesting. There is one area where we adopt international standards by regulation, and that is in the transportation area. That is precisely, I think, to address industry concerns of consistency and uniformity as packages move from country to country.

So in that process, we did go through a rule-making process at that time. I was not around at that time, so I'm assuming we did get industry feedback and tried to incorporate that as best we could within the constraints of the IAEA guidelines.

I guess what -- I guess what I'm trying to find out, how can we communicate better so that people could prepare properly and that we don't find ourselves in a situation five years later where people are without casks, as you just indicated, or unable to ship material. Absent a rule change that's the situation we have. And a rule change will not solve the problem any time quickly.

DR. FISHER: But I think the approval of already approved foreign made casks would help the most. I recognize that a lot of these issues are created by another agency, the Department of Transportation and not the Nuclear Regulatory Commission, but working effectively with DOT is also helpful.

There is also some issues that I have heard that are very difficult, and that's transporting sources between the U.S. and Mexico are very problematic right now, because U.S. carriers are not allowed to transport in Mexico. There are some issues there that your staff have probably been working on already.

CHAIRMAN JACZKO: Well, I appreciate that. And there are other issues too as we meet subsequently to continue to, I think, improve the communication and dialogue that we have there. I think that will be helpful as we go forward.

This is a question, I think, for you, Dr. Mattmuller. Many have touched on the medical isotope issue, and I guess sometimes we take off our regulatory hats and we have human being hats that we put on, believe it or not. And certainly medical isotopes is an important issue.

It does not seem to be an important issue for the nation, which I think everyone has highlighted the disconnect that that presents.

Certainly, my interest and I think the focus for this agency as we go forward is on making sure that we play our role in whatever solutions may develop which is in the regulatory arena and being prepared to review licenses to deal with any applications that might come forward in this five to seven-year period or in the short term.

The question I had on this, and I think it really goes to something you touched on very briefly, I think, at the end of your presentation, you talked about, I think, for the NRC to look at flexibilities and other issues in the regulatory process. One of the things I have done in the last two weeks is ask the staff to look at the regulatory issues.

Now, the B&W approach may have issues. Those are probably statutory issues and not really regulatory issues. They don't manifest themselves as regulatory issues, but they are inherently statutory issues in how we define waste, and that we may have limited flexibility in what we can do there.

But I'm not aware in the other areas -- I mean, these are relatively routine kinds of licensing actions, whether it is looking at targets, whether it is looking at -- really, ultimately, that would be the main issue, imports/exports, which we do on a routine basis.

Are there were specific issues that you were concerned about when you said that we should have flexibilities? Are there particular issues that you can point to in our regulations where you think that there will be inappropriate choke points that we would need to look at?

MR. MATTMULLER: Some of the choke points that exist now, for example, for the Missouri reactor is powered by HEU fuel, and they are undergoing steps to convert to LEU fuel. That's my understanding in order to have an appropriate neutron flux for bombardment of the targets, they will need to raise the power limit of their reactor from ten megawatts, which is the current limit for that type of research reactor to 12 megawatts.

So, in essence, they need a new license for a category that does not exist right now. And I don't know if that would need to go through the complete regulatory process --

CHAIRMAN JACZKO: So, there is nothing -- you're not aware of any specific problem with that regulatory -- just that it would require a regulatory review?

MR. MATTMULLER: Yes. Well, I guess the issue would be that there is not a category -- there is nowhere for them to go into the regulations to get a license right now. It is going to be something new, is my understanding.

And similarly, for the Babcock & Wilcox reactor, in that it won't be a test reactor, it won't be a research reactor. It is going to be 100 percent for the production of medical isotopes. And it is my understanding there is not a category like that for reactors in the current regulations.

CHAIRMAN JACZKO: Well, I thank you. I don't know if any of the staff wanted to comment on the first point in particular, if there is an issue.

The second issue is, again, I'm not sure -- certainly there are categories. I

think we have just never licensed facilities of that nature. So, there certainly are categories to do it, and I think we have just never done it before.

George, I don't know if you have any comments.

MR. PANGBURN: Just this week, a couple of us were at Missouri, Eric Leads, Tim McGinty, myself and a few others. And at that point, you know, we talked with the folks at Missouri. I think they are well aware of the need for an amendment to their Part 50 license.

We had some discussions about other types of licensing and how you might work that within the Part 50, whether there would need to be a separate Part 70 or Part 30 license, because they are looking at making a production facility a processing facility, might be the more appropriate term here. And they have done an awful lot of planning.

So I think they are thinking ahead on it, as you know we have received from B&W, they are thinking ahead. The staff is looking at the issues to try and make sure we were clear with Missouri this week that the agency did not want to be in a position where we were on the regulatory hold point toward the national solution towards the medical isotope issue. And I think both Missouri and B&W are moving ahead with some speed on this.

CHAIRMAN JACZKO: I appreciate your answers.

Commissioner Lyons, did you have additional questions.

COMMISSIONER LYONS: Just couple of additional questions.

Steve, if I could continue the line of questions that Greg was just on,

perhaps a question that really is not directly within the NRC's purview. But in your slides, you had the statement that it is four to five years to any of the solutions on Mo-99.

What determines that time?

MR. MATTMULLER: Those are the estimates that Missouri and Babcock & Wilcox have given us. And sometimes -- and even Babcock & Wilcox might be more appropriate five to seven years as far as the time they think they need to pursue licensing to pursue construction and to become operational.

So, those are coming directly from those two producers.

COMMISSIONER LYONS: Well, I guess speaking just for myself, I would hope that as the importance of this crisis becomes more visible, that -- and again, this is not an NRC -- it is not directly an NRC issue -- I would hope that, perhaps, Congress would be moved to step in, and to the extent dollars can address -- can shorten any of those times, I think it is simply vital to the country that that happen.

A question for Bruce, if I may. You, in talking about the national academy report, made a number of comparisons more from a cost or a dose rate issue if one moved from Cesium-137 to some of the X-ray options. You didn't talk, however, about the efficacy of moving to such irradiators.

And I have had at least some folks in the medical community suggest to me that with the currently available end point -- I don't remember the number, I think it is 180 kilovolts or so -- on existing x-ray machines, that there is a real question on whether you have the same efficacy in terms of the medical effect that you're

desiring.

Could you comment at all on that? Are you aware of work to try to better address that? I'm more than willing to believe that as you go up in energy, eventually, they will be the same but you also increase the complexity of the x-ray system substantially?

DR. THOMADSEN: Yes. This is a confusing issue based on what data is available. There are facilities that do use the lower energy x-ray sources for blood irradiation. They seem to be able to do it just fine. They are subject to the complications that we mentioned in the report, but the doses do seem to be able to serve to inactivate the white blood cells.

There is always the question with those lower energies of what price you're paying due to the fact that you have to give much higher doses to some parts of the blood product. And what is that going to do to the blood products that you want to use and not inactivate? That is not well documented at the moment and not well researched at the moment.

In the reports that we have seen, they do not have long-term data to follow-up on that. We just don't have an answer to that question at the moment.

COMMISSIONER LYONS: I appreciate that it is still viewed as an open question. It strikes me as a very, very important question. And if there is more of a shift towards the lower energy x-ray systems, I certainly hope that that gets the research focus that I think it deserves.

And the only other comment I would have made, Mr. Chairman, I certainly

appreciated Dr. Fisher's remarks on a National Source Tracking System and deficiencies therein as of today.

I just wanted to make the point that the deficiencies that you highlighted, and others, I think are very, very well understood at the staff level. They are well -- we are well on the path towards addressing each of the issues that you raised. And certainly, the staff intent is to vastly improve the operation of the National Source Tracking System.

COMMISSIONER KLEIN: One follow-up question, a question probably for Dr. Welsh.

Based on what you know of the NRC's response to the VA situation, are there any actions that we should have taken that we didn't? Do you think our actions were sufficient for what you know to date?

DR. WELSH: From what I know, it appears that there the NRC has acted appropriately and things are moving in the correct direction.

COMMISSIONER KLEIN: Thanks.

COMMISSIONER SVINICKI: Before you turn off your mike, Dr. Welsh, I will follow-up and say that your presentation talked about a number of questions that you indicated were important questions. As an advisory committee, is there a plan for you, again on these more general themes, to take up those questions and be arriving at a consensus recommendation or any recommendations that might come out of your deliberations of those questions?

DR. WELSH: I don't know if there is a plan for further specific meeting and

discussion between NRC staff and ACMUI on this individual topic. But I am told that there will certainly be more information relayed to us in general, and we look forward to having that information, interpreting it, and providing advice and input as requested.

DR. MALMUD: Commissioner, what usually happens is the NRC completes its investigation, which is, as you know, aggressively ongoing now.

At the completion of the investigation, they prepare a report. They will then brief us on the report and recommendations that they may have made internally with NRC staff. And then ask us for our opinion with regard to the outcome of actions that might be taken and perhaps even unintended consequences of what might occur.

Then we render our advice. They take that advice and then, if necessary, incorporate it into the recommendation.

So, they know that we intensely interested in this. We and the NRC staff both have great concern for the well-being not only of our veterans but of all patients who are being treated. And therefore, we know we will continue to be informed, because that's been the pattern of NRC staff in dealing with us.

And we will happily review the material and offer any constructive advice that can be forthcoming from this group which represents radiation oncology, radiation physics, radiochemistry, patient advocacy, each of the elements that's necessary to deal with this.

COMMISSIONER SVINICKI: And I appreciate that. It is really a

two-pronged response, as I think you're indicating here, there is the reaction to the specific event, but then there are the improvements to our processes that could potentially be recommended as an outgrowth of examining the one specific event.

So I, of course, appreciate and I'm certain that the agency will benefit from the application of all of your expertise to both of those prongs of response to this event.

And I would just close with a comment that the topics that we have heard about today are very dynamic, they are very active issues and a lot is going on, so I would encourage the ACMUI to not hold back.

And again, given the unfortunate infrequency with which we have an opportunity to have the kind of meeting we had today, there are other vehicles for the committee to make if they feel there is any urgent recommendations or issues that need to be brought to the agency or Commission's attention. I would encourage you, speaking only for myself, to avail yourself of other types of communications that would get thing of urgent importance or developments you feel need to be brought to your attention, please do so, and thank you again.

DR. MALMUD: The Chairman has already transmitted that message to us long before this particular issue arose, so we know that we have access, and we will take advantage of it at the right moment. Thank you.

COMMISSIONER SVINICKI: Thank you.

Thank you, Mr. Chairman.

CHAIRMAN JACZKO: Thank you for your presentations. I know the staff

certainly appreciates your interactions and your dialogue. ACMUI is a unique committee. As a staff advisory committee you do play that unique role in interacting with the staff in providing them with helpful guidance as you go forward.

It is certainly I think, periodically useful for us to hear from you directly, but I hope that you will continue to have your interactions with the staff. I think that is certainly a helpful role and some thing that is important as we go forward. And I thank you for your presentation.

We are adjourned.

(Whereupon, at 3:33 p.m., the meeting was adjourned.)