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NUCLEAR REGULATORY COMMISSION

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ADVISORY COMMITTEE FOR THE MEDICAL USE

OF ISOTOPES MEETING

(ACMUI)

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THURSDAY

NOVEMBER 17, 1994

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ROCKVILLE, MARYLAND

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The Advisory Committee met in Rockville, Maryland, at 8:00 a.m., Barry A. Siegel, Chairman, presiding.

COMMITTEE MEMBERS:

BARRY A. SIEGEL	Chairman
JUDITH I. BROWN	Member
LARRY CAMPER	Member
DANIEL F. FLYNN	Member
JOHN E. GLENN	Member
JOHN GRAHAM	Member
WIL B. NELP	Member
JUDITH ANNE STITT	Member

DENNIS P. SWANSON	Member
LOUIS WAGNER	Member
DAVID WOODBURY	Member

ACMUI STAFF PRESENT:

Carl Paperiello

ALSO PRESENT:

Florence Kaltovich

Katherine Seifert

John Telford

I N D E X

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

8:07 a.m.

DR. GLENN: Good morning, ladies and gentlemen. I am pleased to welcome you to Rockville, Maryland on behalf of the Advisory Committee on the Medical Use of Isotopes. My name is John Glenn. I am Chief of the Medical, Academic, and Commercial Use Safety Branch of the Nuclear Regulatory Commission.

This is an announced meeting of the Advisory Committee and is being held in accordance with the rules and regulations of the General Services Administration and the Nuclear Regulatory Commission. This meeting was announced in the Federal Register on October 11th, 1994, and that notice stated that the meeting would begin at 8:00 a.m.

The function of the Advisory Committee is to advise the NRC staff on issues and questions that arise in the medical use of byproduct material. The Committee provides counsel to the staff but does not determine or direct the actual decisions. The NRC solicits the opinions of counsel and values the opinions of this committee very much.

The staff requests the Committee reach a consensus if possible, but also values well stated minority or dissenting opinions. Therefore, any members who do have

differing opinions as to the direction NRC policy should take are encouraged to state those opinions.

The agenda is full and I request that members of the committee direct their remarks as briefly and succinctly as possible.

As part of the preparation of this meeting, I have reviewed the agenda for members financial and employment interests. I have not identified any conflicts from that review based on the very general nature of the discussion we're having this time. I don't see anything that involves any specific institution where there might be a conflict, nor am I aware of any of you who have been -- raised any of the items that are on the agenda as part of a petition for rule making. So, to the best of my knowledge, there are no conflicts. However, should any member of the committee become aware of a potential conflict of interest with regard to a topic of discussion, you are obligated to inform the chairman and myself, and recuse yourself from a discussion of that topic as a committee member.

I would like now to introduce those members of the Advisory Committee and a soon to be member of the Advisory Committee who are seated at the table. To my left we have David Woodbury who is our representative from the Food and Drug Administration. We have Louis Wagner who is our physics specialist. We have Dennis Swanson who

represents the specialty of pharmacy. We have Judith Stitt who represents the specialty of radiation therapy. We have Robert Quillin who represents the states. Larry Camper who is the section leader of the medical and academic section of the NRC. Barry Siegel who is the chairman of the committee. We have Wil Nelp who is our specialist with regards to medical research. A soon to be member but not officially on board yet, John Graham, who represents hospital administration. He has been selected but the paper work hasn't been completed yet so he can participate in discussions but he will not be able to help the Committee reach a consensus or participate in any votes. Daniel Flynn who is also a representative of the specialty of radiation therapy and Judith Brown who represents the public interest.

Just a few administrative items. We do have coffee and doughnuts for the Advisory Committee members. They are not available for the public. There are restrooms at the end of the hall. As you're going down the hall, the men's room is to the left and the women's room to the right. Also to the left there is a vending room and so if you don't wish to have coffee but would prefer a cold drink, there are vending machines that can satisfy that need.

And with those -- Oh, the last thing, with

regard to the microphones, they're very sensitive and if you wish to talk to one of your neighbors, you should move the microphone aside so that you don't have a public conversation.

And with those comments, I will turn it over to Dr. Siegel.

CHAIRMAN SIEGEL: Thanks, John.

Good morning, everyone. We have a full agenda and a lot of fairly meaty topics. We're scheduled to go through mid-day tomorrow. My guess is that without Carol here we probably will be done by noon today because -- but we budgeted the time as if she were here and we're going to miss her at this meeting.

The -- Larry has received no notification that there are members of the public who wish to make statements before this Advisory Committee. And I would just ask the audience if there's anyone who has not so declared that has a desire to address the Advisory Committee some time during the course of this meeting? Seeing none, we will proceed.

As has been true in the past, depending on how we're doing on time and depending on the nature of the discussion, the Chair will reserve the right to recognize members of the public to participate in a discussion or to provide information during the course of a discussion as it seems appropriate.

Dan Berman sends his regrets and is sorry he couldn't join us today but he had a double collision on his calendar and had to deal with it. And for those of you who have still not figured out what your E-mail addresses are so that I can communicate with all of you at 3:00 in the morning, I really would love to get your Internet addresses or that of a secretary who can get a message to you.

And with that, let's begin. And our first topic this morning for the first couple of hours actually will be presented by Dr. Glenn discussing the radio pharmacy rule and how it is to be resolved.

DR. GLENN: Actually, I'll change that comment a little bit to how it has been resolved. So let me update you on the current status of the radio pharmacy rule.

On Tuesday of this week the three commissioners did affirm the radio pharmacy rule. So, with some minor changes they have directed the staff to make in a staff requirements memorandum, the rule will be published in the Federal Register. That publishing will take place before the end of this month. And so by January 1st of 1995 the rule will be effective.

So what I'm discussing today has now become for the most part reality. There may be a few changes and I'll try to mention those as we go along.

Let me do a little editorializing first. Give

you my view of how dramatic this change is going to be for the Nuclear Regulatory Commission. This represents my own personal vision of what's going on. But I think it is a dramatic change in philosophy. I think it will help focus our attention or the -- where it needs to be and also I think it will provide the community with the flexibility that they need.

In the early days of nuclear medicine, the AEC and the community worked very close together and there was almost a daily working relationship. The AEC provided the training for the physicians. New procedures came into the AEC for approval. The drug approval, the Advisory Committee, the predecessor to this committee, would approve new uses,a nd so forth. However, in the '60s and '70s certain procedures became to be routine and the AEC created something called the group concept. And the group concept said, well, if you have a certain basic level of knowledge, you can do anything of a certain type of nuclear medicine. And then we had groups 1, 2, and 3. Groups 1 were uptake and dilution. Group 2 was diagnostic imaging. Group 3 was generators. So we were considered to require a little more knowledge than simply imaging.

I think we made a critical mistake in the middle '80s when we changed our regulations in Part 35 in a dramatic way. And this group concept that we created

within the original Part 35 as a limited set and you only had to have a limited set of training. You could do any procedure. In the middle '80s we made that Part 35 and we forgot about the fact that there had been another group out there that we had been licensing all along that did other things. Like compounded new drugs, did human research. We called those licensees medical licensees of broad scope. But 1986 the rule we published was silent on the existence of anything other than what was really the group concept. And that flushed out some other problems as well.

This rule, I think, resolves all of those problems. I makes clear that medical licensees do in fact have the flexibility to do things with drugs so long as state boards of pharmacy and the Food and Drug Administration don't have an objection. It recognizes that pharmacists have a professional job to do and should be allowed to do it. It clarifies what the difference between a broad scope and a specific license of limited scope are. The regulation now takes care of that. So we've got some fixes in here.

In particular, I'm going to talk about how we've recognized the right of both an authorized user physician and an authorized nuclear pharmacist to prepare drugs. I'll discuss in detail the criteria that we've set

for recognizing a pharmacist as an authorized nuclear pharmacist. A brief discussion of how we're going to look at human research, human subjects. Some simplifications we've made in the process. We've actually, I think, made a big step forward in allowing clearly qualified people to go ahead and participate as authorized users and authorized nuclear pharmacists without going through a big paper review process when in fact the paper review is very simple. It's are you certified? Have you been listed on a previous license? Something that anyone can easily do. And then finally, the specific parts of Part 35 that don't apply to broad scope licensees.

Today radioactive drug preparation is controlled by Section 35.4[illegible] of our regulations. And it restricts the materials to be used in drugs or reagent kits, that they be manufactured, labelled, packaged, and distributed in accordance with a license issued pursuant to Sections 32.72, 32.73, or 32.74, or equivalent agreement state regulations. It does not provide for any institutional preparation of radioactive materials. It says that if it's for radioactive drug, it has to have been prepared by either a manufacturer licensed by the NRC or an agreement state or a pharmacy licensed by the NRC or an agreement state.

How does this rule change that? The new 35.49

says nothing at all about the preparation or the suppliers of drugs. Instead, within the sections that have to do with the uses of radioactive material, we have these kinds of conditions or these kinds of regulations. It can either be obtained from a manufacturer preparer licensed pursuant to 10 CFR 32.72, the old way. Or, it can be prepared by an authorized nuclear pharmacist or an authorized user who meets the requirements of 10 CFR 35.920 for training experience or under the supervision of either. Now, there is still some restriction on the physicians. You have to have the training and experience equivalent to what's required for 35.200 uses. So, it requires a little more training than would be required for using 35.100 materials for uptake and dilution.

The current regulations went beyond just supply. It also restricted use of prepared materials. Currently 35.100 you can only use IND or NDA materials. Current 35.200 you can only use IND or NDA materials, and in addition, you have to follow the manufacturer's instructions or kits and generators, c as modified in the interim final rule, you can make departures under the directions of an authorized user. And current 35.300, it's got to be IND or NDA material. You have to comply with the packaging insert regarding indications and methods of administration or base don the interim final rule, the

directions of the authorized user in the written directive.

DR. WOODBURY: John?

DR. GLENN: Yes?

DR. WOODBURY: What about PLAs?

DR. GLENN: Oh, that's a deficiency in the current regulation which the new regulation, of course, by not having these restrictions in it takes care of.

So, right now there is a problem, that PLAs are not recognized in the regulation as it's read today. However, as the -- when the new regulation goes into effect, if FDA's approved it, they can use it.

MR. SWANSON: Excuse me, Doctor. Florence Kaltovich wishes to be recognized.

Announce yourself just so the transcriptionist can get it.

MS. KALTOVICH: I'm Florence Kaltovich. I work at the FDA Center for Biologics.

My major concern that it doesn't specifically state PLA here could be problems because they are -- there is a total different regulations under our CFRs than under NDA or IND.

DR. GLENN: I have not gotten into what the current wording is but we don't refer to INDs or NDAs, either.

MS. KALTOVICH: In here it listed that it was

and I was concerned.

DR. GLENN: Well, my next line is that as it's received from 35.100, 200, 300, it's received from a supplier who is licensed under Part 32 or prepared by qualified, authorized nuclear pharmacist, or authorized user. And what we're silent on its FDA credentials. So we will not restrict it.

MS. KALTOVICH: Okay. Thank you.

MR. SWANSON: And John, doesn't also the new term radioactive drug as opposed to the term radiopharmaceutical partially address that issue? Because you define it to mean pharmaceutical or radiolabelled biologic.

DR. GLENN: Right. And that's in Part 32 we define -- Well, I guess, no, we define it in Part 35. But yes, we have incorporated the FDA's definition of a radioactive drug. And in fact, in most places in Part 35 we don't even use the term radioactive drug, we just use the term byproduct material to avoid that problem of any implied restriction in terms of the terminology.

We're also changing Part 32 which is the regulation under which we license nuclear pharmacies, conforming changes. Currently under 32.72 they have to receive the material as an NDA material, a biologic product license material, or material subject to an IND. Or, they

have to demonstrate to us that they're not subject to FDA's regulations. So far as I'm aware, we have never had a pharmacy come in and say they want to do anything other than distribute already approved FDA materials on the basis that they're not subject to FDA regulation. There have been arguments about that but so far as I know that has never been the basis of a license that we have issued.

CHAIRMAN SIEGEL: I might just point out that that's because you only regulate byproduct material. And if positron emitters were under discussion, that might be a more interesting discussion.

DR. GLENN: Currently we have a regulation, Part 32, section 32.73, and again, it restricts generators and reagent kits to FDA approved materials, or with the same caveat, demonstrate that you're not subject to FDA's regulations.

I'll mention that 32.73 goes away in this revision of the regulations. Generators, under the new definition of radioactive drug, go into 32.72 and the NRC has removed itself completely from the regulation of kits that do not contain radioactive material. So, 32.73 disappears completely.

The new 32.72 says that we will grant distribution licenses for drugs and generators prepared by FDA or state licensed, or registered, manufacturers or

pharmacies, or nuclear pharmacies within a federal medical institution. Now, we had to include them because they might fall outside all of these other categories and so a VA hospital could come in and ask to be licensed pursuant to Part 32.

There was a letter that was distributed to the members of the committee with comments from Dr. Carol Marcus that did express some concerns about the proposed labeling requirements in the regulation. Currently the NRC's labeling requirements are that the radionuclide be specified, the quantity of activity, the date of assay, the Part 35 listed use. That's whether it's for a use that's in 35.100, 200, 300, so forth. And the regulation says it may be combined with any required FDA labeling.

The new labeling does not differ greatly from that. Rather than the radionuclide, we do say radioactive drug or abbreviation. We still require the quantity. We require the date of assay. Controversial one, we also require the time of assay. That's in addition. However, in the rule as approved by the Commission, that has been limited so that if the isotope has a half-life greater than 100 days, the time of assay is not important. It doesn't have to b eon the labeling. That, I think, involves very few drugs but it does avoid the inconsistency of requiring a time to be noted when the time isn't that important,

where the date is sufficient information to be able to comply with our regulations.

Still requires that the Part 35 use be listed. And the regulation says that it is independent of FDA labeling. If the pharmacy or the manufacturer wishes to include it with the required FDA labeling, that's fine. However, this labeling is NRC's Part 20 labeling requirement and it does not have to be combined with FDA's.

DR. WOODBURY: Does this mean the provider then has then two different labeling things to be concerned about? Isn't that overkill?

DR. GLENN: We tried to word this such that we don't restrict them in any way. Anything that meets our requirements and meet your requirements, it can be combined. It can be separate. Whatever meets the requirements of Part 20 plus whatever meets the requirements of the FDA is acceptable. We're not requiring two labels.

John Telford just clarified for me. There is one sentence that says clearly that one label will be fine if it has the information that we require.

DR. NELP: What do you perceive you would require that isn't already required? I mean, why do you want to get into this arena? I would presume that everything that comes into our hospital and our laboratory,

and to our research unit, is labeled appropriately by the current guidelines and FDA, and users guidelines, and so forth. Why don't you just accept what there is out there.

DR. GLENN: This is the labeling that is required for the medical use licensee to be able to comply with the NRC's radiation safety requirements and misadministration requirements. That's the only reason for this labeling.

DR. NELP: That already exists was my point.

DR. GLENN: I guess we don't know that that exists. There is a Part 20 requirement that applies to all NRC licensees.

CHAIRMAN SIEGEL: Buzz, I'm not sure that this is a practical problem in the final analysis and I would be interested to see what Dennis thinks about that. I -- This information for the most part is already on the label of something that arrives at your shop from a Part 32 supplier. And this applies to Part 32 suppliers.

DR. GLENN: This is the Part 32 requirement, right.

CHAIRMAN SIEGEL: Correct. If you are making something down the hall in your own radiopharmacy and it's going to go from your lab directly into a patient, you don't have to generate this complicated label to go right into the patient. This is when it's being shipped into

your facility by a commercial supplier.

That's correct, John?

DR. GLENN: Yes, this particular requirement. Now, there are some Part 35 --

CHAIRMAN SIEGEL: Absolutely.

DR. GLENN: What has to be on a syringe.

CHAIRMAN SIEGEL: Correct.

Do you agree, Dennis? Or do you still see a problem here?

MR. SWANSON: Well, I have several specific comments regarding labeling and what appears in this regulatory guide. And I don't know if you want to address those now or come back to it later on?

DR. GLENN: I would be fine. I guess let me make one other comment in terms of the labelling. We had in the proposed language a requirement that there be a statement on the labeling that said that this did not relieve people from complying with any other regulations that might apply to a drug manufacturer or a pharmacy. In the rule as approved by the Commission, that sentence is no longer required. So just to make that clarification.

MR. SWANSON: Specifically, why do you require the Part 35 listed uses on the label? It seems that the centralized nuclear pharmacy, according to their license, is restricted to distribute the drugs to people that are

appropriately licensed. Likewise, the Part 35 licensees according to their license, are restricted to receive drugs from people that are appropriately licensed. It seems ridiculous to require that statement on a label.

If I can illustrate an example here of why I'm concerned.

DR. GLENN: Well, I guess one thing I will note, I will be showing you a license later and that is the basic-- that is the way in which we actually list on a license what a medical use licensee may do, is by those 35.100, 35.200, 35.300.

MR. SWANSON: Yes. My concern is that I don't think that needs to appear on the unit dose label that goes from the centralized nuclear pharmacy to the Part 35 licensee. If I can pass these around to the ACMUI, I would just like to illustrate a point here.

And what I'd really like you to do when you get these is just focus on the top two labels, if you would. The top two labels are actually samples of labels from two centralized nuclear pharmacies. I'd like you just to look at the top two labels and tell me which one is easier to read and specifically find a piece of information. For example, the name of the radioisotope or the patient's name, or the prescription number? And just focus on the top two. And I think you can readily see that it's much

easier to find the information on the second label. And the reason why is because the second label has much less material type don that label. And the point I'm trying to make is, I think you really need to look at what your requirements are for labeling very carefully because as you begin to require more material on the label, it actually becomes much more difficult to find the critical material that you need. And in fact, I think that can have a significant bearing on misadministrations and safety because, again, if you can't find, for example, the name of the isotope or the patient's name very readily, that can have a significant impact. And that is an important point, a very important point that I would like to make to the NRC in its labeling requirements in general.

Secondly, I have concerns about for the syringes, and maybe you can answer this question. You require the clinical procedure, or patient, or human subject's name. If a centralized nuclear pharmacy labels a syringe with a patient's name. Let's say they label a syringe of Technetium MDP for bone imaging with a human subject's name. They send that to a hospital for eventual administration to the patient. And let's say for some reason that particular patient study is canceled. At the nuclear medicine department of the hospital they reschedule another patient for a bone scan. And in traditional

practice would be to use that dose that was canceled, we could use it for the other scan. Would that be considered a misadministration by the NRC since that syringe was originally labeled for another patient?

DR. GLENN: Well, certainly the answer about the misadministration would not be because I think if you do the test, was it the right drug? Was this the right route of administration? Dah, dah, dah.

MR. SWANSON: But wrong patient. The point I'm trying to make is I don't think syringes ought to be labeled with the clinical procedure or patient's name. Probably more appropriately labeled with the abbreviation or name of the radiopharmaceutical and a particular lot number referring back to the prescription. Another point, okay, on your specific requirements.

DR. GLENN: Well, since we have the "or" in there, is it really a problem?

MR. SWANSON: I don't think you have an "or" in there at this point in time. You have on the --

DR. GLENN: Can you give a reference?

MR. CAMPER: What are you reading from?

MR. SWANSON: I'm reading from page 46 of the regulatory guide. Top of the page. Actually, the first complete sentence. "The syringe or syringe radiation shield label should also specify the clinical procedure to

be formed or the name of the patient or human research subject in order to prevent errors that lead to misadministration." It does not refer to an "or" with regard to using the name of the radiopharmaceutical.

Also, later on, if you go down to the second paragraph, it says, "That because of the limited surface area on the unit dose syringe, the syringe label may bear the radiation caution symbol, the words 'caution, radioactive material,' and a prescription number that links the label to complete form." I think it would probably be wise there to include abbreviated name of the radiopharmaceutical also.

DR. GLENN: John, do you -- Is John Telford -- In the rule itself, exactly what -- I didn't bring -- I don't have it.

MR. CAMPER: I can read to you, John. I'm reading from 32.72.A.4. It says, "A label is affixed to each container of a radioactive drug to be transferred for commercial distribution. The label must include the name of the radioactive drug or its abbreviation, quantity of radioactivity, and date and time of assay." New words inserted just in the last few days. "For drugs with a half-life greater than 100 days, the time of assay may be omitted. In addition, the label for the syringe or syringe radiation shield must also contain the clinical procedure

to be performed or the patient's or the human research subject's name."

DR. NELP: Why would you want to do that? That's not convention. First place, that's not the conventional practice and is not a requirement in the practice of either diagnostic or research uses of these things. We never -- Well, we could but ordinarily don't put the patient's name on the syringe. And we ordinarily do not put the procedure on the label.

CHAIRMAN SIEGEL: I think we've got three things going on simultaneously here. And I think we need to make sure we're clear about this.

This is the distribution of a dose of a radioactive drug from a commercial supplier, and for the most part, in fulfillment of a prescription, implicit or otherwise, for use in a patient. And if we forgot for the moment that this was a radioactive drug, most of the time the prescription would be very specific. It would be a prescription for a specific patient with specific instructions. And it would be very clearly linked physician, pharmacy, patient. And that's true of the average prescription.

Now, we over the years it has clearly evolved that commercial nuclear pharmacies distribute radioactive drugs with implicit patients in mind without always

explicitly stating who the patient is that's going to get the particular dose of drug delivered to the hospital that morning.

And so stating that Technetium MDP was meant for a bone scan solves that problem. You don't have to have the patient's name on there. It just says this is a 20 millicurie does of Technetium MDP and it's intended for use in a bone scan. Now, the author --

DR. NELP: Well, what else would you use it for?

CHAIRMAN SIEGEL: Whatever else the authorized user wanted to use it for. And the authorized user has the right to alter that prescription.

MR. SWANSON: Correct. The big thing that differentiates traditional pharmacy dispensing from nuclear pharmacy dispensing is that in traditional pharmacy dispensing, we dispense the drug directly to the patient for the patient's own use. In nuclear pharmacy dispensing, we dispense the drug basically to the nuclear medicine clinic for use in patients under the direction of the physician. There is a difference there.

MR. GRAHAM: Well, I don't think it's a difference. It's a sequence. A commercial manufacturer is labeling a drug that is being sent to a licensed pharmaceutical distributor and then there are state

requirements that kick in that cover the labeling, when it's going to go from that licensed, controlled entry point to a patient. And this seems to be backing up the labeling process a step further than it needs to. So it is -- It's placing a limitation in the label that doesn't seem to apply once you get to an authorized user.

DR. NELP: The physician, the materials are dispensed to the physician. He uses it according to his authorization. If I have ten bone scans to do tomorrow, I will order ten unit doses of that material and when they arrive in my laboratory, I will use them as I see fit under the discretion of the timing and the cancellations, and the add-ons, et cetera, et cetera. And I may order more and sometimes I'll have some that are not used.

DR. GLENN: I guess I'm missing the point of what in this requirement prohibits you from doing that?

DR. NELP: May -- It was my understanding that I had to say that what the purpose of the radiopharmaceutical was and that it had to have the patient's name on the syringe. That's not correct?

MR. CAMPER: Let me make a clarification, too, for the committee's benefit.

DR. NELP: I thought that's what Larry was reading.

MR. CAMPER: No, it's an or. Currently in

35.60 the requirements are to identify -- and this is for Part 35 licensees, obviously. "To identify its contents, a licensee shall conspicuously label each syringe or syringe radiation shield that contains a syringe with a radiopharmaceutical. The label must show the radiopharmaceutical name or its abbreviation, the clinical procedure to be performed, or the patient's name."

DR. NELP: Well, why do you want the clinical procedure to be --

MR. SWANSON: That's an or.

MR. CAMPER: I guess I would -- Well, I think fundamental reason would be that the technologist needs to know what's in the syringe.

DR. NELP: The technologist does know what's in the syringe.

MR. CAMPER: Well, if it's labeled they do.

DR. NELP: But not the clinical procedure. You need to know what the radioactive material is. Why do you -- I didn't hear an or.

MR. SWANSON: Point of clarification. Part 35 actually specifies it the way it should be specified. Part 35 says you can label the syringe with the name of the patient, with the clinical procedure, or with the name of the radiopharmaceutical. And appropriately, if I were in our lab, we label it with the radiopharmaceutical.

My problem is in this regulatory guide for Part 32, it specifically states that they have to label the syringe with the name of the patient or the clinical procedure. It does not specify that they can label it with the name of the radiopharmaceutical. The specific point, that needs to be modified to be consistent with Part 35. In that they can label it or with the name of the radiopharmaceutical is the specific point.

Also, if you read on further on Part 32, it says labels for containers of radioactive drugs tagged with Technetium 99M should specify the total activity or concentration of Molybdenum 99. That's another labeling requirement that you don't have on your slide that appears here and again, more information that must be on the label. And I question why. If they have an expiration time for the radiopharmaceutical which we traditionally put on labels, then why do we need to specifically put the Molybdenum 99 concentration on the label? When we receive a Technetium generator from a manufacturer, we don't receive information about the results of their testing on Molybdenum breakthrough on that manufacturer's label. If you look at the bottom label on the hand out I gave you which is iodine 123, which you don't regulate, a significant consideration with the use of iodine 123 is that you get build up of I 125 or I 124 contaminants.

That's why they have 24 hour expiration period.

The manufacturer is not required to put the concentration of I 125 or I 124 contaminants on their label. Why are you requiring the centralized nuclear pharmacies to put the limit for Molybdenum 99 breakthrough on their product labeling?

DR. GLENN: I think, if you -- again, if you go back to Part 35, there is a requirement that medical use licensee in fact know the Molybdenum content of the dose that's to be delivered. And so I don't think actually that that's in the regulation. I guess that's in the guide as a should that that be included there. So that's not an absolute requirement. That is a suggestion that in order for the medical use licensee to know the Molybdenum content of the dose at any given time, that that information be provided. But I don't think that's in the regulation itself.

Am I correct on that, John?

DR. FLYNN: Do your inspectors look for it?

DR. GLENN: No.

CHAIRMAN SIEGEL: What was the answer? John said that is correct?

DR. GLENN: He shook his head yes.

So, that would be something that the reviewer in the licensing process may raise, how are your customers

going to know what the Molybdenum content is. But it would not be a basis for denying the license. And it would not -- if it's not incorporated into the license, it would not be an inspection item.

CHAIRMAN SIEGEL: Dennis, I guess I'm still having trouble. You're --I'm having trouble deciding whether you're objecting to new changes in labeling requirements which we're learning are relatively minor versus objecting to existing changes in labeling requirements and wishing to retrench. Because very little is changing here from what is currently required.

MR. SWANSON: I think the requiring that Part 35 listed uses is a significant change from what's currently required. For example, I'm concerned about Molybdenum 99 breakthrough, for example. I was also concerned about the requirement that appeared in the original proposed rule about requiring that that label also notes other regulatory approvals which you've taken care and it doesn't appear in the new Part, so that was part of my original concerns.

In general, I guess I'm concerned that really, again, the NRC is getting into the whole issue of product labeling when in fact those issues are adequately regulated by state boards of pharmacy and by our nuclear pharmacy practice standards. One of your criteria for recognizing

and authorizing nuclear pharmacy is board certification and if you look at the nuclear pharmacy practice standards that led to the examination for board certification, labeling is one of the issues that's addressed.

And so again, it seems like they're stepping into an area that really is probably more of a professional area at this point in time.

DR. GLENN: I think there is a fundamental problem here in that when we talk about labeling, we're talking Part 20 type labeling. In other words, that information that needs to be on a container of byproduct material that allows our licensees to comply with our regulations. We are not using the term in the same sense that FDA uses the term. We are talking about a tag to a container that permits the person who uses that container to use it safely.

CHAIRMAN SIEGEL: So I guess I'm having trouble deciding whether we've got a specific -- it's probably too late, but whether we have a specific recommendation that he wants clarification.

DR. GLENN: Well, I guess I hear one and that's why in the -- We had three "ors" apparently in 35. We only have two "ors" in 32, and I can't remember any reason for dropping the third.

CHAIRMAN SIEGEL: Is that addressable or is it

too late to deal with?

DR. GLENN: I don't know. I think it's -- the affirmation has already taken place.

MR. SWANSON: And again, I do have problem with the Part 35 listed uses on the label. I just can't understand why that's required.

DR. GLENN: Most of the labeling that we have in Part 35 is that information we think it necessary to prevent misadministration.

CHAIRMAN SIEGEL: And yet, Dennis, it's on this label for Thallium. The non-Part 35 listed use is on the label. So why does it bother you?

MR. SWANSON: Tell me specifically what you mean by Part 35 listed use?

CHAIRMAN SIEGEL: Where it says there, cardiac profusion study, and where it says on the cardiolite label, cardiac study.

MR. SWANSON: No, I'm requesting the NRC to tell me what they mean by Part 35 listed use on the label.

DR. GLENN: Is it for use under 35.100, is it for use under 35.200.

MR. SWANSON: Do we have to specifically state on the label, then, this product is approved for use under 35.100, 35.200, 35.300, is that what you're saying that you want on that label?

DR. GLENN: Can we read what the actual regulation is there?

MR. CAMPER: It says, "In addition, the label for the syringe or syringe radiation shield must also contain the clinical procedure to be performed, or the patient's name, or the human research subject's name."

DR. GLENN: Now where is the part that talks about the label that says the Part 35 use? Does that have to be on the label or is that information that has to be otherwise provided?

MR. CAMPER: It goes on to say, "Furthermore, the label or the leaflet or brochure, that accompanies the radioactive drug must contain a statement that the U.S. Nuclear Regulatory Commission has approved distribution of the byproduct material to persons licensed to use byproduct material pursuant to 35.100, 200, or 300, as appropriate, and to persons who hold an equivalent license issued by an agreement state. The Commission's labeling requirements are independent of requirements of the U.S. Food and Drug Administration. One label is acceptable to NRC provided that it contains all of the information which NRC requires."

MR. SWANSON: And that's my objection. I don't know why that has to appear on the labeling, because, again, you have specifically stated in the license of the

distributors that they only can distribute to certain licensees. You've specifically stated in the Part 35 that they can only receive them -- I don't know why that has to appear on the label.

Also, we do not routinely --

MR. CAMPER: It appears on the label, the leaflet, or the brochure that accompany.

MR. SWANSON: We don't routinely distribute leaflets or brochures with unit doses of radiopharmaceuticals. And if you require that, that's an additional expense that must be accrued by the centralized nuclear pharmacy and eventually the public. I don't know why that's required.

DR. GLENN: Because that's -- the reason it's required is because that's the licensing basis. That's how we license medical use licensees is on the basis of 35.100, 35.200, 35.300. So this identifies the class of licensees that can receive that material.

CHAIRMAN SIEGEL: So, if I understand what you're saying, John, and what Dennis is saying, this label that he gave us for Technetium Cardiolite, the sample that's the top one there, would not be in compliance with that labeling requirement if there was not also a "package insert" distributed with the drug?

DR. GLENN: A statement is distributed with it

that said that is for uses under 35.200, right.

CHAIRMAN SIEGEL: All right. So that clearly is-- Now, and that is a new labeling requirement or that's something that's been there all along?

DR. GLENN: No, that's been in Part 32 all along. Now, I guess the difference is that in the past when you were tied to the materials that were coming from a manufacturer, the manufacturer had in fact been the distributor who had that requirement. Now we're allowing the pharmacies to be the original preparers of the material and so they are the ones who would have to make that call.

CHAIRMAN SIEGEL: Florence.

MS. KALTOVICH: My question is about adding that particular language to a package insert. Are you saying that if that sentence or so were put into a package insert which is reviewed by the FDA for each of its products, that that would comply with this regulation? But then you would say the package insert itself would have to be handed to the patient?

DR. GLENN: We're not saying anything about the package insert being handed to the patient. This is information that's necessary for our licensees, not for the patient.

MS. KALTOVICH: Not for the patient. So, within the package insert would suffice but --

CHAIRMAN SIEGEL: I'm not sure it would.

DR. GLENN: Well, actually, that's how it is done today, is that it's in the FDA approved package insert. That's how it's handled today.

CHAIRMAN SIEGEL: Which is not distributed with every single dose of the drug. I guarantee it.

MR. SWANSON: There is also a difference between the FDA and centralized nuclear pharmacies.

DR. NELP: We'll have a package insert binder that's available to people if they want to look up some details. But it certainly is a source of information but it doesn't come with a labeled dose for a patient.

CHAIRMAN SIEGEL: I'll recognize the member of the public who needs to introduce herself.

MS. SEIFERT: I'm Kathy Seifert. I am the Director of Regulatory Affairs for Syncor International and can represent about half the nuclear pharmacies in the country.

In our labeling in this portion that you're referring to, in the leaflet, what do we call this, leaflet or brochure, my question is, would a packing list that accompanies the package of the radiopharmaceutical be considered to be a leaflet or a brochure?

DR. GLENN: That would be perfectly acceptable.

MS. SEIFERT: Because it's easy to put that one

as part of the computer generated leaflet although as far as being something you give to the patient, it really isn't that.

Also, if that's all right, I mean, that's what we do already.

CHAIRMAN SIEGEL: Patients don't get this labeling information anyway.

DR. GLENN: That is perfect.

MS. SEIFERT: Okay.

DR. GLENN: That's perfectly in accord with what the intent of that regulation is. Is that the medical use licensee receives the information as to what use in Part 35 this material has been prepared for.

MR. GRAHAM: But if I understand this, if you ordered ten doses of the drug to be legally labeled, each of those ten doses would have to have that attached package insert? It's equivalent inside a hospital setting that every unit dose drug theoretically would have to be labeled with the package insert coming off the manufacturer?

DR. GLENN: To be legally labeled. See, I don't think that's what it says --

MR. GRAHAM: I'm talking about a quantity.

DR. NELP: I don't think --

DR. GLENN: Could we read the language again?

DR. NELP: We don't have the final regs and you

have to talk to Larry, and Larry has to get out his pen. I'm not sure we know what we're talking about.

CHAIRMAN SIEGEL: Let's hear it again.

MR. CAMPER: Well, I can read it for you.

DR. GLENN: Let's hear it again.

MR. CAMPER: "Furthermore, the label or the leaflet or brochure, that accompanies the radioactive drug must contain a statement that the U.S. Nuclear Regulatory Commission has approved distribution of the byproduct material to persons licensed to use byproduct materials pursuant to 35.100, 200, and 300, as appropriate, and to persons who hold an equivalent license issued by an agreement state. The Commission's labeling requirements are independent of requirements of the U.S. Food and Drug Administration. One label is acceptable to NRC provided that it contains all of the information which NRC requires."

DR. GLENN: I don't that implies every container. It applies every transfer includes that statement.

MR. GRAHAM: Well, but to assure that as a commercial laboratory, I'm complying with the letter of the law, I can't afford the risk that somebody in my packaging area is going to put five of those doses together and toss that package insert in. So, I'm probably going to have to

attach it to each and every dose. It's just redundant information that we've got floating around.

MR. SWANSON: You would also have to have a different label if you distributed I 131 for therapy than you would for Technetium 99 MDP for diagnosis. So you're going to have to keep track --

DR. GLENN: That in fact is our intent. It is our intent that if it's for therapy uses, that it be labeled as such. If it's for diagnostic uses, it be labeled as such. That is in fact our intention.

MR. SWANSON: No, your intent is not that it's labeled for therapeutic uses and diagnostic uses. Your intent is that the label says that it's approved for use under 35.300 or 35.200. The question I'm asking is, what is the purpose of that requirement? What does it add to the safety of the dose? What does it add to the safety of the public?

DR. GLENN: Well, let me go back. I think, in fact, that is exactly what that labeling requires. It requires you to say whether it's for therapeutic -- I mean, for a therapeutic use or whether it's for a diagnostic imaging use. That is what 35.200 and 35.300 mean within the context of Part 35. It's the structure of our regulations. I guess we could revisit that at another time, whether we should have 35.100, 200, 300, but that in

fact is the way regulate.

MR. SWANSON: I'm not arguing with 35.100, 200, and 300. I'm arguing with the point that you're requiring that statement on the product labeling. It's a very different argument.

DR. GLENN: And we're saying it can have a serious consequences if a material that is for use under 35.300 were transferred and used for a 35.200 purpose.

DR. NELP: Could you translate that in to English, please?

CHAIRMAN SIEGEL: Well, that's not true, John.

DR. NELP: And not numbers.

CHAIRMAN SIEGEL: If a 5 millicurie capsule of I 131 that was intended for treatment of hyperthyroidism was used instead for imaging, for imaging of a thyroid--

DR. NELP: One is therapy and one is diagnosis.

DR. GLENN: Correct.

CHAIRMAN SIEGEL: It wouldn't make any difference. Admittedly, if a doses of Strontium 89 that was intended for therapy was tried to be used for cardiac imaging, that would be unsuccessful and would be inappropriate. But --

MR. SWANSON: If you're really concerned about patient safety, then have the product labeled I 131, sodium iodide for therapy, Technetium 99 MDP for diagnosis. Don't

have the label say approved for use for 35.300. That -- unless you know specifically what 35.300 is, that's not adding anything to the safety of the product. That's just complying with your regulatory issues.

DR. GLENN: Again, though, I think it is information that we think is important in order for the medical use licensee to comply with our regulation. Now, let's take a different example. A medical use licensee is authorized to receive for 35.200 but is not authorized --

DR. NELP: Could you instead of talking in numbers, could you say what the differences are?

DR. GLENN: We have a licensee -- But --

DR. NELP: 35.200 versus 35 --

DR. GLENN: 200 is diagnostic imaging. So, we have a licensee who is authorized for --

DR. NELP: Diagnosis.

DR. GLENN: -- diagnostic imaging. But they're not authorized for radiopharmaceutical therapy. If the drug is not labeled as to what its appropriate use is and Strontium 89 is sent to the diagnostic imaging licensee, and they -- due to the fact that there is miscommunication and the medical use licensee does not pick up this is for a type of activity for which I am not authorized, there could be serious consequences.

MR. SWANSON: Let me ask you this question.

DR. NELP: How did he get it in the first place?

MR. SWANSON: Yes. Do you require the --

DR. NELP: He did not prescribe it himself so how did he get it? I mean, he would not prescribe Strontium 89.

DR. GLENN: Well, we have errors occurring all the time.

DR. NELP: So this is an error at -- the pharmacy's error?

DR. GLENN: Or, you could have a medical use licensee who requests something that they're not authorized for.

MR. SWANSON: Do you require the Part 32 licensees to verify that the materials that they ship --

CHAIRMAN SIEGEL: Yes.

MR. SWANSON: -- to an end user are appropriately licensed to receive that material?

CHAIRMAN SIEGEL: Yes. They do, right?

MR. SWANSON: Right.

CHAIRMAN SIEGEL: That's why the Syncor asks for a copy of your license to know what you're licensed to receive.

MR. SWANSON: And you require that the end users under their license conditions, have requirements as

to what they can use?

CHAIRMAN SIEGEL: Yes.

DR. GLENN: But you --

MR. SWANSON: So why are you requiring this to appear on the label?

DR. GLENN: Well, the way our licenses are written, the way you know what they are authorized to do, is by this nomenclature of 35.100 which is update and dilution, 35.200 which is diagnostic imaging, and 35.300 which is radiopharmaceutical therapy. It is in fact the basis of our regulations and the way we write licenses.

MR. CAMPER: Well, it's also, two -- there are two different things going on at the same time here. One hand you have information which must appear upon a syringe. This is your radiopharmaceutical, its abbreviation, the clinical procedure, or the patient's name. That's the end of it, if you will. At the same time, the language that you're referring to, though, Dennis, focuses more upon the distribution of the product by a Part 32 licensee to a Part 35 licensee.

So, two different phenomenon going on all ending up, of course, in the same place. But the reason this language is in here, and arguably I understand your point about being overbearing, but the important thing is it is about distribution to medical licensees authorized

under the 35.100, 200, and 300 scheme.

MR. GRAHAM: And I think Dennis' fundamental point was, is it going to improve the distribution process? Is it going to reduce the error? And so the fundamental question that he raised originally was, is it information that reduces that error rate? And by adding the restriction that you have 35.100, 35.200, you've added more stuff you have to sort out and work around to get to the more relevant information given that you are indeed licensed under Section 35 to have received it in the first place. It's noise.

So in an age of information, you're always asking is the value of the new information being required greater than the turbulence that it may create? And I'm hearing a lot of concern from a pharmacists that -- eliminate the thing.

MR. CAMPER: And to eliminate it, then, that assumes that the limited specific licensee, this is a licensee of 35.100, 200, 300, which is diagnostic and therapy, understands and confidently assumes that the product has been distributed in accordance with a Part 32 distribution license.

MR. GRAHAM: The regulations that govern their license set up the systems to assure that. So, from the perspective of the labeling, this becomes redundant.

CHAIRMAN SIEGEL: Kathy?

MR. GRAHAM: But I think it's moot.

CHAIRMAN SIEGEL: It may be moot.

MR. CAMPER: Well, it's moot in the sense that this rule has ben affirmed. It is not moot in the sense that it could not go undergo further consideration. Or perhaps even recommended changes by the staff.

MR. GRAHAM: One brief procedural question. Having received an impressive amount of, poundage of paper for today, can we receive a set of those final regulations that you're reading from? I mean, we have everything but that.

DR. GLENN: Let me explain why you do not in fact have a final set of the regulations. And that, because the staff does not currently have the final set. That will be being generated in the next few days and we certainly will get that out to the committee.

But we're coming to the committee in real time. I mean, things are happening and we do not have, in fact, ah hard copy of the final rule as it will be published in the Federal Register.

MR. GRAHAM: But even a marked up draft would have helped.

CHAIRMAN SIEGEL: Well, we've got the next best thing. We've got Larry here to help us.

DR. GLENN: Larry will continue to read.

CHAIRMAN SIEGEL: Kathy.

MS. SEIFERT: I'd like to make one more point. As I said before, it's not hard for us to comply with this licensing or this requirement for labeling if we can put it on a packing slip. And in that regard, we can comply with it. I agree 100 percent with Dennis' point earlier that the more you put on the label, the more noise there is, the more chance there is for misadministrations. And we track misadministrations very closely for misadministrations that occur based on something that happened in the pharmacy as well as what happened in the nuclear medicine department if we are aware of it. And probably the most common cause of misadministration is looking at the label incorrectly. And as Dennis said earlier, the more you have on the label, the more difficult it is to see exactly what it is there. Even though you put in all the human factors that may make it easier to read, it's very difficult. Labeling is very important in pharmacy and I agree 100 percent with the fact that the more you have on the label, the more difficult it is to read.

CHAIRMAN SIEGEL: Bob had a comment.

MR. QUILLIN: John, do you have misadministration data which demonstrates a need for this type of labeling in this particular issue?

DR. GLENN: Certainly I think we do on the point of view of the syringe having sufficient information on it to be able to identify what it is. I mean, people picking up the wrong syringe and not checking the information, having -- not having enough information on the syringe. That kind of thing has caused --

CHAIRMAN SIEGEL: Of course, maybe they couldn't read it because the letters were so small to get in all that other stuff.

DR. GLENN: Again, there's this business about the 35 -- Part 35 listed use is something that's been in there for ages and we certainly did not consider that we were changing anything in requiring that this a part of the information that goes with the distributed material.

And again, it's very clear that it doesn't have to be on the label on the container. It just has to be information that is transferred with the shipment. It's for regulatory purposes.

MR. CAMPER: Just a point of clarification, too. In looking at the language in the existing 32.72 or-- there is a relaxation going on in this new verbiage. Perhaps not enough in the minds of some but there is a relaxation going on in the sense that the current verbiage in 32.72.4.I says the following. And, by the way, you do have a copy of Part 35 in the front of your books which

will help you. I don't think you have Part 32 but we can get it for you if you like.

MR. SWANSON: We do now.

MR. CAMPER: It says currently, "The label affixed to each package of the radiopharmaceutical contains information on" the same things. And then goes on to make the statement that it is authorized for distribution to Part 35 licensees. So, this language, believe it or not, was a relaxation of the current requirement. And I don't know what you've been doing functionally out there with the current requirements or how much of a burden it's posed, but this was an attempt to relax that somewhat.

MR. SWANSON: To my knowledge, this information is not being included on materials currently being shipped to us from centralized nuclear pharmacies. Never is.

CHAIRMAN SIEGEL: All right. Well, we got diverted here. Probably appropriately.

Let me summarize what I think we've heard. I think we've heard that less may be more. And that it's appropriate for you at least to consider along the line, whether everything that you've got on the label is absolutely required for a patient's safety as opposed to satisfy some legal requirement so that you feel you've communicated appropriately with your suppliers and your medical licensees, and I think otherwise that captures -- I

think that pretty much captures the main points.

I think given that this is essentially a done deal, it's unlikely that this is going to change but it's worth reexamining at some point down the road.

MR. CAMPER: Just a comment on the done deal part of it. I agree that it is a done deal for now. But I would reemphasize what I said a few moments ago. And that, comments on the guidance document, for example, we're in the stage with the guidance documents were we're asking our regents to take a look at them, provide comments and analysis. We certainly can revisit the guidance document. That's easy to do.

With regards to the rule language itself, we do have a major revision to Part 35 planned and there's absolutely no reason why we couldn't look at these kinds of issues and problems as part of that process. Or, for that matter, if they were serious enough and could be handled simply and quickly enough, we might consider some other way of dealing with it.

So it is a done deal, I agree, but it's not a done deal with a capital D.

MS. BROWN: I'm wondering about the timing of the deal. Why the vote needed to be taken before this committee met to look at the material?

DR. GLENN: The timing, this is not a rushed

rule. You -- Maybe we're kind of behind the ball on this one. But, I will tell you why the timing was extremely important in this case. The interim final rule expires December 31st, 1994 at midnight. If we don't have this rule ready to go, then we have to have another rule making to do something in order to keep the current rule going or else we drop back to a very restrictive literally by the package insert kind of regulation.

MR. CAMPER: Also, I would add to that. In addition, that we have reviewed this rule at great length with this committee. In fact, we spent probably on the order of half a day to three-quarters of a day going through the rule language line item by line item. And we have met with numerous representatives of the radiopharmaceutical industry and various workshops around the country, and generally got very positive feedback on it. Some of these labeling issues, for example, have not come up until now.

MR. SWANSON: Well, a little bit about my confusion on this. The Part 35 rule is basically a rule that applies to the end user. Where my problems are not with the Part 35 rule but with the licensing guideline for the centralized nuclear pharmacy that appear in our packet which is a Part 32 problem, not a Part 35 problem.

CHAIRMAN SIEGEL: Just a quick clarification.

In terms of the syringe labeling that says clinical procedure, or patient, or a human subject's name, what -- do you have any internal guidance as to what you define as an acceptable description of a clinical procedure? Could it simply say diagnostic imaging? Is that a clinical procedure?

DR. GLENN: I don't think we have a regulatory definition. My gut instinct that we meant something a little more than that. But we don't have a regulatory definition.

CHAIRMAN SIEGEL: I guess that is intended to address the question that asked if I chose to divert that does to some other indication, does that make it easier for me to do that. I, frankly, am not sure I see the problem that Buzz and Dennis raised which is that as a physician, I don't have any problems diverting a dose that says it was for a bone scan to myocardial infarc imaging if that's what I want to use it for.

MR. SWANSON: I think my only problem there is, and I think you identified it, it could be easily corrected by just simply putting or radiopharmaceutical there. If you put the name of the radiopharmaceutical, I think that that addresses the identity problem. It also permits the flexibility to do with that dose what you want to do.

CHAIRMAN SIEGEL: You can speak to us, John.

DR. FLYNN: Well, John is mentioning that we have defined clinical procedures manual in Part 35. And I'm trying to think whether that provides any guidance or not.

MR. TELFORD: John Telford, research. The point I was trying to make is that in 35.2 there is a definition of diagnostic clinical procedures manual. And in that manual are all of the clinical procedures, exactly the point, which have to have been approved by the physician authorized user. So that if in your institution, in your diagnostic clinical procedures manual you have a list of all the clinical procedures that you do. So you have defined for yourself what the clinical procedures are.

CHAIRMAN SIEGEL: I understand that and that's -- Right. But that's why adding the third "or" also solves the problem. Because my clinical procedure manual says that in order to do a renal scan, you take a syringe full of Technetium DTPA, therefore the syringe full of Technetium DTPA doesn't have to say renal scan on it. It could simply say Technetium DPTA. Then, if I also choose to use that syringe instead for a brain death study, I got the option. It's not even momentarily mislabeled if you restrict it to the drug name.

I think I sort of agree with Dennis although I also sense that this is not a budget buster in terms of a

major earth shattering problem that leads to clinical disasters.

MR. SWANSON: I think I'm -- a major concern I have is it goes back to a misadministration rule. If the syringe is labeled with a patient's name or a clinical procedure and you use it for a different patient or a different clinical procedure, are we going to get hanged on that? And --

MR. CAMPER: Well, certainly not in the diagnostic arena because of the threshold.

MR. SWANSON: Wrong. In misadministration the diagnostic area is defined as wrong patient, wrong procedure, wrong drug.

CHAIRMAN SIEGEL: With a meeting a dose threshold.

DR. GLENN: Only if it exceeds 5 and 50.

CHAIRMAN SIEGEL: That's correct.

DR. WAGNER: Yes, but -- that still does cause you a problem in terms of the procedures you have to go through. To file a report, you have to got through various procedures to make sure things were available. That you did have a misadministration, it didn't exceed the level. But you still have to go through a lot of procedures.

That may actually be the fact that I'm in an agreement state and the agreement state has those rules in

there.

MR. CAMPER: I was going to say, we have no such rule. Ours is strictly at a thresholder's reporting requirement. There is nothing -- For diagnostic misadministrations, there's nothing other than that reporting threshold at 5 and 50.

DR. WAGNER: We don't have to report it but we have to investigate it.

MR. SWANSON: All I'm really saying is a simple "or radiopharmaceutical" is going to solve your whole problem here. If you just go back to the Part 35.

DR. GLENN: And I don't remember why it does not exactly parallel Part 35. It seems like it should have.

John, I guess just one question. Clarify with you, I do not think we got any comments on this particular issue about the clinical procedure and the --

MR. TELFORD: I don't believe we did, either, because it is in basically current language.

MR. SWANSON: It's stated correctly in Part 35. Again let me emphasize the point. It's state incorrectly in the regulatory guide. It is stated correctly in Part 35.

MR. TELFORD: Your comments are -- will be well received on the regulatory guide. There is time to do

something about the guide.

CHAIRMAN SIEGEL: Is anyone on the committee who feels we shouldn't make the recommendation that this issue be looked at and that adding that third "or" as either in rule language or at least in the regulatory guide at that level be addressed somehow?

MR. CAMPER: Dennis, would you, for the record, you have it right there in front of you, don't you, still where you're reading from? Would you cite the page and the--so we can focus on it carefully? If you don't, we can carry on.

MR. SWANSON: It's page 46.

DR. GLENN: Page 46. And I think we will also look at the other information that we said there and make it -- and try to clarify the various means by which you can meet this regulation. That a packing slip with the statement on it, all of those would be acceptable ways of meeting this requirement.

CHAIRMAN SIEGEL: Now, the only other -- Sounds to me like the only other major issue you raised with respect to the regulatory guide was whether or not the Molybdenum labeling needed to be in the label. And I guess the collision there is whether or not the Part 35 licensee will be able to know they're in compliance with their requirement if something they get from the commercial

pharmacy doesn't tell them that it's okay and Molybdenum. And Dennis' answer was the expiration date addresses the problem if the Part 32 licensee is following the rules.

DR. GLENN: I guess one issue that I know did come up in the discussion of this rule making is that in fact expiration times and expiration dates may be one of the things that is changed by the pharmacy. So, I guess we have some concern on that.

CHAIRMAN SIEGEL: But they won't be changed to result in a violation of the Molybdenum requirement.

DR. GLENN: Maybe that's what the guide should say is that the pharmacy can have procedures to assure that if it's used within the stated time that's put on the label, or whatever happens, that it would not exceed.

MR. SWANSON: Actually, the guide does say that. That the centralized nuclear pharmacy is required to put an expiration date and time based upon fulfilling the Molybdenum 99 breakthrough. If that expiration and date, and time, is on the label, there ought not to be a requirement that they actually put the Molybdenum concentration on that label.

CHAIRMAN SIEGEL: In current Part 35, 35.204A reads, "A licensee may not administer to humans a radiopharmaceutical containing more than 0.015 microcurie of Molybdenum 99 per millicurie or Technetium 99M." And

then this part B talks about if you do -- if you aliquot your own generator, you have to measure it.

I would interpret A to mean, Dennis, that if you don't have the information, you don't know and consequently it really does need to be in the information provided to the Part 35 licensee. Because this is putting a responsibility-- you could argue that the way 35 is worded is incorrect. And that may be one issue. But currently the Part 35 licensee has to know the Molybdenum concentration in order to know that they are in compliance with 35.204A. And admittedly, it could be done by an understanding of the underlying procedures but having it in the label is more explicit.

MR. SWANSON: Well, I think a better way to address the problem, actually, would be to require in the licensing guide to have the centralized nuclear pharmacies put on their label a Molybdenum 99 expiration date/time rather than the actual concentration of Molybdenum 99 breakthrough in the generator aliquot which would then require the end user to perform a calculation that would also increase substantially the amount of information on the label. So, simply on the label it said, Molybdenum 99 expiration, time.

CHAIRMAN SIEGEL: You actually wouldn't want to have that. I mean, you wouldn't want it to be a different

number than the expiration time for other reasons.

MR. SWANSON: You could have the shortest of the two.

CHAIRMAN SIEGEL: Correct.

Kathy.

MS. SEIFERT: Kathy Seifert again.

I agree with you, Barry, that the expiration time of the drug should include the expiration of the Molybdenum 99 and typically the drug expires before the Moly ever gets to any point that it would be in effect. So, to add that additional labeling requirement would be overkill.

CHAIRMAN SIEGEL: At any rate, there's some concern about the way you're addressing that one as well, although --

DR. GLENN: But that is within the guide and we can certainly work on that.

CHAIRMAN SIEGEL: Continue. So we had our little five minute diversion for questions there.

MR. SWANSON: It was either now or later, okay?

CHAIRMAN SIEGEL: No argument.

DR. GLENN: No, I think -- Hopefully that was the major discussion we'll have.

In terms of who can be an authorized nuclear pharmacist, the regulation, both Part 35 and Part 32, state

that an "an authorized nuclear pharmacist is a person who is either a board certified nuclear pharmacist, is named as an authorized nuclear pharmacist on an NRC or agreement state licensee authorizing nuclear pharmacy, or is named as an authorized nuclear pharmacist on a permit of a license of broad scope."

So, anyone who had bene previously approved can be used as an authorized nuclear pharmacist, anyone who is board certified can be. And then we have criteria for people who aren't any of those things. How you can get yourself listed as an authorized nuclear pharmacists on an NRC license if you're not previously listed and if you're not board certified. The first way is obviously the current certification or a 700 hour structured program that consists of both didactic and supervised experience, and a signed preceptor statement of competency by an already approved authorized nuclear pharmacist.

Some of the comments that we received based on the proposal rule was, would we grandfather, particularly those people who have been working on broad scope licenses for years and years and have never been listed on a licence, obviously have the training and experience. What we said here is, you don't have to go back and find the person who taught them 20 or 30 years ago to sign a preceptor statement. We will recognize their existing

training and experience without a preceptor statement.

DR. SIEGEL: So Bill Biner does not have to get a preceptor statement.

DR. GLENN: That's right. Who would he ask?

DR. SIEGEL: As long as we're talking about authorized nuclear pharmacists, we probably ought to just get on the table for at least momentary discussion the issue of character, since that is a point that we've addressed in previous discussions at the AECMUI and certainly Carol's letter that you provided to us raises indignant concerns about the issue of character.

Just for the sake of getting it on the table, John, can you explain the rationale for having that in the preamble and how the NRC sees it might use that information that you've built into the preamble.

DR. GLENN: Within the Atomic Energy Act itself, it does provide that one of the bases for licensing is character. The Commission can take into account a person's character in determining whether to issue or not issue permission to use byproduct material.

We have also in the last -- I think it was '92 -- within part 30, 40, 70 and 50, we published a Deliberate Misconduct Rule. So we have now in our regulations codified that when an individual is responsible for providing false information or deliberately causing

violations of the NRC's requirements that we can take actions against individuals as well as actions against licensees. That is, in fact, in effect today for all licensees, not just medical, not just pharmacist, not just doctors, but anyone who is licensed by the NRC who provides the Commission with false information or by deliberate act causes a violation of our regulations, that person can be removed from licenced activities. That person can be banned from licensed activities. That's really all that the preamble is making clear.

DR. SIEGEL: Have there been applications of the character provision in micro licensing activities?

DR. GLENN: Yes. There are individuals, doctors and technologists, who have been banned from NRC license activities.

DR. PAPERIELLO: I might add. When it is done, it is done by order, it's done by due process of law, hearing rights. It's done for a period of time and it's not a very common sort of thing. It's not arbitrary that you're somewhere on a list somewhere that nobody knows about. It's a well-publicized thing.

DR. GLENN: We're very sensitive to the idea of blacklisting and that kind of thing. Whenever this action is taken, it's done in public with full rights.

DR. SIEGEL: I'm personally not uncomfortable

with it. I just wanted to get it on the table here so that you all could say what you just said since it has been a point that's been raised publicly.

Continue.

DR. GLENN: One of the other major changes is that the current Part 35 is absolutely silent about human subjects used in research. The fact is, you can say Part 35 does not even reach to human subjects because it defines medical use and that's diagnosis and therapy. There is no mention of human subjects.

The new Part 35 remedies that. In multiple locations the regulation has had to be changed to put in parallel patient and human subject so that everywhere where there's a requirement for measuring dosages to protect patients, there's a requirement to measure dosages to protect human subjects. Where we have notification requirements for misadministered patients, we now have notification, we stuck in human subjects so that the human subject has the same rights as the patient. So multiple places within the regulations that change has been made and our definition of medical use has been expanded to include.

There are two cases in terms of how we're going to regulate human subjects in medical research. One is that we think the majority of cases, it's going to be research that is either conducted, funded, supported or

regulated by another federal agency who has implemented the federal policy for the protection of human subjects. Which case, all we require is that the research you do in fact meet those conditions.

In the inspection process we will look to see that in fact two aspects of that have been implemented. That is, the use of Institutional Review Boards and the informed consent. But we're not going any further. We're not approving the Institutional Review Boards under those circumstances. We're not reviewing informed consent. We are saying that the appropriate federal agency is responsible for seeing that that policy is carried out.

DR. SIEGEL: Let me just seek a point of clarification on this. There is a substantial amount of research done with byproduct material that is not funded or supported or directly regulated by another federal agency, but it is conducted at institutions that have filed general assurances with the Department of Health and Human Services that all of the research conducted within their walls, whether DHSS-supported or not, will be conducted in accordance with the federal policies on protection of human subjects.

One concern that I have is that an inspector might go to an institution, see a research project, look on the Institutional Review Board form where it shows what the

source of funding is, see that there is no federal funding and then might get caught into thinking that this is research that's not regulated by another federal agency.

Are you comfortable that you all have addressed that in your thinking and understand that well, that that's not going to be a problem, because there's a lot of research that you won't be able to directly link the research to another federal agency that already has this in its rules, there's an indirect link.

DR. GLENN: But there is actually a document that would say that they're --

DR. SIEGEL: Unequivocally.

DR. GLENN: I think maybe we need to beef up our guidance to make sure that that's clear, that where that agreement is, in fact, clear, that that brings them under the federal policy. I have no doubt in my mind that it does, but I guess we do need to make clear how you can determine that and what to look for.

DR. SIEGEL: I'd be curious to know if anyone else on the committee is aware of any institutions who file their DHSS assurance and say, And by the way, we're going to exclude things that aren't funded by the DHSS and we're not going to bother doing this. I think the standard of care is to, once you have a DHSS assurance in place, that you make it an umbrella that covers all the research

conducted within your walls.

Does everybody agree that that's the way our institutions operate? Okay. So I agree. I think this is not going to be much of a problem, but you inspectors need to know that, too.

DR. GLENN: Now, we don't know that there's not something else out there that, in fact, doesn't fall under the federal umbrella through one of these mechanisms and we have provided that if such a case is identified, that there must be a specific application to the Nuclear Regulatory Commission to conduct that research. My guess is if we get such applications, we'll probably be coming to this committee looking for advice.

What we have said is that certainly key elements of any approval we grant would be an Institutional Review Board and informed consent.

DR. SIEGEL: I'm going to ask you an even more difficult question. Unless someone came to you and said, I want to do research and I'm not conducted, funded, supported or regulated by another federal agency, would you have any way of knowing that the activity was research? Construct. An individual practitioner who has an license for an office practice is doing something that is not defined in a package label as an approved indication and gets in their mind, I've never heard of this before. This

must be research. And God, it wasn't covered by this.

Is that too far fetched to conceive of?

DR. GLENN: I think that's reaching a little too far because I think that is diagnosis and therapy for a patient. The more likely thing to come up is somebody says, Well, I want to do a screening and so I'm going to test every third person who comes in here for something, whether I think they have a problem or not. Those are the kinds of things, I think, that might trigger our interest. Who approved this? Is there a federal agency involved?

DR. SIEGEL: Again, I don't think this is going to come up very often, but I just would be curious to see how you've thought through these particular kinds of problems.

DR. GLENN: But I don't think this is the back door way for us to get back into off label uses of material. That falls under the normal regulatory scheme of fDA.

DR. SIEGEL: And I would just add to what I pointed out about that individual practitioner. Again, the standard of care is that, irrespective of whether you have DHSS assurance or not, the standard of care of protection of human rights is that you follow the Helsinki Doctrines and you have your research peer reviewed and you obtain an informed consent. So you've just codified it in the case

of an NRC licensee by saying that they have to let you know that they're doing that. That's okay.

DR. GLENN: I mentioned briefly when I started off this morning that we did stick a few things into the regulation to make life easier really for both pharmacies and for medical use licensees.

An amendment is not required to add users to the license if either the authorized user or the authorized nuclear pharmacist is certified by one of the organizations listed in Sub-part J nor if the licensee has a copy of a document that shows the individual is identified as an authorized user, an authorized nuclear pharmacist on an NRC or agreement state license nor if you have a document that shows that the individual is identified as an authorized user, an authorized nuclear pharmacist on a permit issued by an NRC or agreement state licensee of broad scope.

Now, the cost for that is that you do have to tell us who these people are and that there is a notification requirement. But you don't have to delay the use of the individual and you don't have to pay any fees or wait for any approval. You just need to let us know so that in our own documentation we know who the authorized people are at your institution.

I mentioned before that we have explicitly stated those parts of the regulation that no longer apply

to broad scope licensees, particularly Type A broad scope licensees. No amendment is needed to name an authorized user an authorized nuclear pharmacist. That's above and beyond what I was saying before. In fact, the broad scope licensee can apply the Sub-part J criteria and approve users.

No amendment is required to add or change areas of use of specified addresses. The current Part 35 says that if you make any changes in your facility, you have to get an amendment first. That, in fact, is not the standard of practice with broad scope licensees. This simply gives that a regulatory basis. Unfortunately, we've been running broad scope licensees for the last five years by exemption from the regulation rather than by the regulation. This fixes that problem. And, in addition, the broad scope licensees, since they can approve users, don't need to tell us about the users when they change users. So if a broad scope licensee adds a physician or a pharmacist, they don't have to notify us of that.

DR. WAGNER: John, on the pervious page then why is the notification required there because if the person meets these criteria, are you going to do some policing action to make sure that we didn't make a mistake or something?

DR. GLENN: It's not policing action. There is

a current requirement that you tell us when somebody leaves. This is so that we know that you still have qualified persons for the activities that are authorized by the license.

DR. WAGNER: We checked that. We just did that. We did that in those three things above there. We already know that because they meet these criteria.

DR. GLENN: No, no.

DR. WAGNER: Why do we have to notify you?

DR. GLENN: Let's take a limited scope license for medical use. We may have authorized radio pharmaceutical therapy based on a person who is trained, has received the training necessary for that. We currently require a notification if one of those people leaves. So if you send in a notification that person leaves and you haven't sent in a notification that someone has replaced them, the question is whether you are still qualified for the activities that you're authorized for. That's the purpose of the notification.

During inspection, that will be reviewed. The notifications will be reviewed to determine that you're in compliance. It's not going to be a big deal because it should be relatively minor to determine that those conditions have been met. But it will be reviewed.

DR. WAGNER: I presume those notifications will

have to include the qualifications of the individual and everything else. A package will have to be sent to you.

DR. GLENN: I think what it requires is that you send a copy of the basis document that you used. In other words, copy of certification, copy of the license.

DR. WAGNER: I still don't understand it then. I mean if it's that simple, I don't understand the need for the notification. If that's simple, we can do that. That's simple. But what are you doing over and beyond that? Why do we have to notify you? I don't understand what the need is for you to know when we do this as long as we make sure that this person is qualified. I don't see the point. Is that just for your records? Are we just pushing paper or what?

DR. GLENN: No, no. The basis of a license is that you have people who are qualified. You have to have facilities. You have to have equipment. You have to have trained personnel. We need to know at any given time that, in fact, you still meet those requirements. If you don't, then the license authorization needs to be changed.

DR. WAGNER: I understand your point and I agree with that, but it seems to me that we've done that.

DR. GLENN: What you're telling us is that everybody will always comply with their license and there is no need for us to have any verification process. I wish

that were true. But experience has been that we do need to monitor what goes on.

MR. CAMPER: In writing this rule, too, there was some discussion amongst the team and so forth that this is a change for limited specific licensees. They have not heretofore had this authority whereas broad scope licensees have.

DR. WAGNER: I understand.

MR. CAMPER: Therefore, again may it's overkill in the minds of some, but we felt that it was appropriate to monitor how this goes for a while and see how they do. In time, we may have a body of evidence that shows that this has not been a problem for limited specific licensees to exercise this new naming authority and things may change, but we wanted to see how it's being done.

We wanted to give them, on the one hand, flexibility to name users and to avoid an amendment cost when someone is clearly qualified by virtue of board certification and the like. But, on the other hand, we felt a need to monitor this, at least for some period of time.

DR. GLENN: Other changes. The misadministration definitions have been modified to include human subjects. There is now a specific requirement for measurement of beta alpha or beta emitting radio nuclides.

It's not applicable to unit doses received from a 3272 distributor. So a medical use licensee who receives unit doses previously calibrated, either by a manufacturer or a pharmacy, does not have to have a method of assaying dose.

Also, we permit a combination of measurements and calculations in order to determine the dose. So we are not implying that you have to have a single instrument which you can drop the total dose into and get a single assay. You can take an aliquot. You can use liquid scintillation counting for that aliquot and then, based on specific activity, calculate the dose.

DR. SIEGEL: David.

DR. WOODBURG: Do you have standards for measuring the alpha emitters? NIST didn't have standards. What standards are you going to use?

DR. GLENN: Well, no, we do not have standards and, in fact, people who are going to do this, rather than giving them a standard, we're saying, You have to describe how you're going to do your measurements.

The thing is, with liquid scintillation counting, if that's the method, the physics is rather straightforward and I think anyone can do it. I guess we had a recent go round on stromtium 89 where there wasn't a standard, but it turned out that both AMERSHAM and NIST used the same method, which was liquid scintillation

counting, and had very comparable results and so it really didn't appear to be a problem.

DR. WOODBURG: I guess the problem is because if you have different measurements or different calculations from one institution to another, then you don't know what is used as a standard and what you're measuring is the right thing.

DR. GLENN: Maybe if the other committee members want to address that, but we felt that there were techniques out there that we could, in fact, review based on licensee submissions.

DR. SIEGEL: Maybe it might be worthwhile to have Larry read us the specific language that relates to alpha in particular.

While he looks, let me divert us for a second and ask Judy and Dan whether they perceive any problem at the interface between clinical radiation oncology and the new approaches in radiation oncology where there's research being conducted while patient care is actually being delivered in terms of misadministration reporting and how any of this stuff might be changing here.

An example would be the first 100 patients who received hi dose rate brachytherapy were actually getting clinical care but in a research mode. The research was, we didn't know if that was going to work but, by the same

token, the intent of the research and, hence, the reason for bearing the risk was that there was expected benefit.

Do you all see a problem with the fact that misadministration reporting now extends into the research environment? I don't, but I want to see if you do.

DR. STITT: I think it always has. That would be my attitude, and maybe it's easier to contemplate it in therapy than in diagnosis because in diagnosis, I assume human subjects was put in because some of these are not patients. That is, they're folks that are having an isotope given but not because they need a steady donor treatment.

DR. GLENN: By human subjects, we're mainly, I think, referring to volunteers.

DR. SIEGEL: To volunteers.

DR. STITT: Right. Okay. Because you sure don't have volunteers for therapy, at least I couldn't think of any. It's interesting because when we just got in the hi dose rate business, there's not a protocol in our institution that would indicate that that was experimental therapy. The hinge there is, what's innovative therapy versus experimental, and there are some pretty specific descriptions of that. So hi dose rate brachytherapy in most institutions is not referred to as experimental. But no matter how you want to look at that word versus

innovative therapy still would come any kind of misadministration rule.

DR. SIEGEL: I agree with that. I just wanted to make sure that you all didn't think there was a problem.

DR. STITT: It may not look like it, but I'm kind of contemplating these things to see where they cross my territory and where they don't.

DR. FLYNN: I agree with Judy. I mean the isotope used in HTR is radium 192 mostly and that's not new. The dosimetry is not new. So the fraction size or the time the dose is delivered is new and the biological effects may be something of concern.

But what my question would be is -- maybe I'm missing a point here. Which pure alphamitter are you talking about? Can you help me with that?

DR. SIEGEL: Not at the moment.

DR. FLYNN: Because all the alphamitters that I'm thinking of also would emit other --

DR. SIEGEL: These are for unsealed sources anyway. This is for radioactive drugs so we're not talking about Californium 252 for external therapy at the moment. This is in anticipation of an astatine labeled monoclodal antibody that doesn't exist yet that will be used for therapy at some time in the future. Or bismuth.

DR. GLENN: And clearly, I think, the example

that is real world is stromtium 89.

DR. SIEGEL: For beta but not for alpha.

Did you find it, Larry?

MR. CAMPER: Yes. For the Part 32 licensee, it says the following, the rule language. "The licensee shall possess and use instrumentation to measure the radioactivity of radioactive drugs. The licensee shall have procedures for use of the instrumentation. The licensee shall measure by direct measurement or by combination of measurements and calculations the amount of radioactivity in dosages of alpha, beta or photon emitting radioactive drugs prior to transfer for commercial distribution. In addition, the licensee shall perform tests before initial use, periodically and following repair on each instrument for accuracy, linearity, geometry dependence and so forth."

With regards to the guidance for the Part 32 licensee, the pharmacy or the manufacturer in 10.1.2. under Radioactive Drugs Instrumentation it says, "You must describe the instrumentation procedures and method of measurement used to determine the amount of radioactivity in dosages of alpha, beta or photon emitting radioactive drugs prior to transfer for commercial distribution. Measurement may be done by direct measurement or a combination of direct measurement and calculation."

Now here's a note for the reviewer. This is

available, of course, in the guidance. "The regulations do not require commercial nuclear pharmacy and medical use licensees to measure the activity of alpha or beta emitting radioactive drugs if they are received from the manufacturer in unit dosages. Therefore, it is critical that the manufacturer's measurements are accurate and match the activities on the labels of unit dosage containers.

Those calibrator procedures for most photon emitting radio nuclides are well known and standardized. However, you will have to use your professional expertise and judgment when evaluating instrumentation, procedures and measurement methods for low energy photon, beta and alpha emitting radio nuclides."

DR. SIEGEL: I think that's reasonably clear, certainly from the FDA's perspective. You all wouldn't permit a manufacturer to distribute a beta emitting radio nuclide in interstate commerce if they didn't know how much was in the vial and the USP wouldn't allow that in its pharmacopoeial standards either.

So I think that at the manufacturer's side, that is not a problem. At the pharmacy side, as long as it's a pass through of a unit dose, it's not a problem. If a pharmacy is going to be doing though what this rule potentially allows, which is producing a beta emitting radiopharmaceutical in-house from scratch and then

distributing it to Part 35 licensees, that commercial pharmacy has to know that they've distributed a millicurie when they say they've distributed a millicurie. There has to be a measurement method, whether it's alpha or beta, and they have to devise and come up with such a method before they can do it.

Then at the Part 35 end, right now the intent will be that the Part 35 licensees can accept whatever the Part 32 supplier tells them for alpha and beta. Is that correct?

DR. GLENN: That's correct. And again, for the Part 32 licensee, we would look at their method of measurement but it is true that for many of these isotopes standards don't exist. I guess going back to Dan's comment. For radium 192, in fact, a standard does not exist although there is a working standard among the major users.

I'm going to propose that this be the last slide and then we take a break. This will finish the review of the regulations and then we can talk about the actual license that we'll prepare after the break.

One other change that's in the regulations is we have updated the regulations with regards to some of the certifications that can be recognized, some of the Osteopathic Board certifications. These are things that

over the last five years we have recognized as the staff and some of these we have brought to the Advisory Committee. So we're updating the regulations to match the actual practice, as we've instructed our reviewers.

The one in the middle, I'll note that the last time we had a meeting we did discuss this. The Advisory Committee gave us some advice in terms of additional information we needed to get from the board They supplied it, and the conclusion is that for certifications of the American Osteopathic Board of Radiology after 1984, in fact, they did have requirement for the procedures that the Advisory Committee told us to look at. So the regulation will, in fact, note that that certification is good after 1984. And also included, the Royal College of Physicians and Surgeons which is one that we did bring to the Advisory Committee a couple of years ago.

DR. FLYNN: Can I bring up a point? I am sorry I wasn't at the last meeting. I was on reserve duty, military reserve duty. But Osteopathic Board of Radiology, it's my understanding that there were two programs in radiation oncology several years ago. Both programs have closed so I would have specific concerns about the Osteopathic Board of Radiology examining and certifying in radiation oncology. They've examined and certified people in radiation oncology very infrequently. In the past when

I've contacted the board, several years ago I had some questions, I asked them the number of people being certified per year. Sometimes it's zero.

So I have a sort of concern about that. I'd like to express a minority opinion that that should be looked into further. I'm not saying that their standards are not as high as American Board of Radiology but I would have concerns in the area of radiation oncology that they are not certifying enough individuals to make it clear to me that it's equivalent.

DR. GLENN: I will mention. Certainly this rule making, this was too big a topic to take on in addition to the issues that were on the floor. But a major part of this relook at Part 35 over the next few years is going to be to try for once and all to resolve this training experience issue and get it so that we have a system which is clear and the criteria are clear and we don't have these issues. One problem is we add someone and we don't have a way to know when the program changes, for example. We're going to have to look at that.

MR. CAMPER: Let me only add to that. We've heard a lot of comments, somewhat to our surprise, of recent about board certification, what's actually going on, residency programs which are actually going on and so forth. We, as John is alluding to, are going to be looking

at and have committed to going out and looking at this T&E issue as part of the revision of FAR 35. We do intend to go out starting next year and look at some of these 200 hour programs. We intend to look at some residency programs. We anticipate using Dr. Pallico to assist us in looking at some of these residency programs.

I would envision meetings and discussions with the board certifying groups to talk about what's actually going on to address some of the criticisms that have arisen. So we certainly can look at your issue as well at that time.

DR. FLYNN: Well, it's normally the American Board of Radiology which certifies individuals. But the Residency Review Committee of the ACGME, which accredits programs -- I'm on the Residency Review Committee for Radiation Oncology and we put through some additional requirements. For example, if a facility has HDR brachytherapy, the facility must offer training, includ[illegible] safety specifically for their residents in training.

I'm just concerned that for a board certification, in the board certification area, that some people who have difficulty achieving American Board of Radiology certification may use shortcut methods to obtain quote "board certification from somebody" and that the NRC should be very cautious about what is recognizes as

equivalent certification.

MR. CAMPER: It's certainly fair to say, I think, that the NRC has operated under the philosophy in dealing with the certifying boards over the years. We view that as a quality pedigree, if you will. But clearly as we look at the T&E issue and its sensitivity in today's market place, we need to go back and revisit that whole question of the board certifications and what they really mean, what the boards are committing to us, that we end up placing those board certifications in our regulations and so forth across the board. Across the board.

DR. SIEGEL: Yes and no. Let me just comment on that even though it's not part of what we're talking about now. It sounds to me like you'll address whether the current system is rotten or not as opposed to tackling head on what your objectives are. I think that's the backwards way of doing it. I think rather than trying to say that 20 percent of radiology residents really don't provide six months of training or really don't provide the 200 hours, you ought sit down -- as I've said nine times now and told the Commission three weeks ago -- once and for all decide what it is you want to assure. Then figure out what it takes to assure it. And then design the programs to meet that.

And that will extricate you from this turf war

stuff because what you're talking about and what you're alluding is turf war. One way you attack people who are trying to prevent you from achieving a particular kind of practice is to say, Well, your training programs aren't any good either. And then you get the NRC all riled up wondering, Gee, maybe we shouldn't be licensing any of these people, and that's the wrong way to evaluate this problem. You ought to start at the beginning, figure out what the public health and safety issues are, and design the system from the ground up rather than looking at the current system and figuring out what's wrong with it. I really encourage you to do it that way.

DR. FLYNN: But if there are no osteopathic training programs, it's ludicrous to have a board certification method.

DR. SIEGEL: Well, I may be suggesting that board certification might not be the method to do any of this for anybody. We really ought to look and see what the right way to achieve the NRC's objectives is rather than assuming that we've got to investigate what is going on at the Residency Review Committee for Radiology and for Nuclear Medicine and the American Osteopathic Association's review of its programs. I think it's tackling the problem backwards.

MR. CAMPER: I didn't mean to imply that that's

how we're going to approach the problem. As you know, we've talked with this committee on a number of occasions. The T&E issue is a big one. We're going to look at it from the ground floor up. We have an open mind. But, as part of that process, one of the things we want to do is to look at these other training programs that exist, look at the residency programs, meet with the board certifying groups, preferably at some point get the various representatives of the various boards together and talk about this issue face to face.

But it's only an element of a much larger process. I agree with you totally. I mean if that was the approach and the end onto itself, it would be the wrong approach, but it's just not that. It's only part of the overall process.

DR. GLENN: And any change we bring about, we're going to have to be able to say what's wrong with the current system.

DR. SIEGEL: I understand.

Any other comments about this last slide before we take a 10 minute break? Let's do it.

(Whereupon, off the record for a 17 minute break at 10:02 a.m.)

DR. SIEGEL: I think we can go back on the record. Before we start, Tory asked me to just briefly

announce that some members of the public appear not to have signed in and she would appreciate it if you would do so. I also had a request to allow the temperature to come up a little bit and, even though it's against my better judgment, I decided we could do that a little bit. Keep me posted if it's still too cold.

John, continue.

DR. GLENN: For the next part of my presentation, what I want to do is discuss some of the licensing issues and most of the conversation that I'll present will be focused around how we're going to be writing licenses based on this new rule. I think that will allow you to bring up any issues that are in the guide with respect to the new rule.

It presents both an opportunity and a challenge, the new rule, in terms of the way we write licenses. Automatically the licenses are going to be providing more flexibility with respect to both the uses and forms. Essentially, all limited scope licenses of the NRC for medical use are now going to become any form licenses. The old group concept is gone. Everybody can receive material in any form. As I mentioned to Dr. Woodbury during the break, we are completely out of the business of interpreting FDA's labeling as far as the uses. That is an issue that is to be handled between the user and

the FDA as to whether the indications of use and the procedures are correct. So that aspect of our former regulation is gone.

However, we still have the fundamental need to, when we license a facility, know the radiation safety aspects of that operation. And so somehow we have to be able to provide all this flexibility plus put some sort of bounds in terms of the radiation safety. We don't want to have a small community hospital that has only a technologist and no physic support, pharmacy support all of a sudden going into monoclodal labeling in a big way. We would want to know that they in fact brought on the qualified people before we would permit that to happen. Somehow the license needs to take into account the activities, the operations, so that we can properly bound the radiation safety aspects.

We've already had some discussions that the new procedures required for alpha and beta measurements and unusual operations, we're going to have to be reviewing those really on a case by case basis for radiation safety aspects. There is not an existing set of standards out there that we can rely upon. We're going to have to look at the credentials of the people in the program. We're going to have to look at facilities, the equipment on a case by case basis.

DR. SIEGEL: Dennis.

DR. SWANSON: A comment. As I read the regulatory guides again, a concern that comes to my mind is how specific do you see the requirements for information about uses of a prepared radiopharmaceutical? Also, for example, types of preparation procedures, etcetera? The reason for my concern is because if it's a detailed type of information that you want very specific uses and detail preparation procedures for specific agents, then that basically is going to prevent extemporaneous compounding or extemporaneous preparation of these materials without first having the licensing amendment.

DR. GLENN: Something that has been developed since the guide and which I only signed out to the regions as drafts for comments this week is what we call a standard review plan which is based on the guide. In there, you have notes to the reviewers in terms of what to be looking for. Specific to the comment you just made, we're telling them they "should not seek detailed preparation procedure information about the chemical components or reactions having only to do with the drug safety and efficacy. These issues are the responsibility of the FDA and state authorities. You should only seek detailed commitments from the application as our necessary to limit the scope and level of radiation hazard likely to encountered in the

preparation and the use of radioactive material."

So we would hope not to in fact confine you to any drug preparation but if you're going to need a fume hood, if you're going to need a glove box, if you're going to need some special kind of monitoring, we'll try to get you to define those parameters of how you're going to do things and commitments that when you're handling, say, more than 500 millicuries of Vidine 131 it will be done in a glove box with a certain kind of filtration, charcoal of a certain efficiency and your monitoring system. Those are the kinds of commitments we're trying to get through the process.

DR. SIEGEL: So, for example, for uses we could put down -- again, this applies to the on-site preparation, let's say -- Iodine 131 and as a use preparation of radioactive drugs for imaging studies.

DR. GLENN: Yes, and probably we'd go a little bit beyond that. We'd want to know, what's the maximum activity you'll have in any one container at any one time? And then, based on that, what are the handling procedures? Is it going to always be done in a hood? Is it going to be done in a glove box? How often are you going to do wipe surveys? Those kind of things.

DR. SWANSON: But what you're not looking for is, for example, use of Iodine 131 for the preparation of

tag 3 monoclodal antibody.

DR. GLENN: No. We're not interested in that detail.

DR. SIEGEL: This thing that you're showing us here, this is from your licensing guide.

DR. GLENN: Right. And that was handed out this morning. That was the document that was handed out this morning.

DR. SIEGEL: Okay. Maybe I missed it.

DR. GLENN: It's hot off the press.

DR. SIEGEL: I give up.

DR. GLENN: It will look almost identical to the Errata Guide for 10.8.

DR. SIEGEL: It's this thing here that says Errata on the front page?

DR. GLENN: Yes, that's it.

DR. SIEGEL: Okay. Fine. All right. I didn't see that. Oh, and this has the sample licenses in it. Got it.

DR. GLENN: It has sample licenses and in bold face it has the notes to the reviewer. I will mention one thing. Carl is not here right now. He is very concerned that in the future we probably should only have one set of guidance. There shouldn't be the set of guidance for the community and then that set of guidance with additional

information for the reviewers. We should have one set that everybody knows about. And also if we could maybe simplify the process. Maybe we don't need the formality of a licensing guide. Maybe the standard review plans developed by the staff but put out for comment would in fact be sufficient. We don't really need the more cumbersome process that we go through for the regulatory guides.

DR. SIEGEL: And I think I agree with that concept. I think there's always the concern that you put one thing in a regulatory guide but you're telling your internal folks something different, even though the document is one that is accessible through FOIA. I think it is, isn't it?

DR. GLENN: Yes. It's all available.

DR. SIEGEL: So that there might be two sets of standards. I know Carl's goal quite clearly is not to have two sets of standards, and I love that.

DR. GLENN: Carl just walked in. We're mentioning that we don't need both licensing guides and standards. We had not settled on exactly the mechanism we're going to use in the future. But I am very sensitive to your concern that in the need to understand the operations and needing some detail about what's going to go on, we don't somehow tie you into a particular way of

making a radioactive drug. That's not what we're interested in doing.

DR. SWANSON: I don't know if this is an appropriate time to bring this up. Again, in looking at the regulatory guide in Table 1, it talks about types of materials and for those materials that are obtained from a Part 32 supplier, it had a limit of 100 millicuries on the container and I question why the 100 millicurie limit because obviously we receive I31 sodium iodide for therapy from a Part 32 supplier that may be 200 millicuries or we could receive a bulk vial of tekeishium MDP from a supplier that would exceed 100 millicuries.

DR. GLENN: The 100 millicuries isn't etched in stone. That's sort of a default guiding line. Let me describe a little bit about how we envisage in the standard review plan a license being written, and then maybe we can discuss some of the details.

One thing that we need to do. Currently our licenses are written in such a way that it's essentially any byproduct material in 35.100, any form in 35.100 and as needed. There are reasons why we don't want to write licenses that way any more, but we still want to preserve the simplicity of licensing for those people who aren't doing anything unusual. So what I propose to do here is first, to divide byproduct material by half life because

anything over 120 days may be subject to decommissioning rules. So that is a natural thing that we need to have a dividing line in our licensing for because we have to evaluate for decommissioning criteria.

DR. SWANSON: Just a point before you go on. You talked earlier about specifying a half life for whether or not to be on the container and you picked 100 days. Just to keep things simple, you might want to consider 120 days for that also.

DR. GLENN: Well, we had a discussion. I tell you where we came down is we assumed that if you don't put the time on you've got a possible slops 48 hours. The 48 hours out of 100 days amounted to about one percent.

DR. SWANSON: I'm just trying to remember all these numbers is all.

DR. GLENN: This isn't too important because this is on the license but this was chosen because of the decommissioning rule. This would permit any form. That's so that, even though it says received as initially distributed in accordance with the Part 32 license, we are no longer restricting the medical use licensee to keep it in that form. In other words, your pharmacist can add Vitamin C, if they want to, to the drug in order to make it last longer and that would not be in violation of this regulation. You receive it from a pharmacy. You receive

it from a manufacturer. You make changes as directed by the pharmacist or by the ANP or by the authorized user and that's still covered by this blanket authorization.

And then as needed but with a limit so that we can know when the quantities are beginning to get large enough that we need to look for unusual radiation safety hazards. Maybe 100 millicuries isn't the right number in every case, and we would listen to reason as to what it should be. But we chose 100 as one where you're pretty sure that if they are using the common everyday drugs as received from manufacturers and it's not more than 100 millicuries in any one container, that you have limited the radiation safety consequences sufficiently that you really don't need to worry about asking more questions about the processes that are going to be used.

For those licensees who, in fact, want to compound from scratch, we would authorize whatever isotopes they tell us about, any unsealed form for preparation and administration as specified in 35.300. Now, before we would issue this, we would need to know that they do either have an ANP or an authorized user with the appropriate training and the 1.5 curies for iodine here would tell us ventilation, effluent releases. These are issues that have to be looked at in this license.

So we're using these possession limits as the

clue to when we need to look farther into the radiation safety program. They're not meant to limit the radiopharmaceutical uses but to get to the radiation safety issues.

DR. SIEGEL: John, just a point of clarification. You've shown the licensee here as St. Nowhere Hospital. Are you describing a Part 32 license to us or a Part 35?

DR. GLENN: This is a Part 35 license. I'll have a Part 32 license later.

DR. NELP: I missed the comment fully, I believe, on the 100 millicuries per container. I know you said that was a guideline.

DR. GLENN: Essentially in the guidance what we're saying is if a medical use licensee comes in, they're going to get prepared materials. They're not going to have more than 100 millicuries in any one container. The current Part 35 10.8 procedures will be adequate. You really don't need to look any further. However, if it's more than that, then you need to look to see if there are any special handling effluent monitoring requirements for compliance with Part 20.

DR. SWANSON: So basically the 100 millicuries is kind of an internal NRC action level.

DR. GLENN: Right.

DR. NELP: Because if you have your own generator, typically you're pulling off tech that's many times that amount every day.

DR. GLENN: Yes, and that could be authorized in various ways. Either we can list molybademum generator as a separate item or we could put in here, except generators with a higher activity, something of that nature.

DR. SIEGEL: In fact, this license as written here, the way it's written, would not authorize the possession of a one curie molybademum generator.

DR. GLENN: That's true. That's what they requested.

DR. SIEGEL: But the way your license would read is you'd have Item B would say molybademum 99/tekeishlum generator 3.6 curies.

DR. GLENN: Yes.

DR. SIEGEL: So it's done by licensing.

DR. NELP: This is an example.

DR. SIEGEL: And this is the way it's been going on for the last 30 years.

DR. GLENN: Now, we've also included here in some of the sealed source uses and the sealed source would stay pretty much the same way that it is today. You can receive it if it's been manufactured by someone licensed by

either the NRC or an agreement state would have to be material that's listed in 35.400.

The sample license I've given you here is very long. This was sort of, I guess, to make the drug people happy to know that we're really leaning on the sealed source therapy people a lot more nowadays than we are on the radioactive drugs. This license is so long because of this particular authorization. Radium 192, a particular sealed source, two sources not to exceed 10 curies and it's to be used in an HDR device. This license is so complicated because it has an HDR device on it.

But for the sample license for the reviewers I wanted to include this because we're putting a lot of reliance on our reviewers in fact making sure that the HDRs are licensed properly because we had not fixed Part 35 for HDR. So we're really doing it through license conditions.

License condition 10 would be very much the same. You can use material at a facility located at a given place. For a broad scope licensee, you can make changes within that listed facility without an amendment. For a limited scope licensee, you would have to come and tell us about changes of the facilities within the facility that's listed.

The Radiation Safety Officer is named and then we've listed all different kinds of possibilities here for

authorizing users. This catches the fact that you can name your own users. So a physician, dentist or podiatrist is defined in 35.32, working as authorized users in accordance with 35.13. So that says you can name your own users provided that they're certified, listed on another license or on a broad scope permit. Again, same thing with the pharmacist. If they meet any of those conditions in the definition and in the regulation, you can use them without amendment. Or you could submit a name and they can be approved. So the pharmacist could be named specifically. Likewise with authorized users. You can have physicians and the material and uses for which they're authorized.

DR. SIEGEL: Just a question of process. Filling out a license is sometimes not an easy thing for particularly new applicants to do because it's a complicated process and sometimes even for existing applicants. If someone comes in the way you see this now with 12 and only has D, only lists the actual people who are currently practicing in that hospital, would you encourage them under the way you're currently planning it to add paragraphs A and B?

DR. GLENN: This is to be automatic. Any amendment that comes in, we would add these.

DR. SIEGEL: Fine.

DR. GLENN: That raises an interesting question

though. What about current licensees who don't come in for an amendment and you can, in fact, go ahead and do this. This just makes it clear to everyone that, in fact, you're allowed to do that.

DR. SIEGEL: Got it.

DR. GLENN: But the regulation, in fact, is sufficient to allow you to name those users.

The medical physicist is named in this case. This is not a teletherapy physicist. This is a medical physicist because in our guidance for HDR we, in fact, require a medical physicist and we hope to remedy the regulation and get that fixed so that we have within our regulations both the teletherapy and the brachytherapy physicist well defined.

Then we start a whole series of special conditions that had to do with the HDR device, about interlocks, about radiation surveys that have to be made, about servicing the device, about the room that it's located in.

DR. SIEGEL: At the risk of being presumptuous, these look like draft regulations for HDR. Right?

DR. GLENN: I think certainly many of them will show up in whatever comes out in Part 35.

DR. PAPERIELLO: We're going to discuss that later, I think, in a session but you're right. You're

exactly right. That stuff ought to be in the regulations and we shouldn't be writing this as license conditions one after another.

DR. STITT: Let me just throw in a comment. I've been mulling it over since you described the brachytherapy physicist versus the teletherapy physicist versus the medical physicist and you know that that will be coming up. There's no such thing as a brachytherapy radiation oncologist versus a radiation oncologist versus a teletherapy radiation oncologist and we, meaning the NRC, is getting in some turf I don't think that is necessarily appropriate to start breaking that sort of thing down. We'll revisit that.

DR. GLENN: Yes, and one thing, maybe we only want medical physicists. We don't want teletherapy physicists.

DR. STITT: I would suggest that's true. We'll get there later.

DR. GLENN: We'll get there later.

Again, prescriptive requirements that are being done by license condition for HDR. Another thing we have, because of the mismatch between Part 35 as is currently written and HDR, we have to have such things in lieu of an existing regulation, you can do this instead. So we have to grant exemptions to the regulations in order to have

them make sense for the particular application.

And still it goes on. Let me skip to the end here. Some other conditions that have been added on here. There were some sealed sources on this license that were not for medical use and so some of the standard not for medical use conditions are also included on this license.

Currently we will be keeping the tie down condition the way it exists today, and that is that your application and any letters that change the application are referenced in a serial chronological date format and that you are tied to the statements and representations and procedures contained in those documents with the provision that ministerial changes can be made in accordance with Part 35.

Just to let you know. As we're going into this rethink of the way Part 35 is written and the way we do licensing, we're trying to see if we can't come up with a better way of doing this so that there is not this series of letters that somehow taken together constitute the commitments of a licensee but rather have separate compartments, procedures for receipt of material, procedures for dispensing. Segregate the license into clear parts, each of which has to be modified in its entirety when you make change. That way there is always one set of procedures, one set of commitments that clearly

apply to the license at any one time. That's just thinking ahead. We're not there yet. We're talking about a lot of changes and we can't make them all happen at once.

DR. SIEGEL: The problem with this as it relates to the question Dennis asked earlier is, is the potential trap that a licensee might get itself into of overly describing in too much detail how they're going to make I 131 labeled monoclodal antibody and then they realize six months later that they need to do something different chemically and then they've got to file a license amendment or, more likely, they forget that they need to do it and then someone comes along and says, Oh, you violated your license. So in a way you need to get the people who review the licenses to work with people writing these unique licenses to get them not to be too specific. They need to be more general and less specific to give them the flexibility to maintain radiation safety while practicing medicine and pharmacy with enough flexibility to do it well.

DR. PAPERIELLO: It goes beyond just the medical area. It goes into the entire materials area. In the reactor side of the house, we have something we call 5059 which allows reactor people wide latitude to make changes in our procedures without our approval. You have to balance that with the practical matter that we have two

to three inspectors living at every reactor site in the country so if we had a concern, we would know about it. But when we look at how we're licensing, we are looking at everything including the question of whether or not we'll create -- and we put parenthesis around this -- "a 3059." We are far from changing the process and I would tell you by the time we're right now doing the systems analysis to understand ourselves what the process really is and every variation among the regions. We will not be changing anything. You won't be caught short. And of course, what we're doing is going to apply to all material licenses.

We don't know what we're going to do yet because we're still in the very, very initial stages of the process. But we will let you know where we are going once we even have an idea ourselves of where we're going. But some of things to think about is why do we have a five year license? When you look into that, you find out it's tradition. No other basis. These things like this, why do you need amendments to change a procedure when, if you have your staff that can look at it and say, Hey, it's okay. That way we save people the cost of filing an amendment and save ourselves work in doing it. All these things are going to be considered but right now we're in the stages of just trying to find out what happens when you send an application in and a license goes out the other end? How

many people have their fingers in the pie?

DR. GLENN: Dennis will be interested in this. This is a pharmacy license. Some of the same thinking goes in here.

DR. SIEGEL: Do we have this example, John?

DR. GLENN: No, I don't think we have that example yet. You do? Okay.

DR. SIEGEL: I don't have this example. Now I've got many of them.

DR. GLENN: Again, we want to provide the flexibility that for a pharmacy that is going to continue only distributing prepared material from a manufacture license pursuant to Part 32, that they can rather simply define that for us and ask for that authorization. We have not made the cut here though in terms of 120 day, half life and activities because we are assuming that the pharmacy is going to need more material and they're going to be handling more at any one time. So we're proposing, you give us a list of the isotopes and activities you need and then we'll evaluate that as to whether we see any particular radiation safety handling problems.

But then just as in the medical use license, if the pharmacy is going to be compounding from scratch, just tell us what isotopes you need, authorize any form and then list again the isotopes. If you're doing it this way,

obviously we're going to be probably asking a little more information about what you plan to do because this says you're doing something unusual. You're going to be having more processing than you would with already prepared materials. More processing raises the question of more changes for effluence contamination and so forth.

We'll keep something in here for in vitro kits for what's called redistribution. We have to be a little careful about some of these things where essentially the pharmacy is just a pass through for the manufacturer. We want to keep the right description and labeling with the material because we don't want specific licensees getting instructions for general licensees and we don't want general licensees getting instruction for specific licensees. So we have some special conditions to keep that part of the program straight.

Some other types of authorizations here. Some pharmacies also pass on calibration sources and other kinds of sealed sources that medical use licensees may want to use. We would not approve the manufacture of sealed sources on a pharmacy license. We would make them get a different kind of license for that. But some of these are pass throughs. You can see here, we talk about "E) Redistribution of sealed sources as received from the manufacturer." So pharmacies are allowed to redistribute

those things that we would require a different kind of license for manufacture.

Depleted uranium. Any questions on anything?

Most of the rest of these conditions are standard conditions. If you're an authorized user condition, the one that recognizes the pharmacy can name its own users if they meet certain conditions or you can have a listed names of authorized nuclear pharmacists. Radiation Safety Officers also to be stated.

This is a standard leak test condition that we put on all licenses that have sealed source and aren't Part 35. Part 35 has built into it a leak test requirement. Part 30 does not. So if it's a non-medical use we're doing it by condition. Obviously that's something we need to remedy in our regulation so that something that we put on every license in fact is in the regulation and not on the license.

Likewise, there's a general prohibition. If it's distributed as a sealed source, credit is taken for the fact that it's a sealed source, has integrity. You're not allowed to open those things. Inventories, transportation. Again, Part 30 and Part 20 only have a very general decay and storage condition. We essentially give to non-Part 35 licensees the same authorization that is given to Part 35 licensees.

This is a unique condition that appears on nuclear pharmacy licenses. Many of the pharmacy licenses offer as a service to their customers that they will pick up used syringes and vials and so forth and save them the disposal hassle. We will allow that provided that the pharmacy is only picking up their own material.

This is a standard condition that is used if a licensee requests it that eliminates them having to submit a decommissiong plan. In other words, they say that they're going to apply the conditions of the regulation and keep their possession limits down below what requires a decommissioning or emergency plan.

Then the standard tie down condition except again for Part 30 licenses, there is no ministerial change rule and so there is not the same flexibility that's provided to medical use licenses to make minor changes. Again, something that needs to be fixed.

DR. SWANSON: One of the things I noted again in the regulatory guidance specifically discussed the ability of centralized nuclear pharmacies to distribute to Part 35 licensees. It didn't specifically address their ability to distribute to broad licensees which, in fact, does occur.

DR. GLENN: I think the rule change we have makes it clear now that broad and limited scope licensees

are both clearly covered by Part 35.

MR. CAMPER: I'd make a comment at this point as John is winding down. We did recently participate in the all agreement states meeting and myself and some other members of the staff met with a task force of the CRCPD that's working on revising existing model regulations. These regulations are prepared by the CRCPD in such a fashion that they could be used by agreement states and, of course, while we were meeting with them primarily to talk about language associated with the quality management rule, we did at one point get into a discussion about this particular rule and then that evening we met with actual program directors of the states.

An issue was brought up by one of the program directors that I intended to bring up and that is is that come January there will be a substantial disparity in our C controlled states and agreement states with regards to this flexibility in this regulation, authorized nuclear pharmacist and the like. Now, this rule does have a Division 1 definition compatibility. Mr. Graham is a new member. That means the definitions have to be identical. And the rest of the contents of the rule is Division 2 compatibility which means that they need to put in place processes that meet the objectives and requirements of this rule but they can do it in a way that's flexible. It

doesn't necessarily have to be in rule language. It can be in guidance approach and so forth and they have three years to do that.

Now, as a practical matter, what's already starting to happen -- in fact, Don Flater of the State of Iowa brought it up. He had been contacted, I guess, by the University of Iowa. People who are nuclear pharmacists in agreement states are probably going to want to become authorized nuclear pharmacists fairly quickly, if for no other reason than simply this credentialing type of approach. "Well, my friend who lives in Virginia is an ANP and I live in Maryland and I'm not" type of thing.

Now, we did offer to work with the CRCPD folks as they move ahead at some point to develop model regulations for use by the agreement states, but now that's not going to happen in the immediate future. We did simply make the offer. They agreed that at some point they would want to do it. So my point is, just for the record, that recognize come January, there's substantial disparity between the NRC states and the agreement states and I think that it is something that practitioners are going to want the agreement states to move toward or some variation thereof. It looks an awful lot like it because of the flexibility provided. So, just for the record, be aware of that.

DR. GLENN: My final slide just makes some of the points that I think I've already made that some changes on pharmacy licenses. Currently, authorized users may be pharmacists or people who have medical technology background. With this rule change, the only people who will be listed as users on pharmacy licenses are pharmacists who meet the qualifications of an ANP.

Pharmacists who are currently listed on pharmacy licenses, in fact, will be ANPs because if you look at the requirements we have to be a user, the hours and everything are the same as in the new regulation. And the only additional requirement is the fact that there are pharmacists and we put in the grand-fathering condition for the preceptor. So, any pharmacist who's listed as a user today will be an ANP on January 1st. And board certified nuclear pharmacists are not required to be listed on the license.

CHAIRMAN SIEGEL: Kathy?

MS. SEIFERT: A question on pharmacists' ANP.

Occasionally, we get into a situation where we have a staff turnover and we hire someone who is licensed in a state who is not yet qualified to be an ANP. We usually have that person work in conjunct with someone else, perhaps maybe not licensed in that state as a pharmacist but would be licensed in another state. So,

that person would sort of serve as the preceptor in the nuclear pharmacy regard while the other person may have the state pharmacy licensure.

Would that still be acceptable?

DR. GLENN: I'm not sure I followed everything. But I guess the preceptor must be an ANP.

MS. SEIFERT: Okay. Is it required that that ANP necessarily be licensed in the state in which the practice is going on?

DR. GLENN: No. Our regulations, I don't think, would reach to that.

MS. SEIFERT: Okay.

DR. GLENN: Now whether you'd run into trouble with pharmacy law, I don't know.

MS. SEIFERT: Well, that's the reason that we always have a pharmacist that's licensed in the state and that's the question where these people are working together. One has the ANP qualifications; the other one has the pharmacy license and is in training to be an ANP.

MR. CAMPER: Let me give you a parallel that I think will help clarify this.

If you look today -- bear in mind, remember the discussions where the radiopharmacists, by virtue of this rule, now parallels, if you will, the authorized physician user, part 35.

MS. SEIFERT: Yes.

MR. CAMPER: Today, one of our criteria is that to be an authorized user, one must be licensed to practice medicine. You do not necessarily have to be licensed to practice medicine in the state where you're requesting to be an authorized user.

MS. SEIFERT: Okay.

MR. CAMPER: You simply have to be licensed to practice medicine.

CHAIRMAN SIEGEL: But you'd better not practice medicine in that state if you're not licensed.

MR. CAMPER: I meant NRC space.

MS. SEIFERT: Yes. Yes, okay.

MR. SWANSON: Just to clarify for the public record, I think what Kathy is saying is, in that case, the authorized nuclear pharmacist would be working under the supervision of the licensed pharmacists in the state which would cover our Board of Pharmacy regulations. And vice-versa, the pharmacist who is licensed in the state would be working under the supervision of the authorized nuclear pharmacist to address the NRC regulations.

MS. SEIFERT: Exactly. That's exactly what we do. And as long as that person is licensed as a pharmacist in some state and we're covered on the state pharmacy regs, we're okay.

CHAIRMAN SIEGEL: It's cool.

MS. SEIFERT: All right.

DR. GLENN: We're mainly concerned about the competency of the preceptor.

CHAIRMAN SIEGEL: All right. So, that's your last slide, correct, John?

DR. GLENN: That's my last slide.

CHAIRMAN SIEGEL: I know that I had a few items -- no, actually, there's about ten of them. They're not so bad. A few items that were probably just worth questions. Some of them you've addressed already.

Dennis, do you have additional things in the licensing guidance that caught your attention?

MR. SWANSON: Yes, several additional things. Some of them more housekeeping things, and some of them general issues.

CHAIRMAN SIEGEL: It's probably worth, I think, spending a couple of minutes just to address some of these. So, why don't we open to -- just do it this way.

John, do you have your document there? Let's start with the "Draft Guide for the Preparation of Applications for Commercial Nuclear Pharmacy Licenses", which was the first document in the package. The first question I have -- and it's just an information item -- is on page 11. So, if anybody has something before page 11,

we'll do them first.

Dennis, you didn't mark your pages?

Okay, my question on page 11 is, it states that "if the State Board of Pharmacy requires a pharmacist to be physically present at the facility during the preparation and dispensing of prescriptions, then you should confirm that the pharmacist present during the use of licensed radioactive materials is an authorized nuclear pharmacist."

It wasn't clear to me why those were linked. That a pharmacist who is not an authorized nuclear pharmacist could work under the supervision of an authorized nuclear pharmacist who might be responsible for several facilities, but the person who is physically there watching drugs being dispensed at that moment didn't necessarily have to be an ANP.

MR. SWANSON: Yes, I had exactly the same question, especially if you go back to the first sentence of that section where it says that "each commercial nuclear pharmacy must have an authorized nuclear pharmacist to prepare radioactive drugs for medical use."

So, it seems to me that that particular statement just doesn't need to be there.

DR. GLENN: Needs to be under the supervision of. If there's a pharmacist present, that pharmacist has to be then under the supervision. But I see what you're

saying. It doesn't have to be the ANP, right?

CHAIRMAN SIEGEL: But this does say it has to be the ANP.

DR. GLENN: Yes, okay.

CHAIRMAN SIEGEL: So, I think this may need a little technical direction on that one item.

I guess I wasn't aware that the RSO has to be physically present during the operation of the pharmacy. Does it say that?

DR. NELP: What page is that, please?

CHAIRMAN SIEGEL: Well, it says "the radiation safety officer you designate" -- this is on page 12 at the top -- "should be present daily at the facility."

DR. GLENN: Okay, that is a true use of the word "should." We're saying that we think the standard is that the radiation safety officer is someone who is really involved with the program. We have cases where we have absentee RSOs. We're saying that is not the norm that we want to accept for licensing. But it's not, as a requirement, if there's a day that the RSO doesn't show up, that you're in violation. It's that we expect that this is a real employee of the licensee who, in fact, does participate in daily activities.

MR. SWANSON: And of little less concern, it also goes on to further state that "the authorized nuclear

pharmacist can serve the functions of the RSO in the absence of the RSO." So, I had less concern at that point.

CHAIRMAN SIEGEL: Okay. I skip next to page 61, so quite a jump.

MR. SWANSON: I actually have concerns before that with regard to 31, 32, 33. All of the issues related to calibration of dose calibrators. The requirements that are listed there are different substantially from the Part 35 requirements for calibration and QC of dose calibrators. I think it needs to be looked at as to why those differences exist. Do they really need to exist, so on and so forth?

DR. GLENN: Is there anything in particular? I guess we do have the five percents in there when the regulation is ten percent. I guess that's what we're trying to say --

MR. SWANSON: The activity level of the reference standards are different. Another difference is the Part 35 accuracy from the highest dose to administer to the patient to the lowest, and you're using vials here -- highest activity in a vial.

CHAIRMAN SIEGEL: Because it's tied to what's dispensed.

MR. SWANSON: It's tied to what's dispensed.

CHAIRMAN SIEGEL: Right. And if you dispense a

dose --

MR. SWANSON: But you're measuring the dose as dispensed.

CHAIRMAN SIEGEL: -- then you want the dose to be accurate. If you dispense a vial, you want that reading to be accurate, don't you agree?

MR. SWANSON: True. I'm just asking that these all be looked at. You've got a two percent limit on a geometrical error, that's pretty tight, okay?

CHAIRMAN SIEGEL: Where is that, Dennis? I missed that one.

MR. SWANSON: Under geometrical error.

MR. GRAHAM: Page 33, IFP.

MR. SWANSON: Yes, "geometrical variations are significant, greater than two percent."

DR. GLENN: Yes, well, we probably should have caught them. These are coming out of the existing guide and so, we probably should have changed them to match the current Part 35, yes.

MR. SWANSON: Yes, I think that's the point I'm trying to make. We need to go look at Part 35 and make sure where we're differing there, okay, and that they're compatible.

CHAIRMAN SIEGEL: And if you differ that there's a rationale for differing. Because I mean, I do

agree that you don't want to be off by 30 percent if you ship a vial that says it's got 200 millicuries in, just because you only did linearity up to 30 millicuries.

MR. SWANSON: Correct, and I would agree with that, too.

DR. PAPERIELLO: I have a question. Is there an industrial standard -- in other words, some kind of consensus standard -- that either AAPM has or somebody has for those calibrators that we could embrace, rather than create our own guidance?

MR. CAMPER: There is an ANSI standard and the requirements of the ANSI standard and those in Part 35 are very close.

Just a comment on the guidance, in general. I think something I would make here in defense of some of these errors -- and I agree with what John told you. We should caught this. What has happened here is that in this particular rule, we are preparing guidance documents, standard review plans, inspection guidance, to accompany the effective date of the rule. It was a pressed effort, if you will, and I'm sure that we have overlooked some things. So, all the errors that you're pointing out and any that you will point out are greatly appreciated, in fact.

CHAIRMAN SIEGEL: All right, more, Dennis,

before page 61?

MR. SWANSON: I think I've covered some of them.

CHAIRMAN SIEGEL: All right, just a minor -- maybe a minor item on page 61 under "Amendments." In the fourth paragraph it says, "in the past, amendments were usually to add a new nuclear pharmacist or change the RSO. In the future, amendment requests to prepare radioactive drugs from sources other than prepared radioactive drugs are also expected to be common."

That confused me because it sounded like you're likely to be saying that every time you want to do something that the rule now says an authorized nuclear pharmacist can do, you're going to need a license amendment.

DR. GLENN: That's not true, but anytime a new isotope would come along or something like that, we would expect that the people are coming in and getting amendments in order to use that isotope.

CHAIRMAN SIEGEL: Okay. This is a little bit confusing, for whatever it's worth.

DR. GLENN: Okay.

CHAIRMAN SIEGEL: I skip way down the line here. Appendix F, page 1.

So, Dennis, if you or anyone else has anything

first --

MR. SWANSON: The only thing, again, would be Appendix E is the same thing, one dose calibrators, which needs to be looked at.

CHAIRMAN SIEGEL: Right. Appendix F is --

DR. NELP: May I ask why you think the future is going to be different than in the past?

DR. GLENN: Oh, because we didn't authorize it before, so that we expect being authorized for that is going to be more common in the future.

DR. NELP: Okay.

CHAIRMAN SIEGEL: Placing an order for radioactive material. Why does that have to be done by an ANP or a radiation safety officer? Isn't that a supervised activity?

DR. GLENN: Don't we say either/or under supervision?

CHAIRMAN SIEGEL: It's F-1. No, it says "ANP or RSO will place all orders." I interpret that to mean that the pharmacist or the RSO has to be the one who physically types out the purchase order, who picks up the telephone and calls Mallinckrodt and says, "I'd like to order a curie generator."

Do we really mean that level of scrutiny?

DR. GLENN: We mean "will place" in a broader

context, that being monitoring the activity. The follow-on words are what's the most important, "to ensure that the requested materials and quantities are authorized by the license and the possession limits are not exceeded."

I mean, we don't literally mean you'll pick up the telephone and make the call and so forth and so on.

CHAIRMAN SIEGEL: I think you may want to --

DR. GLENN: We can certainly clarify that.

CHAIRMAN SIEGEL: You may want to do a little wording fix on that one.

Okay, that's all I had on that document and I really did not have very much on the --

MR. SWANSON: I'd just like to say Appendix H--

CHAIRMAN SIEGEL: Okay.

MR. SWANSON: -- has the old standards for -- breakthrough, which kind of gave me the preview that this came from the old --

DR. GLENN: Oh, okay. I thought we had found that and fixed that one because I did identify that one.

CHAIRMAN SIEGEL: Yes, one microcurie per millicurie. Oh, excellent.

DR. GLENN: That was supposedly fixed once.

CHAIRMAN SIEGEL: Good pick-up.

MR. SWANSON: Just to point out I actually read it.

CHAIRMAN SIEGEL: I don't have anything on the other licensing guide, and then I skip to the errata on Reg Guide 10.8.

So, Dennis, if you had anything on that other guide.

On page 2 of the errata document that we got in our packages as distinct from the one that came this morning -- because I think they're different -- I just had a question at the bottom. This is under item five. How was a licensee necessarily supposed to decide that preparation of a radioactive drug presents radiation safety hazards greater than those normally encountered by the use of radioactive drugs that are prepared either commercially or by the medical use licensee from commercially available generators and reagent kits? You may need to submit preparation methodologies."

It seemed to me a little vague in terms of when a license amendment was going to be required. I'm wondering if the guidance document needs to give some more specific examples of "if you're currently doing this and plan to do this, you're okay. If you're currently doing this and plan to do that, you'd better file a license amendment because there's an order of magnitude change in radiation safety." So, I think some examples that show what you've got in mind --

DR. GLENN: Yes, I think we were sort of depending on the table to help people tell us enough about what they were doing that we could make that call.

CHAIRMAN SIEGEL: Okay.

DR. GLENN: But certainly, I agree. If the guidance isn't giving guidance, then there's something wrong.

MR. SWANSON: Right. And it comes back to the same concern I expressed before that I would hate to see somebody through their license lock themselves into not being able to extemporaneously compound something that was truly needed for the patient. We need to be very careful about that.

CHAIRMAN SIEGEL: Now, there is an example, I guess, on page 7 that does give a few examples. That second paragraph, and I did notice that, okay. I'm almost done. No, I did that already. That's all I had actually.

Dennis, anything else? Or anyone else?

MR. SWANSON: Just, again, under that section, you refer to either a pharmacist or an authorized user, and I think what you're referring to is an authorized pharmacist or an authorized user.

CHAIRMAN SIEGEL: What page?

MR. SWANSON: It would be on page 3 of the --

CHAIRMAN SIEGEL: Errata?

MR. SWANSON: -- of the Part 35. I didn't look at the errata, I'm sorry, of this guidance document that we received in our packet.

DR. GLENN: The first one?

MR. SWANSON: No, excuse me, it's the errata, the 10.8, page 3, you refer to pharmacist throughout there, but I think you're really referring to authorized pharmacist. To go down to the last paragraph, for example, on that page?

CHAIRMAN SIEGEL: Oh, "either by a pharmacist or an authorized user."

MR. SWANSON: It says "or an authorized user."

DR. GLENN: Yes, yes. The parentheses makes them an ANP, but --

CHAIRMAN SIEGEL: Okay, got it.

Anything else? Kathy, do you have a comment?

MS. SEIFERT: I have one more question.

CHAIRMAN SIEGEL: Yes.

MS. SEIFERT: The qualifications for an authorized nuclear pharmacist, are they parallel, exactly the same as an RSO? Could an authorized nuclear pharmacist qualify as an RSO? Is there anything in --

CHAIRMAN SIEGEL: It actually says that it is anticipated that an ANP will virtually, automatically qualify to be an RSO in a nuclear pharmacy.

MS. SEIFERT: Okay, great.

CHAIRMAN SIEGEL: Did I interpret correctly?

DR. GLENN: Yes, that's correct. It says that.

CHAIRMAN SIEGEL: Any other questions? Okay, good.

DR. GLENN: But it wouldn't work the other way.

CHAIRMAN SIEGEL: Right.

DR. GLENN: An RSO would not qualify as an ANP.

CHAIRMAN SIEGEL: You mean they might actually have to be a pharmacist?

DR. GLENN: That's right.

CHAIRMAN SIEGEL: Understand. All right, good. Productive discussion. We're only 15 minutes overtime. Unless there are further questions on this issue, we'll move on to a less contentious issue, which is the quality management rule.

MS. SEIFERT: All right.

CHAIRMAN SIEGEL: Something everyone at the table can get their teeth into. It's my favorite rule. I like it almost as much as Internal Revenue Code.

MS. MERCHANT: As Barry said, I'm going to talk about the implementation of quality management in this administration rule. For those of you who don't know me, I'm Sally Merchant. I'm with the Medical Section here at NRC. Here's my number if anyone wants to reach me.

CHAIRMAN SIEGEL: She didn't leave it up there long. But I'll give you her E-mail address if you want to reach her.

MS. MERCHANT: Actually, what I'm going to talk about is our continued assessment for the next two years of the overall implementation of the rule. I'm going to talk about the contractor reviews, the results of the inspections, the results of reactive inspections, enforcement actions and the TI field notes. Now, we're collecting data from all of these sources so that over the next two years, we can really do an assessment of what we have and where we're going with this regulation.

Currently, we have two contracts that are supporting the rule. Lawrence Livermore National Lab which is rolling down toward an end. They've completed the review of 1,709 QMPs that were submitted by the licensees. Then INEL who has a contract with us to react to certain events that we call them in on. Usually, it will be a serious misadministration or other event, and we have a contract with them to evaluate it. Both of those findings will be used to evaluate the rule.

The QMP review findings, there were 1,709 letters generated, as we said. There were three categories of letters. Letters number one, which said that the QMP, as written, appears to meet the objectives. There were 35

of those letters sent out, out of the 1,709. Letters number two, which said that the QMP, as written, has weaknesses, but appears to meet the objectives listed in 10 CFR 35.32. There were 278 of those sent out. Letters number three, the QMP, as written, fails to meet at least one of the objectives listed. There were 1,228 of those letters sent out.

We had 168 negative declarations, those who were licensees, who were approved for or had the material listed on their license, but for some reason, were not using it. What it says is that it's not being administered and that they would not use it without sending in a QMP. If they intend to start using the material, they have to send in a quality management program before they can start.

I'd like to clarify the 72 percent of the licensees who got category number three letters. They varied in their safety significance. I wanted to be clear on that. I mean, we don't want to give the impression that 72 percent of the submitted QMPs literally failed to meet. It could have been as simple as a lack of one of the elements in a required directive, written directive. The definitions in 35.2, which gives very specific prescriptive definitions as to what the written directive for each modality has to contain, if a licensee failed to list one of those, we reminded him that he did not list it. Now,

that did not mean that the same licensee wasn't listing all of those on the written directives that he's using, but he failed to commit to do it.

Keeping in mind that these were not really deficiency letters. People take them as deficiency letters. Once we committed to review these QMPs, we were responsible to tell them everything we found. So, as I said, they do vary in their safety significance. So, it could be lack of one element, as compared to failure to do a treatment plan for brachy therapy, which we would consider somewhat unsafe, understatement.

The graphic slides that I've included come from the draft report that Lawrence Livermore provided to us. We haven't got the final report as yet. We are told that the graphs will not change significantly, if at all, but these are from the draft. They show basically what the findings were. And for like radiopharmaceutical therapy -- well, I mean, they're pretty self-explanatory. You can see that a large number of licensees failed to -- I'd like to say that they failed to have at least one portion of the written directive. I don't think that those are licensees that failed to have a written directive, but failed to have a complete written directive.

As you can see, no one, or very few, missed objective two, which says that you have to identify the

patient each time. Everybody did that really well. For radiopharmaceutical therapy, you don't have to meet objective three, which is calculations and computer acceptance testing and that sort of thing. Objective four is the objective that says that you have to assure that what the physician ordered is what the patient got. The others are review processes. Objective five says that you have to identify any misadministration or recordable events and evaluate them.

MR. CAMPER: And actually, any unintended deviation.

MS. MERCHANT: Yes, thank you, Larry.

MR. CAMPER: A comment, too, while you're changing slides there.

If you'll notice -- and you'll see it throughout the slides that Sally is going to show you -- under recordable events and periodic review, those will show up across the board. Arguably, some licensees probably didn't say anything about recordable events or about doing the periodic reviews because, in fact, it exists in regulatory language. Therefore, they may have assumed they didn't need to say anything about it, and that's a valid assumption. However, if they did not mention it in their submitted QMPs, there were some standard paragraphs that were used by the contractor to

remind them of that.

MS. MERCHANT: Yes.

Incidentally, we had been reviewing that language yesterday and in fact, the rule does say that they have to have procedures and had to submit procedures to do that evaluation. That was an argument that we got back from a lot of the licensees that because it was prescriptive, that they did not think they needed to include it in their QMP. But in fact, the rule says that they must submit procedures.

For I-125 and I-131, you could almost superimpose the radiopharmaceutical therapy on this one. The findings are just about the same and I think that you would expect them to be.

DR. GLENN: Sally, maybe I'll make one comment.

I think at least early-on, in reality, one of the true problems we found with QMPs was that many licensees failed to recognize that in this very limited set of diagnostic procedures -- which involve more than 30 microcuries of iodine 125, or 131, did require a written directive. And in fact, that has been, I think, one of the major failures that we've actually detected with licensees meeting the objectives.

MS. MERCHANT: Yes, yes.

Actually, for time, I'm going to skip. You

have these in -- does anybody want me to go through all of them? No, I didn't think so because you had them right in your book.

Okay, on August 1, 1994, we issued a temporary instruction for review of the Quality Management Programs by the inspectors. It will be in effect for two years from that date. The inspectors receive training in using the TI to do the inspections.

One misconception that has kind of come out of this whole thing is that licensees believe that their QMPs have been being reviewed since the rule went into effect. But in fact, we didn't start inspecting the QMPs until August the 1st. The only thing that the inspector did when he went there was to assure that there was a QMP and that people had been trained in it. Other than that, he did not delve into anyone's QMP. So, arguments that we've gotten back were that we found problems with their QMP after they were inspected is a misunderstanding because their QMP was not inspected.

MR. CAMPER: Right. The only exception to that, of course, is in reactive inspections.

MS. MERCHANT: Oh, in reactive, that's true. Yes, thank you.

MR. CAMPER: Right.

MS. MERCHANT: This temporary instruction is

going to be completely entered into a database. We're going to gather all of the information that we find from it. It's important to us because we would like to find out which things are met absolutely all of the time, which things are not met at all. It will have a big impact on what we do with it at the end of the two years.

DR. GLENN: Sally, again, let me mention, it will record data other than whether there is compliance or not compliance either. It will give us information about how people are meeting it --

MS. MERCHANT: Oh, yes.

DR. GLENN: -- as well as whether they're meeting it.

MS. MERCHANT: Yes, I guess I wasn't clear. Even very good, very positive inspections, the whole thing is going to be entered. Not just negative findings, even positive findings.

Additionally, we're getting ready to issue a standard review plan for the review of new and revised QMPs. We're revising the one that the contractor used. Several things: for instance, since all of the licensees failed to some extent, as far as the review process is concerned. We're going to make that as a standard part of the letter rather than a part of the checklist. Just a reminder that you have to do it rather than to check it off

as you go. But the review of the new and revised QMPs will occur -- well, the revised that have been sent in as a result of the letters will be reviewed prior to the inspection by the inspector. It's part of the TI that I just described, and the inspector will review the revised QMP prior to going out. Then all QMPs will be reviewed as part of the license renewal process when new licenses come in, or if you need an amendment. If you're going to add a modality, then the QMP would be reviewed.

Actually, I did it. That's it!

CHAIRMAN SIEGEL: Comments?

I have a few general comments. With respect to the exercise, and I'm not shooting the messenger. I guess the way I would characterize what I've observed with this QMP writing is something I might call as something like "if you can't take a joke, you shouldn't be an NRC licensee."

I'm wondering, and I'll ask you this question, Carl. If you had the opportunity to do this over again, would you have done it this way?

DR. PAPERIELLO: No.

CHAIRMAN SIEGEL: Okay, good. I agree. Because I think what you've discovered is that licensees, although they are perfectly capable in most cases, of following what's in Part 35, are not as good as John Telford in translating it into policies and procedures.

And so, you've said to people, "we're going to create a performance based role and here's what we expect you to do. Now, you go and set a set of procedures in place to achieve that goal and turn your plan into us." Well then when the plan came and it didn't contain the exact language that was in the prescriptive rule, you turn around and say, "no, your plan's no good," even though that licensee may never have had a misadministration, may never have had a recordable event ever, and may never in the future. To me, that's a plan that's working quite effectively.

And so, I think I really -- I'll go on record as saying this, and maybe the Committee would like to join me, that when it comes time for the Commission to reexamine this rule in two years hence as you're supposed to report back, that you might just want to reduce it to the prescriptive requirements that are necessary to achieve your safety goal and get rid of this huge paperwork burden that you've created by forcing people to rewrite your rules into their procedures, and then slapping their hands when you say, "oops, you didn't do that right because this i wasn't dotted and this t wasn't crossed."

MS. MERCHANT: Barry, you will get no argument from us on that. We have learned a great deal, I believe, and I think a demonstration of it, when the standard review plan comes out for the re-review, it's considerably cut

down. I mean, you know, it's something more -- you would be surprised at how -- not prescriptive, how --

MR. CAMPER: Basic.

MS. MERCHANT: -- yes, how basic it is.

CHAIRMAN SIEGEL: Right.

MS. MERCHANT: Did they meet objective one, and anyway they want to do it? That's the way we're, you know --

MS. MERCHANT: I would also add, please don't interpret my comments as being pejoratively critical because they're not meant to be. I think this was a very interesting experiment in rule-making. And I think the experiment provided useful data, but I don't think this is the right way to make rules.

MS. MERCHANT: -- that you are right. We have commented upon the fact that looking at performance base versus prescriptive rule-making, the lessons learned from this will impact upon future actions. It was a lot of work that we went to. I think, as Carl said, if we had it to do again, we would have done it differently. I would -- and this is myself speaking -- but I believe we are trying to do a good thing. The way we had gone about it may have been somewhat overkill before, but I think we're on the right track now.

MR. CAMPER: A comment if I may, and again,

this is a personal observation.

You know, this rule has really been a tough one. I can't tell you how much Dr. Glenn and I have wrestled with this and Carl, since inheriting this rule. One of the things that's interesting about it from my perspective is this.

If one goes back to this performance based concept, you probably recall that that approach grew out of a recommendation by the ACMUI. It said that if you're going to go forward with this type of rule, it should be a performance based rule and you should conduct a pilot program. Well, we did that. Now, the problem -- and this is just me, personally, speaking --

CHAIRMAN SIEGEL: Can I just correct you by saying it was a different ACMUI.

MR. CAMPER: Well, that is true. But it was the ACMUI.

CHAIRMAN SIEGEL: We were doing a character check here. It was an ACMUI of a different character.

MR. CAMPER: You're trying to say this was not during your watch?

CHAIRMAN SIEGEL: That's correct.

MR. CAMPER: So, we had this performance base rule. Now, the problem with performance base rules are that it sounds good. It sounds workable. It sounds warm

and fuzzy, if you will, to the regulated community. But the problem is is when you try to interpret what that means. When licensees try to interpret it, when we try to interpret it, when the contractor tries to interpret it, you get into a real nightmare.

And here's the observation I want to share with you, which I was somewhat struck by. Sally was there when it happened. We were with the contractor, participating in a training session at the subcontractor's facility in a roomful of physicians and physicists who were going to assist the contractor in reviewing the program. Because remember, we had a great deal of interest in having therapy, physicists and physicians and so forth review.

The thing that I found interesting was that I kept trying to hold them in abeyance in the sense that they were going more and more prescriptive, although I kept saying performance base, exercise judgment and the like. If I didn't know better, I would have thought that I was instructing a room of our license reviewers, our inspectors. But in fact, I wasn't. I was instructing a room review, a roomful of people like yourselves.

I think the dilemma is that when you're the regulator, or you're the person who's ultimately responsible for saying something does or does not pass muster, there's a tendency to be prescriptive. There's a

tendency to say that I can walk away from this, and if I'm ever challenged, I can say that I held the line. I took the tight approach. And therein lies the dilemma.

I guess my point in the final analysis, I think in many ways, you're just best to go through a reasonable rule-making process. Lay it out, get comment, discuss it with this Committee and the like. In the final analysis, say what you want, stick with it and be done with it.

CHAIRMAN SIEGEL: I couldn't agree more.

Bob?

MR. QUILLEN: I have to ask a question from the agreement state perspective. That is, if you learned something from this exercise, how is it going to be applied in implementing this in the agreement states?

MS. MERCHANT: Well, I'm the wrong one to ask that question. As I said, that was a comment from myself, just my feelings on it. I think that's being worked out now. I think that you all are negotiating it out.

Let me put it this way. I know what the feeling is, but I'm not really in a position to say just because I'm staff. I don't make the decisions.

MR. CAMPER: Well, I'm only management. I'm not sure I know either.

I'll tell you what I can tell you at this point in time. We did meet with the CRCPD task group that's

writing the model regulation to try to implement this rule. We had some contentious discussions and we had some extremely, you know, friendly discussions. There were a couple of issues. I mean, the definitions are division one compatibility. Like it or not, I understand the sensitivities there. It speaks for itself. And the task group said, "okay, if the definitions are division one, so be it, we'll make the changes."

With regards to the rest of the rule which is division two, they were able to find it workable, with the exception of one thing. That is the idea of submitting the QMPs. Now, a number of the state representatives attending this meeting on the task force said, "look, we simply can't do that because, for example, our state laws say that if we receive something from the licensee, we have to review it and respond within 30 days." Well, if we're suddenly going to get an onslaught of these submitted QMPs, what are we going to do about other licensing actions and the like?

Where that stands is, is that we suggested to the task group that they would write a letter to the Office of State Programs and say, "look, come January the 25th, this QMP is an item of compatibility, division two. It poses a burden and we would offer recommendations to deal with it in the following way." Now, I have seen a draft of that letter from that task group which Terry Prizee chairs.

I have not seen it in final yet, nor have I heard from OSP to take a look at it. But I'm sure we will work with OSP to see what can be done to make whatever appropriate recommendations and so forth that can take place, to allow some flexibility there.

But with regards to the rest of the rule, you know, we have the division one and division two. We have offered to work with the agreement states, the CRCPD, in trying to develop guidance. I did participate in the Agreement States Meeting and shared with them lessons learned from a management perspective. Some of which, you know, caused me to have a lot of bruises and scars. We're willing to do that more, to the extent that it's practical and will help them.

But you raise a good point. I mean, we would just as soon not have to see them go through the same thing we did.

CHAIRMAN SIEGEL: Other comments?

MS. MERCHANT: Yes. I would just have one more and that's that as far as the inspection is concerned, we don't have any expectation that there are going to be a lot of violations. We are not seeing them and we don't expect -- so that when we say 72 percent of the letters fall into the category three, it's not -- you know, part of what it is, we need to find out whether it's going to bear

out on inspection. But at this point in time, we have no reason to think that we're going to have a huge number of violations as far as this is concerned.

CHAIRMAN SIEGEL: A general question in terms of elements of QMPs that go beyond what's in Part 35. It's my understanding that you are not treating those as license commitments, or are you?

MS. MERCHANT: No.

DR. GLENN: No. There is no tie-down of the QMP.

MS. MERCHANT: None at all, none.

CHAIRMAN SIEGEL: Okay, well, that's fairly important.

Any other comments on this? Good.

Thanks, Sally.

MS. MERCHANT: Thank you.

CHAIRMAN SIEGEL: We'll move on to our last item before lunch, the issue of re-examination of NRC's enforcement policy, another very popular item.

Mr. Brach will present this to us.

MR. BRACH: Good morning. I'm Bill Brach. I'm the Deputy Director to Carl Paperiello. I guess this morning I have the honor of being in the hurry up and finish so we can go to lunch time slot, but I'll try to keep within the reasonable time slot, the 30 minutes here.

What I'll be talking about this morning is the NRC's re-examination of the enforcement policy. I want to stress this is an agency-wide effort, where we're looking at the enforcement policy which is contained in 10 CFR, Part 2, Appendix C, and stress that it applies to all NRC licensees. That's commercial power reactors, materials, fuel facilities, as well as medical licensees.

Not like Sally, I didn't have my telephone number up here. But I'm sure if you call Sally's number, she'll relay a message to me.

DR. GLENN: He's already got your Internet address. He figured it out.

MR. BRACH: This past July, the Executive Director for Operations formed a task force to conduct this review of the enforcement policy. The task force is chaired by Jim Lieberman, who is head of the Director of the Office of Enforcement. The review team consists of the Deputy Regional Administrator from our Region 2 office in Atlanta, the director of the Office of Investigations, the associate director for reactor projects in NRR Reactor Office, the deputy assistant general counsel for enforcement and myself, representing the NMSS materials and fuels and medical licensee programs.

Simply stated, the objective of the review is identified in the billets here. One is asking, are the

defined purposes of the program appropriate? Then secondly, are those purposes being implemented through the procedures and programs that NRC has in place? And then thirdly, of course, to be recommending from the task force review activities changes to the enforcement program. Now, to help you as far as understanding what these purposes are, the next slide, slide two, I have out of 10 CFR, part 2, Appendix C, provided a brief summary of what the defined purposes of the enforcement program are.

You'll recognize the first billet is a fairly standard statement within NRC purview on programs. Our basic responsibility of protecting public health and safety, common defense, security and the environment. What I've listed in the four items as far as the four objectives are, really what are the focus of our review activities. That is, is the enforcement program assisting and ensuring compliance? Obtaining or achieving prompt corrective action? Deterring licensees from future violations, as well as encouraging licensees for improved performance?

Now, in addition to our executive director's charge to the task force to look at the purpose of the enforcement program in concert with those four objectives, we had five additional areas identified that we were asked to review. Now, as you're looking at these five tasks, you'll note the very first billet. Of the five billets,

some of these are a little easier to assess than others. Just for example, in looking at assessing or determining the balance between deterrence and incentives. At best, you might say that's a qualitative and maybe, perhaps, a subjective determination. And contrast that to say, for example, the third billet dealing with amounts of civil penalties, there you have something that's quantifiable. And to some extent, you may be able to assess the effect of a civil penalty monetarily on the well being of a company. Again, stressing that we're looking at policy as it applies to large facilities, such as large commercial reactors, large electric utilities, and as well as a supply to small companies such as a small radiology -- a one or two person organization or licensee.

I want to stress the fourth point. This is one area that's really of importance on the NMSS side of the house where there are -- differences in the size of our licensees. Some institutions, some fuel facilities, clearly are fairly large, but a number of our licensees, some medical licensees are fairly small in numbers of people and size of the program. So, we want to, in looking at the enforcement program, be specifically looking at should the continuation of a single policy as applied across all NRC programs be the same, or should there be differences?

I want to identify the very last item, the open enforcement conferences. That was one that was added on. The Agency, throughout the last two years, I believe it is now, has had what I'll call a pilot program of having a few enforcement conferences open to the public. Heretofore, those were meetings that were closed. They were meetings before the NRC and the licensee where there would be discussions of the violation, the corrective actions. It would be an information gathering on the part of NRC and an opportunity for the licensee to discuss their perspectives as far as why the violation, and also the actions they've taken. Over the last about two years now, we've had a pilot program where a few of these have been open. We were asked as part of our overall review, to try to bring closure to that activity as well. Closure from the standpoint of a recommendation of how best to proceed.

I want to spend a few minutes now just going over what the approach of our review team has been for conducting this review. As I noted, we started last July when the team was formed and we put together an overall strategy that I'll say identifies three separate prongs. One is, we're interested in learning from what other federal agencies do in a regulation of their programs. Not that we'll be trying to necessarily copy or replicate other programs, but from the standpoint if they are placed in

very similar situations as we are in regulating an industry, and to the extent they have experiences or lessons learned that we should be looking at and trying to learn from, we want to try to do that.

In that context, we sent over 20 letters to other federal agencies to ask them questions and ask for input on their enforcement program. Right now, we're in the process of arranging meetings with a select few of those agencies to sit down and get a better understanding with regard to particulars of their enforcement program and how we might have lessons learned for ourself from that part of the review.

The second part is we wanted to look internally. That is, we wanted to, within the Agency, touch base with our regions and with our program offices with regard to input from the standpoint on the NRC side of this equation, as far as our experiences from implementing and using the program. We visited all four of our regional offices and have met with all the program offices directly, as well as receive written response on input as to recommendations, suggestions on changes to the enforcement program.

The third prong is to get and solicit input from members of the public. As noted in the fourth billet, we issued a Federal Register notice in August of this year,

had a 60 day comment period. We did something differently than we've done on a lot of past Federal Register notices. On this particular notice, we sent out letters to every NRC licensee as well as a large number of industry organizations, associations, public interest groups, and agreement states, soliciting public comment. We sent out over 8,000 letters requesting their input. As a note, the comment period did close late October on the Federal Register notice.

Now, I want to spend a few minutes going over some of the questions and issues that were raised in looking at the enforcement policy and are included in the Federal Register notice. If a few of you all have jumped ahead to look at page 6 as far as what our recommendations and conclusions are, there's not an omission in the paper. I wanted to stress, we're right now are in the middle of the review. At the end, I'll discuss our plans and schedules. But we are in the process right now, of reviewing public comments.

I'll note that as with regard to comments received, as I mentioned, we mailed out over 8,000 letters to organizations and licensees, and the comment period has closed. We received approximately 50 comments. Of that breakdown of the 50, we received about five comments from medical licensees, medical facilities, or individuals

associated with medical facilities; three comments from agreement states -- well, three comments from states: two agreement states, one non-agreement state. And so far, I've personally reviewed about one-third of those comments. So, some of the comments I'll be offering as I run now through some of the issues will reflect what I've seen so far. The -- one is not an final nor exhaustive review of all the comments yet.

CHAIRMAN SIEGEL: Are you surprised you got only 50 comments?

MR. BRACH: In all honesty, I thought we would receive more, yes. That's one reason I mentioned, we did send letters out to every licensee. And realizing that to take time to review the NRC's enforcement policy, it's a number of pages of the 10 CFR, as well as the Federal Register notice itself, it contained over 100 questions. We were not trying to fashion such a long, detailed questionnaire that would be too onerous or burdensome, but we were trying to ask open-ended questions to solicit input or comment from licensees, the industry, the public on different aspects of the enforcement program, genuinely asking for input. I honestly had expected we would receive more.

CHAIRMAN SIEGEL: Yes, I would have thought so, too.

MR. BRACH: Out of the Federal Register notice, I've picked seven topics that were really more germane to NMSS, Nuclear Material Safety and Safeguard program's medical licensee programs, and areas of interest. There were some others that dealt more principally on the reactor side of the house, asking questions on enforcement discretion in program areas on the reactor side.

What I want to do is run over these seven. I'll give some perspectives on some of the questions asked and also, just an initial indication of some of the comments received. Again, this is just based on my personally having reviewed roughly about a third of the comments and it's not at all a conclusionary in any regard.

First, we started off with a very basic question: what's the purpose and objective of the enforcement program? Does it appear appropriate? Generally, the comments were quite supportive. Now, there were one or two comments that I read so far that were not at all in that vein. But the majority of the comments that I've read were generally supportive that the purpose and objectives of the enforcement program are right. But what they did raise -- and I think this is an important point -- is that with regard to implementation of the program, that sometimes the safety focus of the NRC could use sharpening and I'll say, being pulled back more to keeping a focus on

safety and less with regard to implementation of a rigid proceduralized type of program. I think that's an important point.

On the issue of severity levels, if you're familiar in the enforcement program, there are five severity levels. We classify violations in five severity levels, with severity one being the most severe, severity five being the least severe. Generally, the comments were supportive that that's roughly an adequate breakdown of classification of violations. But there were comments that asked that we provide more definition, more guidance, more examples on the severity levels to help get a better understanding as far as the types of violations and how they're classified.

Coupled with one comment that came from a reactor licensee, but I think it's important. If you're familiar with the enforcement program, we have what's called a supplement that gives examples of severity levels for different types of operations and different program areas. One of the comments that I was reading late yesterday was pointing out a need to keep a safety focus as you walk from one program area to another. The example was raised on the reactor side of the house, dealt with safeguard security violations as contrasted to radiation protection and operational type violations. I think,

again, that was an important message to receive, that we need to keep that safety focus so we're consistent across the board.

The third topic dealing with enforcement conferences. The comments that I've received were all in favor of open enforcement conferences for comments received from non-licensees. That is members of the public, industry organizations, public interest industry organizations. Generally, comments from licensees were identifying difficult and frankness in exchange of information in an open forum. There is one point on the enforcement conferences in the comments that I have seen that I think also is important. We generally hold an enforcement conference when there are one or three objectives to be obtained. One, that NRC feels that we need to learn more information about the violation; need to learn more about the corrective actions taken by the licensee; or third, I'll say a message or the safety significance of the findings needs to be more clearly and directly conveyed to the licensee management.

I mentioned that because a good number of the comments I've seen were observations -- and these were from licensees -- that they felt enforcement conferences, while important and necessary, NRC needs to keep an open mind with regard to the enforcement conference in that the

perceptions that the NRC has already reached a decision and the enforcement conference was just a step in the process that had to be conducted. So, I think, again, that was another important comment that I've seen in the comments today.

I included a fourth item, notices of violation, mainly to point out that between the reactor program and the non-reactor program, there is a difference in how notices of violation are oftentimes communicated. In the materials program, the use of what's called a Form 591 is a form which I imagine a number of you all have seen, where the inspector may at the end of the inspection, leave with licensee management a pre-printed form that the inspector has filled out and checked off whether violations occurred, what the violations were; or whether it was a clear inspection, no violation; or if there were violations, a brief summary of the violation and a commitment on the part of the licensee management to take corrective actions and what those actions from the standpoint of it having been explained to the inspector.

That, oftentimes, will be the end of the documentation of the inspection with regard to what the inspector generates, or what the licensee may see. That contrasts to the reactor side of the Agency where, for every inspection, an inspection report, a detailed report

is written, a formal notice of violation is written and prepared for every violation, including level four's and oftentimes, level five's.

In asking the question to the public on the use of notices of violations, again, one of the comments dealt with the safety significance of violations and don't be solely always compliance-oriented to keep us focused on safety. But also, we were looking for the standpoint of any comment with regard to increased use of the Form 591 in other program areas. There again, I've only looked at about a third of the comments and it's kind of a mixed bag. Some like it, some don't.

The fifth category is civil penalties, one that's gained -- clearly, that's the one that you read about in the press. That's oftentimes what will make a -- not a headline, but the lead-in for an article with regard to the amount of the civil penalty assessed to a licensee. Comments here were reasonably expected from the standpoint of both licensees and members of the public, dealing with the questions with regard to the amounts and the disparity of civil penalties with regard to the type of licensee to which the civil penalty is being applied.

There is an aspect, again, going back to the comment I'd offered about looking at the enforcement policy with regard to its application to small licensees and large

licensees. I was interested, a number of the licensee comments, as well, pointed out that some civil penalties, depending on the size of the company, are I won't say a nuisance, but they don't have as major of an impact as they do, clearly, for small licensees where a civil penalty has not only the media attention, but also the direct financial impact on the livelihood of the company.

We also asked questions about the amounts of the civil penalty and are the amounts right? Should they be escalated? Should they be indexed to inflation? Should there be other indications that we should be looking at as to base amounts of civil penalties? There, from what I've seen, it is pretty a consensus. Of course, it's like asking, do you want to receive a larger civil penalty? But pretty much the consensus was that with the exception of smaller licensees where the financial impact clearly has a direct impact, it's not so much the size of the civil penalty, but it's the occurrence of a violation at that level that requires the Agency's attention to proceed with what we call escalated action that will result in a civil penalty.

The next item dealing with adjustment factors. This is the one area I'll identify, if we go back again, to measuring deterrence and measuring incentive. Adjustment factors is the one aspect of the enforcement program that

clearly lays out an area for incentives to the licensees, based on one, the occurrence of a violation. That violation may be, in part, mitigated based on licensee identification versus NRC identification. It might be mitigated in whole or in part based on the adequacy and promptness of corrective actions to fix the problem, and also based on past performance. Comments that I've seen in the comments so far all clearly support the continued use of adjustment factors. As I point out,t hat's the one area where the incentive to improve as a result of NRC enforcement actions is present.

The last item dealing with timeliness of actions. This is one area I had expected we'd see more in the way of public comment. The only comments I've seen so far have dealt with questions/concerns raised where as a result of a violation, the NRC conducted an investigation, or Department of Justice was perhaps involved, to review. They were just raising questions about, simply put, the amount of time it takes from the identification of the violation to the NRC completing an enforcement action.

Now, that's a very brief overview of the Federal Register notice and some of the comments received to date. As I mentioned, there is not a page 6. We're right now in the middle of the review. Our schedule as currently laid out, calls for completion of the effort by

January. My personal observation is that I think it will be a little bit later than that. As I mentioned, we have meetings that we are right now int he process of trying to arrange over the next few weeks with representatives from other federal agencies. That, coupled with completion of our review of all the public comments and then leading to a consensus within the team and then going outside to our various offices for recommendations and changes, my guess is it will be after the January date.

Let me stop there. I'll answer or respond to any questions if anybody has any.

CHAIRMAN SIEGEL: Dan?

DR. FLYNN: I have a question or a comment.

In radiation oncology, let's take an example where you have a large licensee who has well staffed. And let's say in teletherapy, they have a program by which a prescription is written, calculations are done, doses are being delivered daily. And let's say a big physics staff has physicists who are double-checking other physicists. The initial calculations are done by one physicist. They're being reviewed on a weekly basis by a second and then a third physicist. This large licensee has a well developed quality management program. They are more apt to discover problems occasionally as they have thousands of treatments per month.

As opposed now to a small licensee which is not well staffed, has one physicist or dosimetrist. The calculation is done once. It's checked by the same person who has done the calculation, who is less likely to discover their own error. Violations occur, but the licensee either doesn't discover them or discovers them and doesn't realize it qualifies as something that's reportable. But as you collect information, you will get the false impression that the large licensee is deficient in the quality point of view. Yet the small licensee who doesn't report anything must be doing a great job.

So, my question would be, as you discover, let's say, a misadministration, but you discover the misadministration not because the licensee has reported it, but because it becomes known for some other reason like a source setting off alarm in Ohio from a facility in Indiana. Or let's say, the NRC inspector goes to the facility and asks to read the Radiation Safety Committee minutes and discovers that things were being discussed in those meetings that were actual reportable misadministration by the definition, but weren't being reported, how do you define in terms of severity level -- because I can't quite remember the definitions way back when when I first read them -- if a licensee voluntarily reports a problem and in terms of civil penalty versus a

licensee who doesn't report a problem. It may be that they didn't realize it was a reportable problem. Or let's say in another scenario where they should have realized it was reportable. It was clear that it should have been reported but wasn't. When I first read the severity level several years ago, it seemed to me that failure to report, in some instances, was less of a severity level than the actual problem itself.

MR. BRACH: Well, there are two aspects. One, failure to report would be another violation of what it was they were to have reported. We need to look at those --

CHAIRMAN SIEGEL: Step a little closer to the microphone so the transcriptionist can hear you.

MR. BRACH: Oh, sorry.

With regard to the failure to report, there's an event or an activity that they failed to report, so that both the failure to report and the occurrence on whatever the activity was or event they should have reported, would be looked at in concert.

Now, your other point with regard to identification, say, by the licensee and their implementation of the program versus identification by the NRC inspector during an inspection, or if it was self-exposing as a result of some other event, that -- when I was talking before about the adjustment factors with regard

to the, if you will, mitigation or escalation? That would be addressed in looking at the adjustment factors with regard to -- or would be considered with regard to who identified the event and how it was identified.

DR. FLYNN: I think if the licensee has a very aggressive program to identify reportable events, let's say, you should encourage that. In other words, what you want to do is encourage reporting.

MR. BRACH: Well, that's what I'm trying to say. One of the adjustment factor -- actually, the very first adjustment factor, I believe, is called a debt licensee identification. That's in there, I'll say, from an incentive standpoint that if the event were to occur and is identified by the licensee, that one of the considerations for determining should there be a penalty would be the consideration of the adjustment factor of who identified it. If it was identified by the licensee, that clearly is the incentive to the licensee to identify it because that would also, perhaps then, be a mitigation of any penalty that might result from the occurrence of that violation.

There are other factors that would be incorporated too, as well as corrective actions. If it's identified by the licensee, but then subsequent events are also identified, but corrective actions on the first or

second either were deficient or not complete, that would also be part of what would be looked at. But who identified the violation, clearly, is one aspect that's looked at. The incentive would be for the licensee to identify as far as perhaps mitigating any resulted penalty that might come from the event having occurred.

DR. FLYNN: My opinion would be that that should be a very strong factor.

MR. BRACH: In some of our deliberations, there are three of the factors that we spent quite a bit of time on, looking at, with regard to incentive, I'll say. It deals with licensee identification -- who identified it, NRC or the licensee? Corrective actions being not only prompt, but complete or, let's say, adequate, and the third one being looking back from a repetitive standpoint. Is this a repeat problem or violation in the same area, which would give you an indication on the adequacy of prior corrective actions. So, those three all need to be looked at together.

CHAIRMAN SIEGEL: Lou?

DR. WAGNER: I'd like to just make a comment about the severity level issues. I've been a proponent for some time that excessive paperwork and documentation, record-keeping and paper exchanging is contrary to the principles of ALARA. ALARA says we must keep our exposures

as low as reasonably achievable and we can't do that if we have to spend too much time in our office documenting things galore, that are needless. This happens continually.

The severity level five issues are often just paperwork problems that do not really impact any safety issue, but they are non-compliance issues. I would strongly encourage that they not be issued as violations. Your idea of non-cited violations is very good. I would even go further and I would just say they are items of non-compliance. In that case, they can be corrected very simply and should use a very minimal of record-keeping to document such violations.

MR. BRACH: Okay. You've pointed out one of the areas we had asked questions on, dealt with severity level five violations and the extent to which and how NRC would communicate that to a licensee, whether through a normal -- I'll say normal -- the past routine practice of a notice of violation, if that were to be documented in the inspection report as a non-cited violation. That also would be contingent upon appropriate corrective actions either already taken or committed to be taken by the licensee at that point in time. But that is one area we were looking at.

Specially, again, levels one through five with

five being the least safety significant to all the violations. Oftentimes, the more the procedural paper type of violations are in that lower category.

CHAIRMAN SIEGEL: Question. A lot of the data you're gathering in discussions with other federal agencies is going to be looking at opinions and subjective impressions. Are there better scientific measurement tools to figure out whether an enforcement program is set at the right level? Have you all considered randomizing your enforcement options to control the experiments to find out what would happen if we deregulated or de-enforced this half of the licensees, and we continued where we are with this half of the licensees?

It seems to me that the regulator's viewpoint on this has got to always be, we can't possibly retrench. And so, consequently, you never learn the consequences of what would happen if you backed off. General history teaches us that you'll continue to ratchet upwards over time.

MR. BRACH: A couple of questions have been asked. The first one, in our going to the other federal agencies, is to genuinely learn how they've gotten to where they are in their enforcement program and what they may be doing -- they, being the other agencies -- that we ought to be considering in ours. It's not solely from the

perspective of what can we add to our program -- you know, a new wrinkle, a new enforcement tool -- but from the standpoint, stepping back from the fundamental policy, should we, NRC, revamp?

Your second question on a pilot sample, no. Personally, I've not considered that. I'm not aware of it being a candidate. That might be --

CHAIRMAN SIEGEL: Well, maybe learn something from your Medical Advisory Committee. I mean, an enforcement program is a therapeutic intervention, correct? And the way in medicine we document that therapeutic interventions work is, we do randomized controlled trials to find out what happens with the drug versus the placebo, or the radiation therapy -- not so often -- versus the placebo, but perhaps versus surgery.

I would encourage you to consider actually gathering some real data about whether these enforcement programs work. Now, a lot of the time, you're operating almost at the noise level and you're operating at event frequencies that are so low that you'd have a hard time proving statistically that your therapeutic intervention is worth a darn. I recognize that scientific problem, but I suspect there are scientific tools that could be brought to bear rather than just finding out that licensees don't particularly like large fines, which I think you already

knew.

MR. BRACH: Yes. I appreciate it and I'll carry the comment back. As we're talking, there have been occasions in the past where maybe NRC has implemented a new rule or regulation or made a substantial change in a particular program area or an aspect of the program where enforcement has been held in abeyance for some given period of time to allow implementation of the new program requirements. but that, really, was not along those same lines as far as a sampling, as far as a controlled sampling of populations of samples or groups to somehow try to measure or assess. But I'll carry the comment back.

CHAIRMAN SIEGEL: Wishful thinking.

MR. BRACH: It might be a very difficult one to go forward with, yes.

CHAIRMAN SIEGEL: Dennis?

MR. SWANSON: Just as another comment and it goes along the line of deterrence and incentives. We always see the NRC publications and notifications of violations. It would be really helpful to the community, as inspectors go out and see things that are done better at one place versus another, if we got that information. Certainly -- identify good practices or things that are being done perhaps differently that you recognize as good practice, to let us know that information. That would be a

real help to us as a community. And that would be an incentive because it would be a positive thing, a positive identification.

MR. BRACH: I appreciate your comment. The one difficulty that puts us in is, as a regulator we are all the time guarded against putting ourselves in the role of either an advisor to, or a consultant -- not directly consulting, but putting us in a role where we are suggesting to a licensee how they could do their activity, I'll say, better as opposed to drawing the distinction between compliance and non-compliance.

I understand your comment. Sometimes an information notice is perhaps the opposite of what's being told in an information notice where we'll identify an experience of one or two or three licensees in a respective area and the difficulties they ran into. The corollary of that would be the example of the licensee that did those things in a better, or did the opposite, perhaps, of what was described. It puts us in a difficult situation if we're advising -- if we're communicating to a licensee in a way that might be advising them on a "better way to do" whatever it is they're doing when their current methods and activities are in compliance with our rules.

I understand your comment, but it puts us in a difficult quandary.

CHAIRMAN SIEGEL: But only because that's your mind-set. I mean, we've told the Commission at a briefing a couple of years ago that the whole concept of quality by inspection isn't necessarily the way to achieve what you want to achieve. Quality by TQM, CQI, continuous quality improvement might get you exactly where you want to be with a much less adversarial nature.

The notion that the way you get people to comply is to scare them with respect to the consequences may not be the best way to get people performing where you want them to be, especially since it has a high cost. The high cost is, as we've said before, it takes the good actors and forces them to do an awful lot to prove that they're in compliance that they might not have to have done otherwise. It creates a huge paper trail and a substantial personnel cost and resource allocation cost that may have nothing to do with the ultimate quality of the activity.

So, maybe once again, we'll encourage you to look at the paper by Berwick in the New England Journal of Medicine about six years and at least think through that concept again.

DR. FLYNN: You know, one way you could do this without actually trying to endorse someone's practice is that if you went to a large licensee and you found that their program was outstanding -- you can't maybe come out

and say that as an endorsing of their practice. Maybe with your limited resources, you could inspect them slightly less frequently and focus your attention on, let's say, the drunk driver who is always getting in trouble. Focus your limited number of resources and inspections on programs that may be problem programs.

DR. PAPERIELLO: We are doing that. There's a draft version of our Inspection Manual, Chapter 2800, that's going out to comments about the agreement states in our regional offices. In fact, that's what we are going to do. We are going to stretch out the interval for licensees who either have clear inspections or merely a violation noted on 591s.

Actually, there's a subjective inclination with the inspectors to go out more often for people who clearly have problems, and an unwillingness to back off on people who are performing well. What I'm going to do is change the procedures to coerce them to do that. So, yes, you're right.

CHAIRMAN SIEGEL: Good.

DR. WAGNER: Is there a way we can get a copy of that, that was sent out to the states? Could I get a copy of that somehow?

DR. PAPERIELLO: I don't see why not.

MR. CAMPER: Yes, it's to the regions, not the

states.

DR. WAGNER: Okay, but could I --

DR. PAPERIELLO: I believe we did distribute it to the agreement states, too.

MR. CAMPER: Oh, have we? Oh, good, okay.

MR. BRACH: Yes, a copy went to the agreement states.

DR. WAGNER: I haven't seen it, but I'd like to get a copy of that if I could.

CHAIRMAN SIEGEL: Other comments, question?

If not, Bill, thank you very much.

We are adjourned for lunch. Since we are 15 minutes late, we will resume at 1:15, John? Is that okay?

DR. GLENN: Sounds good to me.

CHAIRMAN SIEGEL: 1:15.

(Whereupon, the meeting was recessed at 12:14 p.m., to reconvene at 1:15 p.m., this same day.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:20 p.m.)

CHAIRMAN SIEGEL: Larry has one announcement he needs to make before we resume.

MR. CAMPER: Toward the end of the discission this morning, we were talking about the inspection guidance that Dr. Paperiello referred to in terms of making changes as far as lengthening the time for good performers and the link.

Now, that information has gone to the regions. It has gone to the states. And in the back of my mind, I was operating under the assumption that that was going to be releasable in January publicly. As it turns out, it is now in the PDR. So we will make a copy available to you promptly.

CHAIRMAN SIEGEL: And Judy reminded me if any of you didn't get my E-mail message or fax, this is the book, "Breaking the Vicious Circle" by our newest Supreme Court Justice Stephen Breyer. I urge everybody on the Committee and, actually, everybody in this building to read this book.

DR. WAGNER: I did look into that, Barry. And my secretary told me that the only place she could find it was at the Library of Congress.

DR. STITT: Oh, no. Borders Book Store has it.

DR. WAGNER: I mean in a library.

CHAIRMAN SIEGEL: It actually briefly went out of --

DR. STITT: Oh, in a library.

CHAIRMAN SIEGEL: -- print because it had to be reprinted because it sold so well when he was affirmed for the Supreme Court, but it's back in print again.

DR. STITT: Several people asked me if "Breaking the Vicious Circle" was some sort of sociology or psychology or dysfunctional family book, and I said "Yes."

CHAIRMAN SIEGEL: Yes. Okay. Let's go back.

DR. POLLYCOVE: Barry?

CHAIRMAN SIEGEL: Yes?

DR. POLLYCOVE: Just one quick comment about this. Did anyone see Joe Biden's response on McNeil-Lehrer when they were being confirmed? He spontaneously without Breyer saying anything jumped on him and said "Who are you to be substituting," talking about the book, "your elitist view when the public feels differently?" And it was a five-minute temper outburst in Congress. So maybe that's why.

CHAIRMAN SIEGEL: Were those Joe Biden's original words or did he borrow them from someone else?

DR. POLLYCOVE: I don't know.

CHAIRMAN SIEGEL: I don't report to Congress.

Let us continue. Now, next is a progress report on the National Academy of Sciences Institute of Medicine study. Pat is going to tell us what's going on.

NAS PROGRESS REPORT

DR. RATHBUN: Good afternoon. Thank you for the opportunity to report on the progress of the study being carried out by the National Academy of Science. I'm going to just talk about three things that are underway with the NAS. One is their meetings. Two is the committees, the subcommittees, that they have commissioned. And then the third is the papers that they have commissioned to date.

They held their second committee meeting on July 10th through 12th. At that time they introduced two committee members that are relatively noteworthy. One is John Villforth, who is a former executive from the FDA. And then the other is Ted Phillips, whom you may know, from UCSF. So those were significant additions.

There were two presentations of special note. Dr. Siegel gave his presentation representing the ACMUI. And Bob Alvarez, former Senate staffer, gave his position. It was really very interesting because Barry gave the normal talk on how hard we are on the regulation community and Alvarez gave the normal talk on how easy we are. So it gave the committee an interesting perspective, I thought.

And I know Barry is going to tell you more about that in a minute.

They had their third committee meeting October 13th and 14th. That was also an especially interesting meeting because each one of the NRC commissioners personally went down and spoke to them. They all encouraged the NAS to be fair and objective and stressed that they were not looking for any pat answers or preordained answers, that it was up to the NAS. And they were asking for a fair and objective report, but it was whatever they thought would come out.

In my view, that was a critical meeting. And I almost saw the NAS kind of change at that point. They had been kind of, frankly, milling around a little bit in my view. And at this point they sort of took off, marching smartly down the road in pursuit of something.

(Laughter.)

DR. RATHBUN: They also held a workshop at that time. And the transcript from that workshop will be available to you. Barry is going to speak to that later. And they held a full-day session on the quality management rule, which John Glenn represented the NRC as our person down there.

The next meeting is going to be in California in January. What a shame. But this is a critical, pivotal

meeting. This is their last meeting before they've got to come up with their draft or -- let me say it another way -- when they come together again after January, they will have to have the draft in their hand because by June of next year, they have to go into the National Research Council peer review process. So, really, they don't have much more time. Thus far, I have no reason to believe that they're not on schedule, and they're certainly well within their budget.

They have commissioned four subcommittees, which are very interesting and parallel to a large extent what we asked them to do. They have a committee on data and risk. They have one on regulatory issues. And they have one on quality management. And then they have another one, which is pretty much their creation. And that is on education and training.

Thus far they have commissioned four papers. One is the risk of exposure to low-level radiation, a second paper on the cost of NRC regulation, a third paper of misadministrations, and a fourth paper on regulatory issues. And they are still in the progress of commissioning some more. I spoke to them, actually, this morning. And they're hoping to play some more, but they weren't willing to discuss yet what they were.

They've had a lot of talks from the NRC in

addition to the commissioners relating back to your presentation this morning by Bill Brock. Jim Lieberman gave them a talk on the enforcement program. Stewart Treby, who is the OGC attorney, gave them a talk on the whole issue of OGC's role in regulating, and then Richard Bangert on the agreement states.

That's really all I have to tell you about the NAS, but I would be happy to answer any questions that you might have about their study.

MEMBER NELP: It wasn't clear to me who the heavy hitters might be in the NAS that are relating to the medical use issues that we ordinarily address in this Committee. I know I saw the name Hendlee. I presume that was Bill Hendlee. Were there other people that we would be familiar with?

CHAIRMAN SIEGEL: It's a broadly based group that has all different kinds of expertise, as we heard at the last meeting. The chairman is Charles Putnam, who is a diagnostic radiologist and actually now a Vice Chancellor for Medical Affairs at Duke University. I think that's what he is these days. He keeps changing jobs.

Barbara Croft is on the committee, -- so she's quite familiar with our issues or nuclear medicine issues -- Ted Phillips for radiation therapy, a physicist named Dave Goodin from Oklahoma City. And then there's a mixed

group of other people that I really have not known much about, but they were very interesting folks to listen to their kinds of questions. There's some --

DR. RATHBUN: Cardiologist. What's the name of the cardiologist, Dr. Pollycove?

DR. POLLYCOVE: Barry Zarret.

CHAIRMAN SIEGEL: Oh, Barry Zarret; right.

DR. RATHBUN: Barry Zarret.

CHAIRMAN SIEGEL: There's a couple of lawyers. There are some people who are into -- risk assessment-type folks. So it's a good --

DR. RATHBUN: Lester Lave, who is an economist, who has done a lot of work on nuclear power plant risk, is working with them on that. He's had a lot of experience with the NAS.

I can bring you the composition of the group. I didn't realize --

MEMBER NELP: I think it was probably passed out.

CHAIRMAN SIEGEL: It was at the last meeting.

DR. RATHBUN: Okay.

CHAIRMAN SIEGEL: In my humble opinion, I think that it's a very well-put-together group to provide a broadly based answer that isn't going to come up with any one constituency's agenda. It's going to give an answer

that "This is our critical analysis of the situation." And I think that's the way it should be.

DR. RATHBUN: Well, they've brought the right people together. Their methodology of holding workshops and -- oh, they also have taken two site visits. So they're going out in the field. They're going to hospitals. They're going to licensees. They're doing the right kinds of things that it should work out.

MEMBER NELP: Good.

DR. WAGNER: Are they visiting any facilities in agreement states? Do you know?

DR. RATHBUN: Yes, they are.

CHAIRMAN SIEGEL: I would just point out that in your packages, you should have had a copy of the transcript of my presentation as well as the slides, which many of you, most of you, saw before I gave the talk there. And I really didn't present anything that we had not presently presented to the Commissioners because I figured that was the best source of materials to use as the ACMUI briefing.

Whether it came with this package or whether I inserted it, you also should have received the sort of press release versions of the comments made by each of three Commissioners at the October meeting. And I have the transcript of the public meeting that was held on October

12th, a couple of hundred pages worth, which I'm going to turn over to Tori. And any of you who wants to have a copy of this transcript can get it copied and sent to you.

MEMBER BROWN: Barry?

CHAIRMAN SIEGEL: Yes, Pat, you can have it.

MEMBER BROWN: Barry?

CHAIRMAN SIEGEL: Yes?

MEMBER BROWN: The only thing I noticed in using the slides and reading your presentation was that when we gave the presentation to the Commissioners, in several cases where there was a dissenting opinion, that appeared. But in here it seemed like there was a pretty uniform group.

CHAIRMAN SIEGEL: I actually made a few statements, I thought, where I said that "Not everybody on the ACMUI agrees with this viewpoint."

MEMBER BROWN: Okay. I'll read those closer.

CHAIRMAN SIEGEL: I tried my best to be sensitive to that.

MEMBER BROWN: I just wanted to point that out because the slides were the overall group opinion.

CHAIRMAN SIEGEL: Correct. Okay. Next. We're on brachytherapy issues, fractionation in particular, plus other therapy issues. Trish Holahan and Judy are going to help us out here.

BRACHYTHERAPY FRACTIONATION ISSUES

DR. HOLAHAN: Dr. Stitt has been working with me, and we've had some numerous discussions in terms of what's going on and helping develop the questionnaire and those issues. Since the last meeting, we have been developing a program where we're looking sort of specifically at some of these brachytherapy issues. And, as the slide shows, I'm the project manager for some of these and working on that.

This slide is an update of what you saw at the last meeting, basically looking at the trending of the number of misadministrations since '91. Basically, again we have seen a spike in the number of teletherapy misadministration in '92, but that has been pretty much leveled off. Manual brachytherapy has been relatively constant. As I say, that's up to the end of June in '94. And there have been a couple of more since then.

Remote afterloading brachytherapy. These are misadministrations, as defined. And I'll get into it a little bit more. This doesn't include errors in a single fraction of an HDR treatment.

Strontium 90, the eye applicators, we've had two up to the end of June. And I believe there has been one since that time. And in the radiopharmaceutical therapy, there have been at least one more since the end of

June, one in August. What I'd like to do is go through some of them.

You should have all found at your places, I think you all now have a copy of the slides that I'm using. And also you have a copy of some of the case summaries of some of the recent misadministrations and also other events that have not been classified as misadministrations but focus on some of the areas that we do have concerns and that we're looking sort of for some input.

These are some of the types of brachytherapy events that we have seen in the computer errors, both in data entry and also either defaults within the computers or actual malfunctions in the computer.

Treatment planning, misplaced sources and dislodged sources. I'm going to sort of differentiate a little bit between that. Misplaced is sort of where they've actually been implanted in the wrong location or they have fallen out of the applicator, the applicator has been inserted, source has been loaded, source has fallen out without the authorized user recognizing it and has either lain in the patient's bed next to the patient or something like that. Dislodged sources is where we're seeing that the applicator or the ribbons have shifted slightly: The applicator slips by a centimeter or two; the ribbons move, but they're still within the treatment

volume.

Patient intervention. We have had numerous cases where either the patient has moved about in bed and the sources become dislodged or the patient has actually pulled the source or the ribbons out of the treatment site.

And finally and in many of these is human error is also involved, either in the data entry, loading the applicators, the sources that have been selected for treatment.

What I'd like to do is -- and I know that a number of you have been consultants on recent misadministrations, but some of you may not be familiar with some of the recent cases. And I'd just like to highlight a few just to sort of give you the spectrum of what we're looking at.

In manual brachytherapy, we recently had a case where the patient -- it was a prostate implant -- was to have 112 seeds implanted. The seeds that were implanted were 10 times the activity that was prescribed. The dose consequences were significantly mitigated from if they had just left the seeds there. The original planned dose was 160 Gray.

The same day of the implant, they removed 69 of the seeds by doing a prostatectomy. And then they were able a couple of days later to surgically remove 15

additional seeds.

There are medical consequences in that case. The patient has had problems, especially with where some of the remaining seeds have been localized. One or two have remained. And so we're continuing to follow that case.

The direct cause was the failure of the dosimetrist to verify the activity of the seeds prior to bringing them up to implant. The sources were ordered telephonically. Apparently there was a miscommunication in the ordering. So what was received was 10 times the activity. However, the shipping label did indicate the correct activity. When it was entered in, it was logged in correctly, but when the dosimetrist pulled the sources out, he just believed it was an error in the entry.

So that's one case. As I say, that one is also written up in a little bit more detail in the case summary you've got. A second one is several patients received brachytherapy doses greater than intended because of errors that were in a treatment planning computer in the dose calculations. And 11 patients received doses 5 to 30 percent greater than prescribed. So not all of the cases were misadministrations.

What happened is a computer file had been lost. They had manually reentered the data. There was a default in the computer that the users were not aware of. The

output of the computer system was inadequately verified. They used the incorrect table to verify the output. And, therefore, they weren't able to detect the error. It appeared that it was within five percent, when in actual fact it was on the order of 25 percent.

In both of these two cases, part of the complicating factor was it was a lack of management oversight of the program on the part of the licensee management. There were contractors involved, and the licensees relied entirely on the contractors.

DR. STITT: Trish, let me toss a comment in here. She gets to do all of the work, and I think we agreed that I'll sort of interject some things here and there.

DR. HOLAHAN: Please.

DR. STITT: All I want to do, I want to make a comment because it's going to come up later. Certainly the first case that she described, this man has major sequela, including a perineal-urethral fistula that will probably never heal and some other major problems. So the medical consequences of this particular prostrate implant are significant.

There's something that's ironic about the second group of cases that are misadministrations. At least a portion of them were by definition. However, the

interesting thing is that because of these increased doses that all of these patients received, it put them within a much better therapeutic range.

This whole group of patients is treated at what most institutions -- I'll be very careful, but I will say would be called under-dosed. Their practice is very low dose to try to control these early stages of cervical cancer.

Again, I'm bringing those up as comments because then they come up a little bit later as we try to look at some of those issues.

DR. HOLAHAN: In addition, too, this was also, in addition to external beam.

DR. STITT: Right. That's right, another important point because we'll get to that later. For a lot of the issues in therapeutic radiation oncology, we're talking about combining brachytherapy, be it high dose, low dose, pulsed dose. It doesn't matter, just isotope work with external beam therapy. And it makes it even more complicated, but there may be some truth to be found in trying to put some of those doses together as we develop new regs.

MEMBER NELP: Dr. Stitt, in your work as a general rule, how close do you think your estimates are? And what variance do you have from your estimates putting

it on a workday basis?

DR. STITT: As far as what you're actually giving or where you want to be?

MEMBER NELP: Well, you calculate the dose, and it's an estimated dose. How close do you ordinarily think those doses are to reality? They vary plus or minus 10 percent of the facts or --

DR. STITT: Well, the problem with brachytherapy is --

MEMBER NELP: It's hard to confirm it.

DR. STITT: -- that, number one, I am at the total good graces of my physicist, which is why I try to work very closely with him because I in general have no way of verifying other than going through check sheets.

The biggest problem with brachytherapy is that you move two millimeters away from a source. And your dose is just dramatically different. So it becomes hard to answer that.

In the overall scheme of things, clinically as a physician I'm looking at a range of doses. And you're commonly using external beam therapy plus brachytherapy to come up with some places where you want to get to as an end result. And there are different ways, different permutations. It's very common that you're going to adjust some portion of that, either your brachytherapy or your

teletherapy or some of both, depending on a variety of things.

Even though something as simple as Thanksgiving weekend is coming up, clinicians across the country are making adjustments in their doses. This is nothing to do with misadministrations, but this is the practice of medicine. And so we need to if we're looking at regulation make sure we don't have something that's so minutely detailed that you simply can't carry out medical care.

MEMBER NELP: The reason I mention this is plus or minus 25 percent may be the real world.

DR. STITT: You're right.

MEMBER NELP: That's why my --

DR. STITT: And Trish will get to the questionnaire. The questionnaire -- I mean, I helped her develop this. I'm not saying, "Trish, you did this all by yourself. Don't look at me." But it's very hard to answer the questionnaire.

And that's one of the things we've gotten back from the folks who have tried to. We've asked you to pick a line, 10 percent, 20 percent, 30 percent. And the responses that are most helpful are "Wait a minute. We can't do that. We can't mark a box" because you're right. And plus or minus 25 percent may well be perfectly acceptable.

MEMBER NELP: When we were --

DR. STITT: That's why I brought up this comment about the misadministration which got these people a lot of forms to fill out, site visits, fines, actually put these patients at a dose level that most people in the country would name as their lower end of the dose rate.

MEMBER FLYNN: I know when I was in the task force with my prior physics training, I was concerned initially when the quality management was written that we would be looking at dose gradients, for example, like Judith was alluding to, but we went to the concept of calculated administrative dose or instead of worrying about if you're going to prescribe your dose point on a very steep dose gradient with the doses changing very rapidly, we've got another way of prescribing. An alternate way of prescribing the dose or the prescription was the total source strength in the time that you intended to have the sources in place.

I think generally the calibration of sources -- is that what you're asking? The physics people I think assume plus or minus five percent is a --

MEMBER NELP: No. That's easy. That part of it's easy. I'm talking about what you think actually arrives in terms of interview deposit in the tissues, like I do a lot of internal radiation dosimetry estimates and

correlating with biopsies. And if I get within 20 percent, I think I've done a great job. And that's a different ball game. But I'm sure that's why we emphasize the word "estimates." I just wondered what sort of the rule of thumb is on a working day basis, how close you really think you are when you make an estimate.

DR. HOLAHAN: Okay. As I say, I don't want to belabor some of these too much. I just want to sort of point out the different types of things that we're saying and where I'm coming up with a list of the various areas that we're looking at.

This is a series of HDR brachytherapy misadministrations at one facility where eight patients who were to be treated for cervical cancer inadvertently received an exposure to their knees. What had happened was the hospital was using the wrong length connector tube on the HDR device. And so when they set up the source distance and everything else, it remained outside the patient, instead of going inside, the transfer tubes. They were 50 centimeters longer than expected.

In most cases there were no consequences except for one patient demonstrated definite erythema. And, again, this was a failure to verify the treatment parameters. It was somebody that was different. A second independent check wasn't being done that everything was

verified.

CHAIRMAN SIEGEL: Were the cancers being under-treated?

DR. STITT: Yes. They got zero dose. I was a consultant on this one, too. Actually, the woman who had the most significant injury, she has a third degree injury there, fairly good size of deep moist desquamation and necrosis of the skin.

They were all post-op endometrial cases, and none of them received treatment to the treatment site. They all came back for repeated treatments. And this brings up a whole issue of knowing what your equipment is doing.

DR. HOLAHAN: Okay. And then, obviously, as we mentioned before, we wanted to look at dose fractionation. In the regulations in terms of the definitions, the definition for written directive for teletherapy includes the dose per fraction be included on the written directive. In the definitions for misadministrations, one of the criteria for misadministration is looking at the difference between the calculated weekly dose, weekly administered, versus your weekly prescribed dose. And, again, this is getting at the issues recognizing that it's given over multiple fractions, that you could have a series of errors that the dose in a week could be significantly different

and could have some implications or consequences.

However, for brachytherapy, radiopharmaceutical therapy, and gamma stereotactic radiosurgery, there is no mention in the regulations of dealing with fractionated treatments. The definitions for brachytherapy and gamma stereotactic radiosurgery talk about total dose. For radiopharmaceutical therapy, it's the administered dosage. There is no reference to total dosage, but, again, there's also no reference dose per fraction.

So we looked into this a little bit more. And we have had a couple of instances where there is infractionated treatment. And it can be an error either in temporal or spatial in terms of fractionation. I'll get into that in the gamma knife case.

This is a fractionated HDR error where there was an error in the treatment parameters. The HDR device accepted information in the European date format. It was entered in the American date format, which is month-day-year, as opposed to day-month-year. And so the calculation was done for the decay of the source at a longer time. And so the prescribed was 6 Gray, and they actually administered 10.4 Gray.

However, it was caught after that treatment. And so the total dose was still within -- it was to be two 6 Gray fractions, and it was within 20 percent of the total

dose. So it is not by definition a misadministration, but it was a significant error. And, again, a contributing factor was no verification of the data entry.

We've seen this in radiopharmaceutical therapy. And I'll discuss a little bit further as to why this is a misadministration and the others are classified as incidents or errors. This was three administrations of rhenium 188 antibody. And for the second treatment, the authorized user had changed the written directive to reduce the administered dosage, but it wasn't verified. The technician didn't verify the dosage against the written directive and actually gave the higher dosage. Following that because of the possible dose to the bone marrow, the third injection was cancelled. And, again, it was poor communication and failure to verify the dosage.

Just recently there was an incident with a gamma knife, gamma stereotactic radiosurgery, that in one treatment there were to be 10 treatments within one period of time where it was spatially moved. And during the 6th of these 10 target positions, the couch failed to withdraw from the unit. And so the patient was treated for longer than intended at this one particular site.

Actually, in this case the backup unit also -- it was a failure of the hydraulic valve. And that also operated the backup emergency. And so eventually they had

to manually extract the patient.

Overall dose consequences were minimal because the unintended dose was only about five percent of the total dose for the day. So there were no expected consequences. And, again, because it was only five percent, it was not determined to be a misadministration. But it obviously has significant implications in other cases.

I know these are brachytherapy issues, but I wanted to address very briefly radiopharmaceutical therapy, too, because the list of issues and questions that you have also addresses it.

This was just a recent misadministration in which the wrong patient received four millicuries of strontium 89. And so there was significant dose to the bone marrow and the bone surface. And it was a failure of the technologist to read the syringe label.

Okay. Well, we went out to the ASTRO meeting and had an exhibit out there. And we had a list of issues and questions which, as Dr. Stitt --

MEMBER NELP: May I make a comment at this point? I was consulted on this inadvertent administration of a 24 percent over-administration of rhenium 188. I think this falls into the category of "much ado over nothing." It was absolutely a very small amount that was

over-administered in terms of the therapy dose, like 8 millicuries, instead of 31 millicuries, or something in that range.

DR. HOLAHAN: Yes. It was to be 40. And they gave 32. You're right. It's --

MEMBER NELP: And they cancelled the subsequent therapy for reasons that partially related to this, but for other medical reasons. And they must have spent 20 hours of somebody's time calculating, questioning. The total dose that the patient got ended up being less than the intended total dose in the beginning. And it was an examination of the facts surrounding. And the people at that site said they had determined that it wasn't a misadministration because they weren't adding up the fractions, they were adding up the total.

So, really, it was an example of being costly inspection of something that was very minor. It should not be classified as a misadministration in the ordinary sense of the word at all.

DR. HOLAHAN: Yes.

MEMBER NELP: I don't know if that was your -- it certainly wasn't the impression at the NRC. They took the whole thing to task but would not listen to the logic of the site.

DR. HOLAHAN: Yes. Well, I think in terms of

defining it as a misadministration, it went back to looking at what the definition for written directive --

MEMBER NELP: Right, exactly.

DR. HOLAHAN: -- and the question of: --

MEMBER NELP: The question about it --

DR. HOLAHAN: -- Is radiopharmaceutical therapy typically fractionated? I don't know if --

MEMBER NELP: In that setting it was an experimental treatment of an antibody. And it typically is given or may well be given in split doses. But the whole thing was a very minor thing, and it was treated as if it had major consequences.

DR. HOLAHAN: Well, I think, too, when we're looking at some of these things -- and the consequences do come into play in terms of when we're looking at the enforcement action to a certain degree. But also --

MEMBER NELP: I simply wanted to put it into --

DR. HOLAHAN: -- the generic implication isn't --

MEMBER NELP: I wanted to put it into perspective for the Committee.

DR. HOLAHAN: Yes. I appreciate that.

MEMBER NELP: But I got very involved in it.

MR. CAMPER: Let me add a comment to that on the perspective. Your point is very well-made that many

misadministrations; in fact, I'd say most misadministrations, do not carry with them deleterious consequences. And in many of the cases, the dose that is inadvertently or mistakenly delivered through a misadministration still falls within a range of clinical acceptability.

The perspectives point, though, is remember that the misadministration is an error in the delivery process. In other words, what was administered to the patient, albeit it non-consequential, was not what was intended to be delivered by a percentage threshold. So it's an error in the delivery process.

DR. HOLAHAN: That's a good point. Thank you, Larry.

Anyway, we did develop a list of issues and questions to try and flush out where there may be real problems. As we're proceeding looking down at some of these, primarily again brachytherapy issues, is what is perceived as a problem. Are there voluntary standards and guidelines out there? Is there a need to revise the regulations? Is there a need for additional regulations and guidance? And at this meeting last May, this Committee sort of advised us to go out to the community and find out if there is such need.

We published the list of issues and questions

that you have in your briefing books. We did publish in the "Federal Register" on November the 3rd.

And primarily we're addressing HDR manual brachytherapy. And there are just a few questions on radiopharmaceutical therapy. We're focusing on this dose fractionation issue, source calibration, source placement, localizations, assay of sources, and then training and experience. I had to bring that in at least.

Okay. In terms of the brachytherapy, one of the things we're trying to find out is: The existing brachytherapy regulations that are currently in Part 35, are they adequate? We've discussed before the need for additional regulations for high-dose-rate brachytherapy. Also what is the availability and the adequacy of industry standards and procedures?

And when I have been going out and talking to people, some of the feedback that I have been getting back is in terms that although there may be voluntary standards developed, very often the only way that all licensees are really going to adopt them is to put them into the requirements, into the regulations. I have received this comment from more than one individual. So let the professional organizations develop the standards, but then they should be considered to go into the regulations.

Another question is whether we should have

quality assurance checks in calibrations for brachytherapy similar to teletherapy. And I handed out to you -- it's in Part 35, but just for your ease because we'll get to this question again later -- the requirements for teletherapy versus brachytherapy so you can reference those quickly.

And then this issue of fractionated brachytherapy: Should we revise the definitions to include an error in a specific fraction? We are going out now with a generic letter to request licensees to report all errors in fractionated brachytherapy so that we can get a better handle on how frequently this occurs and what, if any, are the consequences.

Some of the other issues that we're looking at are training and experience. Should there be additional training and experience for physicists and for physicians who are specifically doing HDR? As we mentioned earlier, there is a definition for a teletherapy physicist, but should we expand this to either have it as a medical physicist or specific requirements for physicists who are doing HDR?

Also in terms of a lot of the treatments that are now done through computers, treatment planning, what sort of acceptance testing is there? How do licensees verify that what's coming out of their computer is what they want? I mean, is that information adequate? I think

that misadministration with a series of 11 patients is: What do licensees need to do to verify their computer treatment planning systems?

And another question is the characterization of treatment site. We've had numerous cases recently where -- and this gets into the dislodged sources -- the applicator slips slightly but one or two centimeters. So it's still within the overall treatment volume, recently a case in which out of 12 ribbons, one of the ribbons slipped. It was in an area that would have received a dose of radiation within the normal tissue volume. Should that be classified as wrong treatment site? Is there a definition of what is the right treatment site? So how do we differentiate to know when we're in the wrong treatment site space?

So these are some of the questions that we're trying to flush out. With radiopharmaceutical therapy, some of the issues -- and this is not in the list of issues and questions -- are the adequacy of training and experience, how beta-emitting patient dosages are assayed, -- and that discussion came up this morning in Dr. Glenn's talk -- and also this whole issue of the fractionated radiopharmaceutical therapy. Is it only sort of in the experimental that you would see fractionated? Is it normally typical that one written directive would be prepared for every administration or would a written

directive be prepared for a series of fractions? What is standard in nuclear medicine and in radiopharmaceutical use?

CHAIRMAN SIEGEL: Trish, you have the questions at the end; right?

DR. HOLAHAN: Yes.

CHAIRMAN SIEGEL: Okay. Good. Just to keep track of it.

DR. HOLAHAN: I'm just going to give my lead-in as I'm going.

CHAIRMAN SIEGEL: No problem.

DR. HOLAHAN: Anyway, you have a copy of the draft generic letter in your briefing books. That gets into the issue we'll mention that fractionation can either be temporal and/or spatial. In the case of the gamma knife, more often than not it's a spatial error that's either the wrong volume or in the case that I cited, in addition, it was temporal.

For radiopharmaceutical therapy, the written directive does not include total prescribed dosage, but it just indicates the prescribed dosage. And then the definition for misadministration says "when the prescribed dosage differs from the administered dosage." Therefore, even if it's given in a fractional regimen, each fraction is considered as a separate administered dosage.

In that one case that I showed you, it was a misadministration because it was for that individual fraction that the error was greater than 20 percent.

CHAIRMAN SIEGEL: Was there original written directive --

DR. HOLAHAN: Yes.

MEMBER NELP: What happened was the person was supposed to get 30-30-30 millicuries approximately.

CHAIRMAN SIEGEL: Right.

MEMBER NELP: They gave the first 30 millicuries. They did the dosimetry and said, "Oops. The sacrum is getting more radiation than we thought it would. Our protocol says if it gets so much, we should cut it down." So they said, "We'll cut the next dose down to 24" or whatever the number was.

DR. HOLAHAN: And they did revise the directive.

MEMBER NELP: The guy prepared the 30 and gave the 30 as if it wasn't -- there was a miscommunication, but the whole thing was -- and then they stopped at that point.

CHAIRMAN SIEGEL: Right.

MEMBER NELP: So it was one of three total planned doses that was --

CHAIRMAN SIEGEL: Yes, but there are two issues here. And we will definitely come to this. One is the

whole issue of how much machinery gets put in place for an error when no harm is done -- and that's one that we've talked about many, many times and we're going to talk more about today -- versus the NRC's right to know that there is a problem because there may be some systematic problem that's worthy of correction some need to let licensees throughout the country know that "This kind of an error has occurred. And you might make this mistake. And so be aware of it."

But I think in general for radiopharmaceutical therapy -- and I think what you're telling me is correct -- is that each individual fraction would have its own separate written directive. They may have had an intent if everything went according to plan to give 3 doses of 30 millicuries, but they probably didn't write one written directive.

DR. HOLAHAN: They did have three separate written directives --

MEMBER NELP: Right.

DR. HOLAHAN: -- of what they considered. And basically what Dr. Nelp is saying is they considered all three treatments as one treatment, all three fractions as one treatment.

MEMBER NELP: Which was not --

DR. HOLAHAN: But they had three separate

written directives.

MEMBER NELP: This was really nitpicking on everybody's part. I don't think it's worthy of any further discussion.

DR. HOLAHAN: Okay. Now, for brachytherapy and stereotactic radiosurgery, if the entire treatment is written on one written directive; for example, four fractions at four Gray per fraction, in order for it to be classified as a misadministration, the total administered dose must differ from the total prescribed dose by the limits specified in 35.2, which is 20 percent for brachytherapy and 10 percent for gamma stereotactic.

However, if a separate written directive is written for each fraction, which we have seen on occasion, -- and I don't know how extensive that is; what I've seen is that it would appear that that's more the exception than the rule for HDR -- is then each fraction is considered independently. So if there is an error in one fraction that exceeds by more than 20 percent, it would be considered a misadministration.

So the intent of the generic letter is basically to clarify these interpretations and request that licensees report to us errors in a fractional dose. Even though it is not a misadministration, we are looking to see if there are generic implications; if there is a problem,

how frequently it occurs, does additional action need to be taken?; and basically to see the extent of the problem.

And so we've got the generic letter in draft form, which we hope to issue after we -- well, we'll go for OMB clearance before it goes out.

MR. CAMPER: We do have a question where you can provide some comments on the GL.

DR. HOLAHAN: Right, yes.

MR. CAMPER: Right.

DR. HOLAHAN: Okay. Then this is leading into what is our future direction. We're going to be doing a major revision of Part 35, which Janet will talk about more tomorrow. We would like to adopt or incorporate industry standards where they're available. And that's why we're trying to find out exactly what industry standards are out there now.

We're going to be conducting public meetings to discuss the regulatory criteria to address a lot of these emerging technologies, the new uses in the radiolabelled antibodies and things like that and as gamma knife is being used in more areas now. And then also the input from the NAS study which Pat discussed earlier will be used.

Some of the workshops that we've already got scheduled are last month we did go out to the ASTRO. And we had an exhibit there. We actually had a booth. And I

brought my show and tell. It is over there if you'd like to have a look at it. That was what we had at the exhibit.

We also handed out the case summaries. We had available the new reg, which was published from the Idaho National Engineering Lab on their contract of the misadministration event analysis, where they went out and reviewed seven misadministrations and did a root cause analysis and basically looked at the implications, if the quality management program had been implemented or if it was adequately implemented, could the misadministration have been prevented or mitigated.

Since that time they have also looked at two additional misadministrations for us, the two brachytherapy ones: the one with the treatment planning system error and also the one with the I 125 seeds. And we have some information on that.

We're here, obviously, now. At the end of the month we've got a workshop at the RS&A meeting, basically just letting the medical community know what we're trying to do and trying to start to solicit some input.

Next month we're going to the American Brachytherapy Society. Dr. Stitt is actively involved with us in that workshop as well.

And then in the spring we're going to have a public meeting with the professional societies,

manufacturers, and other interested parties, members of the public, the community at large. We're going to have it announced in the "Federal Register." And then also we'll be holding multiple public workshops.

The objectives of these workshops are primarily fourfold. It's to identify and evaluate some of these therapy errors, to include the fractionated therapy doses, discuss the current standards or industry practice, discuss the need for quality assurance checks and calibrations for brachytherapy, and then discuss the need to modify the current regulations to incorporate licensing guidance on remote afterloaders.

Currently since the incident in Pennsylvania, we have revised the policy and guidance directive on licensing of remote afterloaders. And so the question is whether or not the regulation should be revised to incorporate some of those licensing requirements into the regulations.

MR. CAMPER: Just a point to add. You might recall that you saw many conditions this morning on the example license that Dr. Glenn used. There are several conditions. Those are now what we refer to as standard license conditions that are showing up on all HDR license facilities. And those come up the upgrade to P&GD 86-4.

So the point that Trish is making is the kinds

of conditions you saw this morning and some other things that are contained within licensing space, should they be within regulatory space, specified clearly in the regulations, as opposed to added in by a license condition?

MEMBER FLYNN: Some of those items were part of NRC Bulletin 92-03, which was a few days after Indiana and Pennsylvania. And I helped write that and 93-01.

DR. HOLAHAN: That's right.

MEMBER FLYNN: And so it didn't look very much different to me than those. There were a couple of points added, but I think the key elements were there: physical presence, training, emergency equipment, and a separate survey of the patient.

DR. HOLAHAN: And then the question comes in: Should we get those into the regulations, which they are not currently?

MEMBER FLYNN: But aren't the licensees required to comply with Bulletin 93-01 except I guess in agreement states, they're not? Is that right?

DR. HOLAHAN: That's right. Well, in agreement states, they are not.

DR. GLENN: And it doesn't have the same force as a regulation. Essentially the bulletin says "You've got to tell us if you're not going to do this." There is the understanding that it will be done. But it may not be a

violation if they don't do what's in the bulletin.

MR. CAMPER: That's correct. If we receive an inadequate response from a licensee to a bulletin, there is a process that we go through, additional questions to the licensees, communications, letters, telephone calls. Perhaps we will ultimately move to a confirmatory action letter. Perhaps we will ultimately move to an order as opposed to the process that you would take that was clearly and emphatically stated in the regulation.

MEMBER NELP: I have a couple of questions. Are all sealed radioisotopics orphans of byproduct material?

DR. GLENN: No. Byproduct material was produced in a reactor, either through fission or by exposure to neutrons.

MEMBER NELP: My question is --

DR. HOLAHAN: That are used in brachytherapy currently? Is that what your --

MEMBER NELP: -- byproduct material.

DR. HOLAHAN: Are there any --

MEMBER NELP: Are all brachytherapy sealed radioisotopic sources considered? Is there any non-byproduct material? I think they're all byproduct material.

MR. CAMPER: Radium, radium.

MEMBER NELP: Radium is not? Is anyone using radium today?

DR. GLENN: Yes, unfortunately.

DR. STITT: Occasionally. They probably shouldn't.

MEMBER NELP: The second question I have --

DR. STITT: Those are the ones that really ought to be looked at.

MEMBER NELP: Why, yes. Now, if I manufacture an I 125 or I 125 source for therapy, what's the FDA's role in that particular -- is that considered a device or is that considered a pharmaceutical? It's probably considered a device. Is that correct?

DR. WOODBURY: Yes. It would be a device.

MEMBER NELP: So they're concerned with the safety of the device as a piece of equipment?

DR. WOODBURY: Yes.

MEMBER NELP: Thank you.

DR. HOLAHAN: Okay. I've got -- and this is sort of a summary of some of the questions that were in the briefing book. You've all hopefully had a chance to see the list of questions and issues. Do you believe these questions and issues are appropriate to try and focus on some of these problems? And I recognize that some of them seem to be very, very specific, but what we're trying to

get a general feedback to see if people do believe that th[illegible] a problem. Do you have any general thoughts on the[illegible] questions? And are there any additional questions or additional approaches that we should be looking at?

MEMBER FLYNN: Have these questions already gone out?

DR. HOLAHAN: In the "Federal Register," yes. Yes.

MEMBER FLYNN: Is it too late to modify these questions? I'm not sure why you -- have these already gone out to the --

DR. HOLAHAN: These have. But, I mean, we could be developing additional questions or modifications to be used at future workshops and things.

MEMBER FLYNN: I would just ask that maybe in the future you could circulate the questions in draft form to all of us on the Committee before you send it out and then ask us to comment on the questions after it's in the "Federal Register."

DR. HOLAHAN: Okay. That's a good point.

MR. CAMPER: Comment. Good point, Dr. Flynn. In the case of the questionnaires in terms of the timing and why you didn't see them before now is we were preparing them in preparation for distribution at the ASTRO meeting to make them available to participants at that meeting.

Now, obviously we would have been better served by going through the Committee first and getting input, but then again, these timings just didn't let that happen.

Now, we can certainly adjust the questions. As Trish has pointed out, we published them in the "Federal Register" notice. We're going to be discussing them to some degree during the American Brachytherapy Society meeting in December, the big meeting next spring. So we certainly can adjust the questions and will be happy to do so.

MEMBER FLYNN: For example, I guess I'm the only one here besides Judith who is interested in brachytherapy, teletherapy, radiation oncology who is on the Committee. So, I mean, if I would have seen them, I could have given a response within 24 hours. But I haven't seen them until now.

DR. STITT: Well, I don't think the questions are the issue. The answers are the issue. These went out at ASTRO. The physics community has been responding. We're going to talk about some of the things. Are you going to talk about what you've been getting back in a minute?

DR. HOLAHAN: Yes.

DR. STITT: Okay. Then I'm just going to be --

DR. HOLAHAN: I will be honest. I have had a

few responses back. I've had numerous phone calls from individuals who are interested in responding. And I think they've also contacted Dr. Stitt.

I know that the American College of Medical Physics was going to send it out to all of its members. The AAPM, it was given to the Radiation Therapy Committee of the AAPM. And they were going to address it.

And so in terms of some of the feedback, basically what I've heard is: Yes, there are some standards. There are some issues that should be addressed, source verification or source activity.

A lot of the questions that I got at the ASTRO meeting as people were to ask me is: Why are you doing this? I mean, is there a reason? And I would show them the case summaries. And I would get a response "Well, how could this happen?" And that was sort of the frame that I was trying to say. Well, this is why we're trying to get feedback as to what is current practice, what's accepted practice.

MEMBER NELP: May I ask you a question? What's the denominator on your misadministrations? How many brachytherapy applications or therapies are done on an annual basis? Because the numbers of misadministration seem relatively small. And I imagine as a percentage of the total effort, it must be very, very small indeed.

MEMBER FLYNN: Brachytherapy is approximately, I believe, about 40 to 50 thousand and teletherapy with cobalt about 2 million.

MEMBER NELP: So if you say 50,000 for the brachytherapy, you've identified -- I forget that number -- on the list might be 25 if you added them all up, something like that?

MR. CAMPER: Yes, around about 30 to 40 therapy misadministrations a year in NRC-controlled states. Right.

DR. HOLAHAN: Yes. There are about -- for example, last year there were 21 brachytherapy misadministrations in NRC states. And if you think that there are approximately twice as many in agreement state licensees --

MEMBER NELP: That's 2 parts out of 5,000 or 1 in 1,000, 2 parts out of 5,000 or 1 in every 2,500 applications may have some identifiable error.

CHAIRMAN SIEGEL: We've been over this round before.

MEMBER NELP: It's very small.

CHAIRMAN SIEGEL: But at the risk of getting us diverted into an area that has been explored by this Committee over the last 20 years repetitively, we probably should not worry about whether we think the frequency is too low to worry about because whether we believe that or

not, the NRC is worried about it. And it's not evident that they're going to change their mind about the frequency issue any time soon.

MEMBER NELP: I think they should be reassured that they're doing an excellent job. I mean, that's how I would comment on those numbers. To get below those numbers is trying to avoid human error, --

CHAIRMAN SIEGEL: Correct.

MEMBER NELP: -- which I don't think you're capable of doing. But 1 out of 2,500 and by the definition of your misadministrations, which take in relatively minor events, two major events, including major events, I think it's admirable.

CHAIRMAN SIEGEL: We've pointed that out many times. And that's one of the --

MEMBER NELP: If you wanted to fix something, I'd find something to fix.

MEMBER FLYNN: Do you want us to comment on the questionnaire now? Is that what you're asking?

DR. HOLAHAN: I don't know how --

DR. GLENN: Maybe it would be better to move to the specific questions and then maybe come back and ask the generic question "Are there additional ones?"

DR. HOLAHAN: Oh, okay. Go through the questions?

DR. GLENN: Yes.

DR. HOLAHAN: And then come back to the individual questions? Okay. Yes, that --

DR. STITT: Trish, are we going to hand this questionnaire out, these questionnaires out at the other meetings?

DR. GLENN: They have them.

CHAIRMAN SIEGEL: Do you mean this?

DR. STITT: Yes, those.

DR. HOLAHAN: I'm going to make them available, yes.

DR. STITT: Okay. I just don't want to spend ions of time on that because I think that's missing the point.

DR. GLENN: Okay.

MEMBER NELP: Why don't we look at them over the evening? And maybe we could have specific comments.

CHAIRMAN SIEGEL: We didn't get them today.

MEMBER NELP: Pardon me?

CHAIRMAN SIEGEL: These were in the briefing books.

MEMBER NELP: Okay. I'm sorry.

DR. STITT: All I'm trying to say is we don't need to spend 45 minutes rehashing details of those questions because there are some major questions out there.

And these are some very specific questions about some of the major issues that we have been getting information back from the different groups around the country on and will continue to. I just hate to see us go until 3:00 o'clock over 10 percent versus 15 versus 30.

CHAIRMAN SIEGEL: Especially when there's no right answer.

DR. STITT: Right.

CHAIRMAN SIEGEL: It's a site-specific answer.

DR. STITT: Well, it was meant to stimulate discussion. And we have gotten some comments back. And I think that was one of the goals.

DR. HOLAHAN: That's right. And we did exactly. I'd like to reiterate it. That is, it was a starting point to get people to address in general if they wanted to expand upon it.

MR. CAMPER: I think the emphasis would be: Are there any additional questions that we have not covered in that list of questions or, for that matter, if you see any significant problems with the questions that were asked, as opposed to, as Judith was pointing out, going through each and every question? Any additional questions or any major problems with the questions asked?

MEMBER FLYNN: Well, for example, one that I've been keenly interested in previously was Question Number

17, "Do you believe that all nurses handling brachytherapy patients at your facility have adequate training?" And the reason for that is because for inpatients who are getting low-dose-rate implants during the daytime, you literally have a small army of staff with physicians, physicists, technologists present, but during the nighttime and during the weekends, when things sometimes happen, it may be only the brachytherapy nurse who is with the patient with the radioactive source by themselves.

Now, when you ask the question "Do you believe that they have received adequate training, 'Yes' or 'No'?"; I mean, it would help me a lot. I'd be keenly interested in if they answered it "Yes," put how many hours per year, if they answered it "No," how many hours per year, and whether they answer it "Yes" or "No," why did they answer the question the way they answered it, rather than simply checking off, because later on it doesn't help me at all if 125 people answer "Yes" and 40 people answer "No." That doesn't help me at all.

I'd be interested in how many hours per year and the reason why they think their program is adequate or the reason why they think their program may not be adequate because many programs that I have seen, the nurses themselves are overburdened with other work they're doing on the floor. Then they get one hour per year. It may be

an hour where they're on vacation, they're not even there at the training.

CHAIRMAN SIEGEL: I don't think these questions were meant to be any sort of a referendum and the answers were going to be tallied up and that's what was going to be done. I think this is a vehicle to introduce discussion at workshops and to gather data without any intention to tally up the "Yeses" and "Nos" and then base action on that. It's to try to get an understanding. It's just a way of getting the discussion process started.

DR. HOLAHAN: That's right.

CHAIRMAN SIEGEL: I hope that's correct.

MEMBER FLYNN: That is right.

DR. HOLAHAN: And to see where individuals feel that there is an area of concern.

MEMBER FLYNN: Right.

CHAIRMAN SIEGEL: And I think you could design a series of very complicated sequential questions, but as questionnaires get more and more daunting, people get less and less likely to work their way through them. And it's better to start simple and let the discussion flow. It gets too complicated.

MEMBER FLYNN: Well, see, they did ask the question "Why?" in other questions.

CHAIRMAN SIEGEL: Okay. No problem. I was

actually puzzled by the Question 22.

DR. STITT: Twenty-three is my favorite.

CHAIRMAN SIEGEL: I want to know what the right answer was, number one. And I wanted to know if the correct answer is "I would call the NRC."

DR. HOLAHAN: No, I don't think that was necessarily. It was: Within your facility, do you know where to -- I guess I didn't say that. No. But I'd just like to reiterate that you're correct.

I would anticipate that we would get different types of responses, depending on who is responding. Whether it's physicians or technologists or nurses or physicists, I would not anticipate that the answers are all going to look similar.

CHAIRMAN SIEGEL: I would suggest that with respect to the questionnaire itself, that the issue of additional questions or fine-tuning of these questions are things that we can respond individually to Trish about.

I would also add and just to reiterate something that Dan said, even though you were on a time crunch to get this out to use at the ASTRO meeting without convening this Committee formally to provide a consensus, you have as your purview the right to use each of us as individual consultants any time you want to show us a document and say "Any ideas about this?" You're not

looking for any consensus judgment. You're just looking for thoughts of another set of individuals and in this case people who are doing this for a living who may have some ideas.

And so I would encourage you in the future when you have something like this. Send it to the Committee. Only three people out of 12 may respond, but you may get some useful input.

DR. HOLAHAN: Yes.

CHAIRMAN SIEGEL: I don't think that does anything that violates PACA or anything like that if you do it that way because we all are consultants.

DR. HOLAHAN: Good point.

CHAIRMAN SIEGEL: All right. So why don't we work through your broader questions and some of the other --

DR. HOLAHAN: Okay. Yes. The --

CHAIRMAN SIEGEL: -- specific things on this?

DR. HOLAHAN: Okay. The next broad question is the generic letter. I don't know if you've had an opportunity to read through it. But is it clear in the message that we're trying to get across? And are there additional issues that we should be addressing in that generic letter to try and get additional information on some of these fractionated errors?

MEMBER NELP: Is that a recent handout or is that --

DR. HOLAHAN: That was in your briefing books.

MEMBER NELP: And what page is that, please?

DR. HOLAHAN: It's right after the questions.

MEMBER NELP: Okay. Thank you.

CHAIRMAN SIEGEL: It says "Draft."

DR. HOLAHAN: Yes. It's got "Draft" stamped all over it. And, if you'll note, what we've used for the generic letter is we're using a threshold of 20 percent based on what was used for the total dose. We're just using that for now to try and get some information.

So if you have any comments on the threshold or any comments on the issues that we have addressed, whether or not we should address anything further in that, we'd appreciate them.

MEMBER FLYNN: My opinion is that 20 percent is a good number, as good as any.

And I ask Judy this question because I'm not sure how you do it at your institution. But sometimes when the HDR is fractionated, it may be initially listed as a plan, a prescription, if you will, 600 centigray, 600 rads times 5. But at each HDR treatment, at least at my institution and the ones I'm familiar with, the individual treatment prescription is signed by the authorized user,

physician, radiation oncologist, there at the time of the treatment for each treatment. Is that true, where each time an HDR treatment is performed, a physician is signing something, either if it's a Nucleotron machine, the tab that comes off the printer?

DR. STITT: Signing about 12 things every time, but --

MEMBER FLYNN: Right. So that --

DR. STITT: -- the initial description and overall treatment plan or whatever quality management rule is a different issue.

MEMBER FLYNN: But my interpretation has always been that every time an HDR treatment is given, every fraction can also be interpreted, at least in my view, maybe not you, but as a separate treatment. And so that the 20 percent deviation should be on every single treatment that's given. Even though the original prescription may be 600 rads times 5, each fraction is prescribed.

In recent low-dose-rate brachytherapy, for example, many, many thousands of patients with cancer of the cervix before HDR were given two Fletcher-Suit applications and so many rads to Point A. But each of those two treatments -- and these are many thousands of patients -- were considered a separate treatment, separate

prescription because the prescription is written again at the time that the treatment is performed.

And then two weeks later the second of the two treatments was given. And that was always considered, at least among the physician community, as a second treatment, not as a separate fraction of one prescription.

DR. HOLAHAN: So you're saying at your facility, you would write a written directive prior to each treatment?

MEMBER FLYNN: The plan may be 600 rads times 5.

DR. HOLAHAN: Okay.

MEMBER FLYNN: And that could be in a consultation note. It could be in the patient's chart. But each time the treatment is given, at least, -- I'm just talking about what I'm familiar with -- the prescription for the 600 rads is signed off again at the time of the treatment.

CHAIRMAN SIEGEL: I understand what you're saying, and I think that part of the problem is trying to pick a percentage and assume that that does the job perfectly. And it really doesn't, which is why when we worked through the new definition of misadministrations with the rewrite with the quality management rule, we spent so much time trying to figure out along with John Tellford

what the right prescription was for a teletherapy misadministration versus a brachytherapy misadministration versus a radiopharmaceutical misadministration.

And in the case of teletherapy, I think it was acknowledged, for example, that a 20 percent error in one fraction was generally kind of a "Who cares?" So it was backed off to being an error during the weekly dose.

MEMBER FLYNN: Right.

CHAIRMAN SIEGEL: I think one can make the argument that a brachytherapy fraction treatment error should be linked not just to a percentage, but to some other threshold as well, like 200 rads or pick a number. I'll let you pick a number because in some ways it may be site-specific. But it shouldn't just be a percentage of the fraction per se.

MEMBER NELP: How do you really know when you have a brachytherapy error unless you have some sort of an incident? I guess you could have an error because you go back and check your calculations and "Oops. I made a mistake" in the original calculation, like the computer.

CHAIRMAN SIEGEL: Well, you know you had an error when the source is supposed to be a minute and it stays in three minutes.

DR. STITT: I think what --

CHAIRMAN SIEGEL: That's one way.

DR. STITT: -- we're finding and the reason we're struggling here, --

MEMBER NELP: Okay. It's time activity error and/or --

DR. STITT: -- what's happened recently since so many places are starting to use HDR is that what we used to think and how we used to work both clinically and if you're looking specifically at NRC and regulating is that you've got significantly different sorts of technology.

So in low-dose rate, errors were more the patient pulled the sources out, a source fell out, the applicator was on the floor. And the doses, I'm just guessing, weren't quite so much the issue because those can be very easily adjusted.

In high-dose rate, there are a million gizmos that are clocking everything, including the rotation of the earth, it seems like, enormous numbers of data that you can look at in any way, shape, or form. And so we're seeing a lot of different sorts of material being gathered, for one thing, maybe even different types of misadministration.

This business of -- you know, I jotted down your phrase, Larry -- the error in delivery process to me would be -- that's what you're doing in misadministration. And that could either be a technical misadministration because you can document that the pitch, roll, and yawl is

a little bit different, and we had it virtually set up in another fashion. And then that's something other than a medically significant misadministrations.

I think the other thing that we're really having to deal with and we really have to look very carefully at, -- and it's what you brought up, Dan -- I would be very careful in saying that one fraction yet out of total of five or six combined with 60 Gray whole pelvis can give you a misadministration. You write a general treatment plan that includes external intracavitary.

I think we're finding from the information that we get back from these questions that most places that are doing fractionated high-dose rate do include the total dose, the number of fractions, and the dose per fraction. That gives you a good ballpark that you can work within.

And then when you're signing off the 12 pieces of paper for each fraction, that's really confirming "Here's what we gave today," but that's not rewriting the prescription. And I don't think that itself should be -- I think we have to be very careful not to interpret that as a potential misadministration. It's really documenting what you gave based on what you have written in your quality management or your treatment plan, basically. So those are some bases we're dealing with.

MEMBER FLYNN: To be consistent, though, at

least previously with low-dose-rate brachytherapy, for the many, many thousands of Fletcher-Suit applications given for cancer of the cervix, the plan may have been, let's say, 2,000 rads to Point A for two separate implants, but each implant was treated as a separate --

DR. STITT: Right, but I think that is the issue.

MEMBER FLYNN: Each time there was a misadministration in low-dose-rate brachytherapy, each of these implants were considered as --

DR. STITT: Right.

MEMBER FLYNN: -- independent prescriptions and independent treatments.

DR. STITT: But I think that's why we're having some trouble struggling here because high-dose rate has a lot of characteristics that are very different than low-dose rate. And I think that's why when we come up with something, we're going to see some differences. And it's not going to be --

MEMBER FLYNN: I just worry that if a licensee has 6 HDR treatments planned and one is over by 70 percent, they come back and say "Well, the other 5 we went under by 10 percent each one. So we committed a misadministration during the first one because the overall percentage was less than 20 percent.

DR. STITT: Right. And that could happen, I think, but that's unlikely. And if you have some sort of a threshold which may well be part -- and certainly what I'm hearing from the physics groups is they'd like to see some sort of an absolute number that you could use as a threshold.

MEMBER FLYNN: We've seen some misadministrations where the dose was supposed to be 600 rads and it was 1,000 or 1,100.

DR. STITT: And that probably is no big deal in brachytherapy work.

MR. CAMPER: Let me redirect your thinking just a little bit. What I'm hearing right now, interestingly enough, is sort of the discussion of: What is the appropriate threshold for a misadministration involving a fractionated brachytherapy event?

The GL has a different purpose, if you will. And that is we have learned by virtue of licensees reporting to us fractionated events in HDR in manual brachytherapy, in gamma stereotactic radiosurgery space.

By definition we don't have fractionated misadministrations for those modalities. Licensees reported them to us because of concern, perhaps confusion on their part as to whether or not it should even be reported. And so the generic letter has been created to,

say, in a formal fashion report such events to us.

The threshold that's been chosen is 20 percent. Now, as Barry has correctly pointed out, if you looked at fractionated misadministration thresholds in teletherapy or, for that matter, if you looked at the misadministration in gamma stereotactic, which is at 10 percent, you'll find that there are great difficulties with what percentage to choose on.

What we have done here is pick 20 percent as a reporting threshold for information-gathering purposes. At some point when we get into the consideration of whether or not we need to revise the rule language and establish a threshold for misadministrations, then we will be having the very kind of discussion that you've gotten into now.

So with that in mind, I guess what I would ask is: Is the 20 percent given that any percent that you choose is flawed a reasonable threshold for the 3 different modalities for purposes of reporting and gathering information under this guise? Is it a reasonable threshold?

MEMBER NELP: This is for each? I'm still not clear whether you mean this --

MR. CAMPER: Each fracture.

MEMBER NELP: -- for each fracture.

MR. CAMPER: Yes, sir, I do. I mean for each

fractionation.

MEMBER NELP: Isn't your mission to determine if patients have been subjected to harmful event?

CHAIRMAN SIEGEL: Yes and no.

MR. CAMPER: Clearly it is. Well, yes, it is, but --

MEMBER NELP: And it seems to me that if I am over-administering by 20 percent in one fraction and I'm giving the patient 20 fractions that doesn't harm the patient nor doesn't even come close to harming the patient, then you don't want to know about it.

MR. CAMPER: No, but --

DR. STITT: But the question --

MR. CAMPER: That's true. I believe, though, based upon the discussion we had last time with the Committee, there was some indication that there could be events of consequence, even in a single fractionation.

MEMBER NELP: There could be. But is there an example out there?

MEMBER FLYNN: I'll give you an example, a patient in Virginia.

MEMBER NELP: I mean, if it were 200 percent over, it would -- yes, but the whole thing would be over.

MEMBER FLYNN: There was a misadministration in Virginia for a different reason, but the patient had gotten

very high-dose external beam to the pelvis with a radio-sensitizing agent, five FU, and was given an HDR treatment.

The prescription was to a certain depth, which was deeper than usual. I'm sure Judy will agree. I think it was at three and a half centimeters from the source. And that patient was given, I believe, 1,000 rads, instead of 500, at that point.

That could produce some pretty significant complications, especially added with the fact that it had external beam treatment plus a radio-sensitizing agent.

MEMBER NELP: That was a single administration, wasn't it?

MEMBER FLYNN: But we're talking as to whether there were 3 fractions that were scheduled and that fraction difference was 500 rads. And I think in that case, it could produce a harmful effect because it was such a large fraction added on to everything else the patient had gotten.

And the fraction was prescribed at a certain depth in tissue, which is the key thing. It wasn't prescribed at one centimeter from the HDR source, but at three and a half centimeters.

MEMBER NELP: I know, but I'm trying to deal with the real world and what I think the function of this

Committee is to advise the NRC what is going on in the real world. And I don't believe if somebody is getting 10 fractions or 15 fractions or 20 fractions of a therapeutic modality that you want to know if one of those 20 is over by 20 percent.

DR. HOLAHAN: But I think with HDR, we're not --

MEMBER FLYNN: HDR is usually two to five.

DR. HOLAHAN: -- seeing 15 or 20 fractions. We're seeing two to five.

MEMBER FLYNN: Two to five.

DR. HOLAHAN: So we've got many fewer fractions.

MEMBER NELP: You want to know if that patient at the end of the therapeutic modality was over-treated more than 20 percent of what should have been treated because if you know that she got 20 percent overage on one fraction, you're not going to know about that until way after the fact anyway.

DR. STITT: What will we get from this? This is going to be a letter sent out?

MEMBER NELP: I mean, it's a --

DR. STITT: Data is collected?

DR. HOLAHAN: Yes.

DR. STITT: Then what do we do with it?

CHAIRMAN SIEGEL: It gets analyzed.

DR. STITT: What do you do with it?

CHAIRMAN SIEGEL: It's analyzed. And decisions get made about regulatory requirements.

DR. STITT: So we need more information.

MR. CAMPER: That's the point of it. Let me just interject a point. I think --

MEMBER NELP: I think you have a mind-set on this that fixed. I don't see any negotiability or flexibility at all.

MR. CAMPER: I think the mind-set that we have is if a mind-set is fixed, it's one of gathering more information. What is the extent of the problem?

MEMBER NELP: You do not have a problem.

MR. CAMPER: Well, sir, we don't know that. We don't. Currently it's not defined in the regulations. It's not required to be reported. Those events which we have learned of have been learned of by happenstance because licensees were uncertain as to whether or not they needed to be reported. I would submit to you that we do not know the extent of the problems in fraction --

MEMBER NELP: You don't currently have a reporting requirement?

MR. CAMPER: Sir?

MEMBER NELP: You don't have a --

MR. CAMPER: Not for fractionated events. That's the problem. And what we're trying to do --

MEMBER NELP: What about for total events?

MR. CAMPER: We do, yes. For misadministrations, we do. We have --

MEMBER NELP: For total misadministrations?

MR. CAMPER: By definition currently in Part 35 for the therapy modalities, you are dealing in total dose, total-dose phenomena, misadministrations.

MEMBER NELP: What in God's earth would want you -- if I'm to get 6,000 rads to my lung and I get it in 10 doses and one of them is 20 percent over, my total dose is 6,100 rads or whatever the number, why would you want to know about that fraction?

CHAIRMAN SIEGEL: Why don't you let me answer the question because we've been over this ground many times before. You weren't here for the times.

MEMBER NELP: Well, I missed this. That's what I --

CHAIRMAN SIEGEL: So let me explain it to you. There are a couple of issues on the table here that need to be clarified. A physician sees a patient and develops a treatment plan over time for that patient. Okay? No argument there.

The treatment plan is then converted to a

series of directions that tell all the ancillary staff who will be involved with that patient's treatment "This is what you are to do." The part of the process that the NRC is concerned with is how those directions are carried out and what things lead to errors in this directions.

Now, the big problem that you're having -- I can see it because I've seen it a lot of times before.

MEMBER NELP: I don't have problems, Barry. I just have solutions.

CHAIRMAN SIEGEL: I understand, Buzz. And the problem that the medical community generically has with this whole process is the fact that arbitrary differences from the original plan get defined as misadministrations.

And two things happen as a result or three things happen as a result of misadministrations, one of which is good and two of which may not be good. One that happens that's good is that the NRC gets a piece of data that says "Here was a problem. And the NRC is in a position as the national repository of the data to try to determine if there are trends that are occurring that are of concern to the public health and safety" because any one licensee is unlikely over the course of its practice to encounter enough events to recognize systematic problems, problems with the devices that need to be fixed, problems with the way we practice that need to be fixed, because

most of us only make one mistake if we make any mistake during the course of our practice of this kind of magnitude.

MEMBER NELP: Barry?

CHAIRMAN SIEGEL: And that's a good thing. The NRC has that job.

MR. SWANSON: And if that's the goal, then there really ought not be limits at all. We ought to be reporting every time that we have an abnormal incident if that is truly the goal, it's to identify systematic errors. But it ought to be reported in the --

CHAIRMAN SIEGEL: Right, but there also has to be a practical balance between reporting every minor variation versus variations that potentially have significance. And the reporting threshold is set below the level that can cause harm because fault analysis teaches us that if you want to detect the meltdown, you have to first look for when the valves are leaking. Okay?

That's the mind-set of the NRC. But the truth of the matter, Buzz, is I agree with it because that's how you figure out when disasters are going to occur by looking at a lower level.

The problem the medical community has, especially under the current misadministration administration, meaning the way NRC administers the rules,

is that the minute you make that phone call, you are reasonably guaranteed that sometime tomorrow an inspector is going to show up. And so that's an unpleasant event.

The other thing that's unpleasant is that irrespective of whether any harm has been done to the patient, you're in the loop of now having to talk to the referring physician, talk to the patient, write letters to the patient.

And that's the other unpleasant part of the event. As everybody around this table knows, I completely support the NRC's right to gather all of that data. The problem I had and most of us have had is the disconnect between gathering that data and all of the other things that get in the loop when no harm has been done.

Right now, at least with respect to HDR brachytherapy, where they are is the point of gathering data. The rest of the machinery won't get activated, at least I hope, based on this generic letter.

If you get reports, are these going to launch inspections?

MEMBER NELP: I'd like to respond to your remarks first. It's a very eloquent argument about a problem that I might have. The problem I have doesn't refer to a meltdown or a disaster. The problem that I have is I see from what you know if they're supposed to be

reporting to you misadministrations that are 20 percent or greater of the total effective estimated dose given to patients, that one out of 2,500 events each year gets reported. Now, that has nothing to do with a meltdown or nothing to do with a disaster.

Now you are going to request that they take those 2,500 events and subsegment them into, say, 25,000 events and attempt to report to you a 20 percent overage in any one of those 25,000 events when they're totally inconsequential to the patients' health and to the patients' safety.

Now, if you want to be gathering information, you can gather that information. But it's not going to point you towards picking off a meltdown or a disaster.

If you're concerned about high-dose radiotherapy as a potentially dangerous form of therapy in the public domain that is being administered by equipment that may be faulty or people who are not well-trained, then focus on that. If you give two doses of high-dose radiotherapy, why don't you say "When you do high-dose radiotherapy, we'd like to know about it"?

But you don't want to know about the times that somebody is giving conventional radiotherapy that has been done for years in multiple doses and they go over by 20 percent. You have no basis to need that information.

So that's my counter. We're not trying to head off a disaster. We're trying to get some information. And if you focus it, why don't you say it, "Tell me what you're doing in high-dose radiotherapy." That's what I hear you're worried about.

CHAIRMAN SIEGEL: This letter says --

DR. HOLAHAN: That's right.

CHAIRMAN SIEGEL: That's precisely what it says.

MEMBER NELP: But you're saying it to all radiotherapy and all brachytherapy.

MEMBER FLYNN: No. Just HDR, just the high-dose rate.

CHAIRMAN SIEGEL: That isn't how --

DR. HOLAHAN: No, no. It does apply to manual.

MEMBER NELP: It applies to radiopharmaceutical therapy.

MEMBER GRAHAM: If you read the actual request, it says that -- and it's on Page 4 of 6 of the GL itself.

MEMBER NELP: Now, is it true that it applies to all brachytherapy? This just says it applies to everything.

DR. HOLAHAN: Every fractionated because --

MEMBER NELP: Everything that's fractionated?

MEMBER GRAHAM: Right.

MEMBER NELP: If you want to know about HDR, why don't you ask about HDR? You don't want to know the rest.

MEMBER GRAHAM: I guess if I could back up just a second because it's that whole flow in the letter that I need to understand before I can jump into some of the rest of this. Bear with me. I'm new.

MEMBER NELP: That's one of my problems.

MEMBER GRAHAM: I tend to agree. What I've been hearing is that this group and the NRC need to collect data to determine whether there is an issue that needs to be regulated because of a justified risk to the patients or the public. So you generated a letter.

If I need to collect information inside our medical system and I send out a letter to all of my staff, saying "I want you to report every error," where I've defined this as being the error, I have made it negative from the onset. So at least if you say you want to collect data on incidents, then you're implying you're only collecting data.

The problem with the way the letter is worded is if you get to Page 3 at the bottom, "Therefore, the staff has determined that when fractionated radiopharmaceutical therapy doses are individually prescribed on a written directive and the dosage

administered for any fraction differs from the prescribed dosage by more than 20 percent of the prescribed dosage, the event should be considered a misadministration," the way I understand, as soon as you throw out that word "misadministration," then you've turned on this regulatory machine.

DR. GLENN: I'm sorry. Where are you reading?

MEMBER GRAHAM: I'm reading -- it's the bottom of Page 3 going to the top of Page 4. So if I read this right, the staff has just redefined what is a misadministration. And if I were in a facility, I assume I have to go to -- and I went to that section of 35, that I'm supposed to do everything that gets triggered there by a misadministration.

DR. HOLAHAN: No. It's not a redefinition. It is --

MR. CAMPER: No. First of all, it sure reads like that, but that's a good point.

MEMBER GRAHAM: I thought it was for 20 percent over on total therapy, not for fraction.

MR. CAMPER: The sentence that you're referring to deals with radiopharmaceutical therapy. That is, that sentence is designed to provide clarification that radiopharmaceutical therapy is clearly addressed currently in the regulations. Later on we talk about where gamma

stereotactic, manual brachytherapy, HDRs for fractionated processes are not.

MEMBER GRAHAM: I guess then when I go on to the request, it nowhere clarifies that it's HDR. So, again, I guess I do tend to agree with Dr. Nelp that it would appear to read that it's any 20 percent over fraction for those procedures.

MEMBER FLYNN: The low-dose-rate brachytherapy is not fractionated anyway. And, as I say, when they were administered in two treatments --

MEMBER GRAHAM: Anywhere?

MEMBER FLYNN: Well, when they were administered in 2 treatments and have been so for the last 50 years, each one of those treatments has always been considered for reporting requirements by the physicians as an independent treatment with an independent prescription.

So I think it may say "brachytherapy," but the low-dose-rate brachytherapy is not being administered now suddenly in five fractions or six fractions or seven fractions. It's only the high-dose-rate brachytherapy.

Would you agree with that? Do you think that the low-dose-rate brachytherapy now is being fractionated out in multiple fractions?

DR. STITT: No, it's not, but the reason that you could easily consider high-dose-rate brachytherapy in

the same type of general total course of treatment is that it is the same dose rate as teletherapy.

And that's why I think the folks, particularly the physics comments that we're getting back about this, are making the comment that you don't want to look at just one administration of high-dose rate. It is very different than low-dose rates, the same dose per time as an external beam teletherapy, whether it's cobalt or a linear accelerator.

I'm back to the point I was making before. If we want to collect data, we have to be careful. And I agree with you. This looks like the way you interpret it, that phrase is a little bit alarming if I'm reading the letter. Plus, it's enormously long. But maybe that gives it some clout.

I think that collecting data is one thing, but we have to -- this makes it look like -- I don't know. It's a pretty hostile letter the way I read the thing.

MEMBER GRAHAM: Yes.

DR. STITT: And it looks like we're making more regulations. It doesn't come across like we're gathering data, even if that's a --

MEMBER GRAHAM: I guess this is the fundamental clarification question. Is there a reason it has to be labeled as "an" error? Why don't we just call it an

"incident"?

MEMBER NELP: Why do you want to know about it if it isn't important?

DR. HOLAHAN: Because when we're calling it an --

DR. GLENN: I guess we consider "error" more neutral than "incident," to tell you the truth.

MEMBER NELP: Let me tell you what happened. I don't think radiopharmaceutical therapy would even be an issue for fractionated therapy. There is a very small nucleus of people out there who are doing it. It probably will never become an event that is of serious consequence or importance in terms of numbers or exposures.

What happened at the site that I was asked to investigate, the guy said, "Oops. They wanted 30 millicuries and I gave 38." And I presume out of respect for the NRC, he notified the NRC of this event. Is that how it went? I mean, the NRC had to know about it from him notifying you of this event?

DR. HOLAHAN: I cannot recall --

MEMBER NELP: They didn't inspect?

DR. HOLAHAN: -- at this point whether or not they notified us or if it was discovered during an inspection. I just don't know the answer to that.

MEMBER NELP: But considering the fractionated

radiotherapy was totally inappropriate because the patient got two-thirds of what was prescribed. Even though it was over, the total dose was considerably under. And the reason that she got less than she was prescribed was because she got ill for other reasons, couldn't complete the experimental protocol.

And this is something you didn't need to know about because there was no health consequence. And it engendered tremendous amounts of paperwork and tremendous amounts of hostility.

MR. CAMPER: Well, again, it is --

MEMBER NELP: Now you're focusing this in the regulation and in the letter that relates to one event, one experience that you've had that was totally inconsequential both in terms of the concept of misadministration and in terms of any health or hazard to the human race.

MR. CAMPER: Two points to make, one I think I've already made. And, again, I can only tell you that you are right. Our reporting thresholds are not established at consequence. You are correct. We don't think it's appropriate to establish reporting thresholds at consequence.

MEMBER NELP: You arbitrarily said "We will consider this fractionated misadministration." And their radiation safety committee and their radiation physicist,

who is a nationally known figure, who is very sharp, who knows more about it than anybody in this room said, "We didn't consider it important, and we considered it a total dose deal, and she got 60 percent of what she was supposed to get. What is the fuss?" And you made a "fuss" (quote/unquote) because of the way you interpreted the regulation.

DR. HOLAHAN: That's how the regulations are written. But the other point that I'd like to just raise, too, and I --

MEMBER NELP: And I would like -- you know, I think you ought to -- why -- that's one incident, and now you're putting it in as a --

MR. CAMPER: Well, it's not one incident. I mean, in the generic letter alone, for example, we're citing at least seven or eight incidents that I can count off quickly looking --

MEMBER NELP: Radiopharmaceutical.

MR. CAMPER: No, no. Not only radiopharmaceutical.

MEMBER NELP: I'm talking about radiopharmaceuticals.

MR. CAMPER: Well, we're talking all fractionated events that we're aware of thus far.

MEMBER NELP: My comments are strictly to the

one event that you're aware of, which was a radiopharmaceutical, i think is blown totally out of proportion.

DR. GLENN: Let me make one observation here. I think one comment is that the generic letter is going to have to be simplified. It obviously is too complicated, and it is unreadable. If you go to the requested action section, you will see that we have defined rather clearly what we are asking for, and we are not asking for radiopharmaceutical reporting.

What we've done in the text of the letter is to tell you that we have -- in consultation with our legal staff, have looked at it and determined that there is already a requirement for radiopharmaceutical fractionated treatment.

DR. STITT: In fact, John, I think the very last paragraph on page 5, which is sort of ironically under Paperwork Reduction Act statement --

(Laughter.)

-- if you flip out that one and then stick it with requested actions, you'd have a one-page letter, and all those trees would be saved.

(Laughter.)

DR. GLENN: I think that's really what I'm hearing, that we have made this letter so complicated that

no one is understanding what we're trying to do.

DR. HOLAHAN: We were trying to explain it and ended up I guess confusing the issue.

MR. CAMPER: Right. The issue was it's not addressed in the regulations, but these things have been reported. We attempted to clarify and establish a background as to why we were going out and asking for this reporting process to take place. And in the course of doing that, we apparently have made it lengthy and cumbersome.

And the other thing I was going to say is that, as Dr. Glenn has pointed out, Dr. Nelp, we have taken our the radiopharmaceutical therapy reporting.

MEMBER NELP: Not in the letter I just read.

DR. HOLAHAN: Well, no. We're saying that it is already a requirement.

MR. CAMPER: Under requested actions --

DR. HOLAHAN: It's not under the requested actions because it is already a requirement.

MR. CAMPER: -- radiopharmaceutical therapy is not addressed as an action licensee under requested action. Other fractionated events are -- HDR manual and gamma stereotactic.

DR. STITT: It's confusing because you talk about radiopharmaceutical therapy in two different spots in

the letter.

MR. CAMPER: Correct. We understand.

DR. STITT: Let me ask you a question. When would this letter go out? Will it go out before -- no, it won't -- before the brachytherapy meeting?

DR. HOLAHAN: No, it won't, because --

DR. STITT: Okay.

DR. HOLAHAN: -- it needs OMB clearance.

DR. STITT: Well, I think that, you know, this may be something we want to bring up at that meeting, "Guess what, folks? Here is what's coming," and try to explain it in user-friendly terms because the group of people at that meeting will be primarily M.D.'s, but we've got a lot of contacts going on with physics staff literally across the country, working through AAPM, ACMP, and ASTRO. So it's --

DR. GLENN: Well, I think one thing we have done in the past is to take background material, stick it into an attachment, so that the letter itself is nice and short and crisp --

DR. STITT: Right.

DR. GLENN: -- and tells people what we really want them to do, and then we can pass on all of this other information as a separate document.

MR. CAMPER: Yeah. The other thing is, as I

said, we don't -- certainly, for HDR, perhaps for manual and certainly for gamma stereotactic, we are operating under the assumption that even a single fractionation in those modalities can be of consequence. And secondly, we do not know the extent that events are occurring in the fractionated arena. We just don't know.

DR. HOLAHAN: I would just also like to address, too, for Dr. Flynn is the reason that manual brachytherapy went in there was that we did have an incident reported, but they did classify it as fractionated manual brachytherapy. Although they did have separate written directives, it was -- I believe they were separated by two weeks, but they considered it the first of two fractions.

And so we just wanted to clarify that, you know, if you're going to call it two fractions, then we are concerned with an error in one, and that was why manual came in there.

DR. STITT: One quickie question. Back to the letter -- what is the -- on the last page, it says, "Attachment is, number one, a list of recently-issued generic letters." Are there going to be -- what does that mean?

DR. HOLAHAN: Oh, that's just the NRC recently issued generic letters. They -- we don't have any in the

medical area, but it will be -- because this is an NRC document, it will list all of the NRC generic letters that have been issued in the last year or --

DR. STITT: Is that going to be one page or 12 pages?

DR. HOLAHAN: One.

DR. STITT: Okay.

MR. CAMPER: It's a format thing, Judith. We're do the same thing in information notices.

DR. STITT: Just asking, because if this came in my mail, I would immediately lock all of my files because it looks like you're after something.

MR. CAMPER: Yeah.

DR. STITT: Really.

CHAIRMAN SIEGEL: Okay. Bob?

MR. QUILLIN: Question on page 5 where at the top of the page you're requiring that this reporting be done forever after until your new rulemaking supersedes the reporting requirements.

Have you thought about having some finite period of time for the reporting requirement, rather than just it's going to go on and on and on?

DR. HOLAHAN: Well, I think we would probably look at, you know, in the revision of Part 35 that's done, we would look at it at that point in time. But the thing

-- the reason that we don't have sort of, say, a very short period of time is because not knowing the frequency of how long it's going to take to get in information to see what the extent of the --

MR. QUILLIN: Why don't you --

DR. GLENN: That's a very good comment.

MR. QUILLIN: Why don't you ask for a year's worth and then extent it if you need to, instead of leaving it open-ended and cutting it if you need to.

DR. HOLAHAN: We can consider that.

CHAIRMAN SIEGEL: Bob?

MR. AYERS: Bob Ayers, Medical and Academic Section.

Since we don't have any specialists in that modality, I just wanted to mention something about stereotactic radiosurgery that didn't come up. The important point is that is spatially fractionated and not time fractionated, and they treat to a full dose for a unit volume, and the different fractions, or as they are sometimes referred to as "shots," are done to encompass a volume. So a significant error in one fraction is an error to that volume of tissue.

A good example is a recent one we had -- the licensee reported it at a five percent error in the overall treatment, but it was over 100 percent error to a volume of

tissue, and they -- often in the treatment plan, if they're particularly doing a tumor treatment, to destroy the tissue and go to - very close to the limits that they can go to to adjacent tissue they don't want to harm.

So in that particular modality, a single -- an error in the single fraction could be medically quite important.

CHAIRMAN SIEGEL: All right. Now that we've exorcised our souls a little bit on that stuff --

(Laughter.)

-- let's move on to the rest of your questions before we take a break.

MEMBER GRAHAM: I guess this -- for the purposes of rewriting the letters, so would this letter finally discuss reporting these errors with respect to a prescribed volume of tissue? That is an issue that has been raised by radiation oncologists that I've talked to.

DR. STITT: Well, I don't know that that's in the genetic -- the generic letter.

MEMBER GRAHAM: It isn't in the generic letter now, but --

DR. STITT: Well, actually, it's the same thing that he just brought up with stereotactic. I mean, they use a different set of phrases, but it still refers to what are definitions of treatment site and the wrong treatment

site, and it's -- I see it as the same rather than different, whether it's stereotactic or high dose rate or low date rate, interstitial or intracavitary. I don't know that that's part of the generic letter. Is it?

CHAIRMAN SIEGEL: Well, yeah. Well, it really is, because it says --

DR. STITT: Does it say that?

CHAIRMAN SIEGEL: -- differs by more than 20 percent from the intended dose, that may incur in one or more fractions of fractionated gamma stereotactic radiosurgery and brachytherapy treatments.

Now, and I -- maybe what needs to be made clear, and you may have done so earlier, is that a fraction is the draw time at an angle of 30 degrees pointing at this place. That's a fraction, and then it moves to the next position, and that's a fraction.

MEMBER GRAHAM: And it might make the data collection a lot easier if you discussed with the ABS meeting coming up how they would recommend defining what it is you're going to collect the data on. If you could get buy-in from that group, it would be a lot easier.

MR. CAMPER: Yeah, it's interesting. Some of the comments that you're making, John, are -- if I go back in time about four years ago or so, when we were -- in '90 and '91, we were having meetings with various professional

societies about the definitions that exist today from misadministrations, which by the way for the record are about twice what they used to be.

What are now recordable events used to be misadministrations, but we had lengthy discussions about what all should be included in misadministration criteria, particularly in the realm of brachytherapy; it's very complicated.

And, frankly, we talked about, you know, the volume, we talked about a number of different things, and in the final analysis we were all just absolutely mentally exhausted trying to deal with it because it's very complicated. And so we said, you know, "Okay. Let's do the most simplistic." A percentage error -- and there is all kinds of problems with a percentage error, and we all recognize that, but at least it is something that you can settle on in the final analysis, that it's an error in the delivery; it rises to a level of reportability.

I think Barry has correctly captured -- the unfortunate thing, the stigma associated with misadministrations, or whatever you'd like to call them, is unfortunate. But from a pure event reporting standpoint, it's probably -- 20 percent is probably about as good as anything.

CHAIRMAN SIEGEL: Reporting a variance is

intrinsically a neutral event. The fact that having so reported it, it's sin by definition, to use Carol's term, even though she's not here, is the unfortunate part from the medical perspective, because we all know -- and I agree with you completely, Buzz -- there is a lot more things that go on every day in the practice of medicine that are much more consequential than these areas.

MEMBER NELP: As a corollary to the 20 percent, do you have a percentage point where you're going to say "oops"? Is 30 percent, 40 percent, 50 percent, going to be subject to some sort of inspection or -- I mean, if you could tell -- I don't know what you have in mind in that regard. What is your thinking? Say, 20 percent --

MR. CAMPER: Oh, do you mean on the GL?

MEMBER NELP: I'm not concerned about 20 percent; I just want to know about it. You're not going to reprimand anyone or discipline anyone or punish anyone.

MR. CAMPER: Well, let me just say this. The purpose of --

MEMBER NELP: What is your percentage?

MR. CAMPER: Well, the purpose of the GL is for reporting, is to gather data. I cannot sit here and tell you, though, that some event in a single fractionation might not cause an inspection, or for that matter, depending upon the circumstances of the event, might not

result in enforcement action. I mean, one never knows that, but that's certainly not the intent of the GL.

I think it's highly unlikely that it would, but -- I mean, there can be circumstances where they would warrant more than just a review by us.

DR. HOLAHAN: Well, I think, too, I'll use the gamma knife incident as an example. It was not a misadministration; it was a narrow one fraction. But an inspection was done and we are reviewing it to look at the root cause problem of why the couch failed to retract.

I mean, it does have generic implications. In this case, there were no consequences but that doesn t mean that that type of error in another case --

CHAIRMAN SIEGEL: As John and I just discovered, as the letter reads right now, you won't actually get any reports, because the letter contains no instructions as to when you should report. It just says, "Begin gathering data and continue making such reports," but it doesn't say when to report in relation to an event.

(Several comments made simultaneously from unmiked locations.)

So that means you want the reports to the NRC Operations Center on these, too, a regular way? So you're turning this into an ugly event.

MR. CAMPER: We may need to reconsider that.

DR. HOLAHAN: Yes.

CHAIRMAN SIEGEL: But this is supposed to be a neutral data-gathering kind of thing right now and --

(Laughter.)

-- you're turning it into something a little nastier, I think.

DR. HOLAHAN: Yeah. Well, I don't think that is our intent.

MEMBER NELP: If you tell them what you told me, I don't know if you're going to get inspected on the basis of this report, but you might.

MR. CAMPER: Well --

MEMBER NELP: I can't guarantee that it's not going to --

MR. CAMPER: But you're asking me to --

MEMBER NELP: -- some adverse effect. So I'm not sure that you don't want to connote that. That's the whole conversation; you don't want to connote that, you want to say, "Hey, guys, I need some help adding up this information and turning" --

MR. CAMPER: I understand, and then that's clearly the intent of this GL. But again, I cannot tell you emphatically that a reported single fractionated event would not result in an inspection, or for that matter would not ultimately result in enforcement action. It would

depend upon the circumstances.

MEMBER FLYNN: For example, if five treatments were prescribed, and the single fraction is over 100 percent overdose, then just by dividing the five fractions into the 100 percent plus, then it would be more than 20 percent for the total dose anyway. So it would be a misadministration, or would it? I assume it would be. There's no debate there, is there?

CHAIRMAN SIEGEL: Well, only if it was the fifth dose, because if you modified the remaining three doses, if it was the second dose, then you could control it within the original prescription. If it was the fifth dose, you haven't got that choice.

I would encourage you to try to keep this as low key as you can while you're gathering data to maximize the cooperation of people in trying to get you data, just so we can help find out whether there's really a problem here.

MR. CAMPER: The answer to the second question was a resounding "yes."

CHAIRMAN SIEGEL: Yes.

(Laughter.)

MEMBER NELP: Would it be possible to get the denominator in this questionnaire, how many did you do? It would seem to be very simple, if you asked me how many

radiotherapies I do each year --

DR. GLENN: Since we're going to OMB anyway, why not? Yeah.

MEMBER NELP: And then you'll know -- I mean, you say you don't know if you have -- I'd say you don't have a problem, and you say you don't know. It will help you to find out.

CHAIRMAN SIEGEL: There may an OMB problem, though. One is in event reporting versus a periodic summary reporting --

DR. GLENN: Yeah, I guess there is one issue here. We can certainly do that with respect to those people who report events; we can ask for the total -- we can get the denominator for those who report an event. But we can't get a report from everybody who didn't have an event. That would greatly expand the --

MEMBER NELP: Right. This would be your worst-case scenario probably.

MEMBER FLYNN: But for HDR brachytherapy, and Bob Ayers can correct me if I'm wrong, I think there is approximately 320 HDR machines out there. It is not an undoable number to gather information as to how many fractions are administered per year, to get a good denominator, to see what the --

MEMBER NELP: Now, where does this -- this

reporting will get translated into state regulations, too, I presume.

MEMBER FLYNN: Not necessarily.

MEMBER NELP: You're sampling a very -- a relatively small piece of the pie.

MEMBER FLYNN: That's correct.

CHAIRMAN SIEGEL: Okay. It may be more difficult to get the denominator than meets the eye.

Continue.

DR. HOLAHAN: Okay. Well, let me get to another quiet topic.

(Laughter.)

CHAIRMAN SIEGEL: Right.

DR. HOLAHAN: In the briefing book, I described a couple of incidents in which sources had either become dislodged or ribbons had become dislodged. Now, one of the questions -- the reason for this question is as part of the written directive, the authorized user needs to include the treatment site.

Well, the question then comes down to, if that's -- on the written directive, if they just include either a dose to point A, they obviously don't include the isodose curves within the treatment site. But if a source becomes dislodged and the treatment is within the volume that may have been the isodose curves, is that considered

the treatment site? What is a wrong treatment site?

And I'm just sort of trying to get a feel from the committee as to -- we're trying to develop a working definition of treatment site and wrong treatment site.

MR. CAMPER: May I just add to something that Trish said so you'll fully understand where we really are here.

Currently, wrong treatment site carries with it no threshold, and it is not defined at all. It just says "wrong treatment site," and that can result in a misadministration -- and has.

Now, and Trish's emphasis here is exactly the right one I think in the sense that while the regulation says "wrong treatment site," we think it's probably more appropriate to tackle this problem by saying, "What is the right treatment site? What is the treatment site?"

We find ourselves, today for example, spending a fair amount of time in terms of staff resources, which troubles me immensely, looking at events in which the source has slipped a millimeter or two, or a centimeter or two, and yet this slippage is occurring within either the treatment volume or the irradiation volume. And so what we really need is -- I mean, what is the boundary at which we would be thinking that we are in wrong treatment site? Or where does treatment site stop?

DR. STITT: Two things come to my mind right away, and one was when I was new -- now that I'm an old and experienced person -- I thought it was absolutely hysterical listening to this group try to describe "patient." Do you remember "patient"? That just cracked me up.

Now I see why we spent all this time -- and I think if you thought "patient" was tough, wrong treatment site is not going to be doable. I would try to stay away from making an official regulatory definition of wrong treatment site.

CHAIRMAN SIEGEL: Somewhere in the Milky Way? Is that sufficient?

DR. STITT: I agree with you that it is -- you need some sort of parameters because you're stuck with two millimeters.

Now, in low dose rate, wrong treatment site goes on all the time because those sources are on the move. I'm not talking about sources that have slipped a centimeter or sources that are on the floor. But the anatomy of the human body is such that low dose rate applicators and their sources are moving around a lot.

We, again, back to high dose rate, just know a lot more about what we are doing right and what we are doing wrong. So I don't have a pat definition, but I beg

us not to start working on a definition of wrong treatment site as a -- now, maybe we ought to define right treatment site, and it needs to have some parameters, and maybe there is a threshold. So I'm leaving it with those comments.

DR. HOLAHAN: Well, that was why we had started off with treatment site, because if there is an error -- and I'll go back to the fractional case with HDR -- is your written directive specifies an overall treatment volume, but each fraction is to a separate area within that treatment volume, and there is an error in one of those.

Is that wrong treatment site when it's within the intended treatment volume? I mean, it's perfectly clear that if you intended to treat the right arm and you treated the left, or the sources come out and you tape them to the wrong part of the body, that that's wrong treatment site. But I think it's these type of issues that we're unclear on.

MR. CAMPER: Yeah. You see, that's the point. If only the definition could be so simple as, you know, okay, you irradiate the wrong eye, or the wrong hemisphere of the brain, or the wrong lobe of the lung, or that type of thing, or the wrong leg. Unfortunately, those are the easy calls. The problem is is when we're in this realm that we're discussing now, within the irradiated -- within the planned irradiated volume, or within the planned

treatment volume. That's the dilemma that we are in.

MEMBER FLYNN: I think it has to be taken on a case-by-case basis, because for example I've looked at these summaries here, and I recognize many of these that I was the NRC consultant on.

There was one in Connecticut, for example, where a low dose rate source fell out and went unrecognized in the patient's bedding. The patient sat on it, and later on got a very open, painful ulcer. Well, to me, there's no question that that's a wrong treatment site.

(Laughter.)

But had that source been there for -- had the source been there for a few seconds, and there was no ulcer and no consequence, then I would say not the wrong treatment site -- a dislodged source. I think you have to really - I think it's -- I agree with Judith. It's going to be so difficult with the other -- with sources in different parts of the (quote) "volume" -- let's say, in the pelvis -- it has to be a case-by-case basis. I don't think you can come up with a definition.

DR. HOLAHAN: But I think you're getting at the second question that we have, which is, if it's wrong treatment site, but then should there be a threshold dose considered --

MEMBER FLYNN: Yes.

DR. HOLAHAN: -- for the wrong treatment site?

DR. STITT: I think what we're getting from people around the country -- and again, in response to the questionnaire -- they may not have been the world's greatest questions, but we are getting responses, and I think the responses are at least better than the questions are. But there is a fair number of people who have independently said that for a wrong treatment site, maybe we don't want to define wrong treatment site, but there should be a threshold; and that may take care of the issue.

And for a working definition of a treatment site, I think it's a little bit easier to come up with what is a treatment site, with some parameters and some plus or minus --

MEMBER FLYNN: Instead of harm to the patient, because of -- could it be, for example, you make a judgment as to whether there could be any reasonable medical consequence, whether it be harm or not harm, but leave it to individual case reviews.

DR. STITT: Well, the NRC hasn't been interested in that sort of --

MEMBER FLYNN: There are not that many that you could be -- that you couldn't ask individual questions.

DR. HOLAHAN: Can I ask how you would define treatment site?

DR. STITT: Pretty generally.

(Laughter.)

MR. CAMPER: Such as?

DR. STITT: Yeah, patient -- right. Now, how do you mean that when you say "patient"?

(Laughter.)

CHAIRMAN SIEGEL: I remember, that's somewhere in the pelvis.

(Laughter.)

DR. STITT: Well, some of your -- the cases that you illustrated are good examples of things that aren't really the wrong treatment site -- a nasopharynx catheter, where part of it is in in the volume, and the -- you know, a bit of it's outside. If you had a threshold for part of that tissue, then you'd probably have that taken care of without having to make that into a major investigation.

CHAIRMAN SIEGEL: One kind of combination concept would be to have, first of all, a threshold, period, some bottom level below which it just is silly to report. I mean, we've got a threshold for radiopharmaceutical diagnostic misadministrations, and we don't bother to report them if organ doses are below 25 rems.

I am aware that there have been wrong treatment

sites reported that -- where the dose to the thigh is a few rems, and that just doesn't make a whole lot of sense, or even less. So a bottom threshold at one point would be a good thing to do.

The other thing to do would be to consider alteration of the total dose within the irradiated volume beyond what would have been expected if the treatment had been conducted exactly as planned, so that -- and that could be a percentage. So, a) above 25 rems, and some percentage above what the right orbit would have gotten if the treatment had been conducted exactly as planned.

DR. HOLAHAN: So you're saying based on the isodose curve for what --

CHAIRMAN SIEGEL: It's an "and."

DR. HOLAHAN: -- you would have.

CHAIRMAN SIEGEL: That's an "and." Yeah, it would be an "and."

So in the one case, let's say the treatment site was meant to be the right eye, and you treated the left eye. Well, you wouldn't report incorrect treatment to the great toe, because it didn't even -- even though it was also included in the treatment, but it didn't get, say, the 25 rem number.

MEMBER NELP: Why do you say 25 rem?

CHAIRMAN SIEGEL: I'm pulling that number out

of the air, but I'm pulling a number out of the air that is the same number that is currently in the diagnostic radiopharmaceutical misadministration reporting threshold. It's 50, excuse me. I'm sorry.

DR. STITT: Is this for an organ?

MR. CAMPER: Yes.

CHAIRMAN SIEGEL: Well, my rule is confusing.

DR. STITT: We're looking at something that we -- meaning, there's some information that part of the two committees that I'm working on nationally have something like a threshold of 200 rad, and we're talking about for a spot. We're not talking about for an organ or a volume.

MR. CAMPER: Yeah. We can --

DR. STITT: I mean, we can fill in the blanks as we go along. But I think that combination would be workable, usable, and above all it makes sense, and I think it would eliminate some of the stuff that you spent time doing, you know, or that the source train got halted on the way out, and therefore you've got a wrong treatment site, because there was a --

MR. CAMPER: Then, what I think I'm hearing is, you know, ultimately to clear this up would require rulemaking. I mean, that's the ultimate solution to our problem. But of course, unfortunately, these events are occurring. I mean, we have had three or four this week

we've been working in the staff, and we have to interact with the Office of General Counsel, and it takes a lot of time and effort and resources.

What I think I'm hearing you say, though, and correct me if I'm wrong, is I think we're going to attempt to develop a working model, based upon the comments we've heard in the last few minutes, and then we can distribute that to you.

DR. STITT: To the committee.

MR. CAMPER: And you can provide us with some feedback that we can then further refine the working model that we can use as we go about evaluating these events and interacting with the Office of General Counsel. And we do intend -- we do want to meet with the Office of General Counsel, probably next month, after we've had this meeting and gotten this input and after we meet with the American Brachytherapy Society, for purposes of trying to -- given that it will take rulemaking, obviously, to fix this, at least a working definition to hopefully reduce the amount of staff resources that have to be devoted to literally events where we're talking millimeters or centimeters within a planned irradiated volume.

Does that sound like a workable approach?

DR. STITT: Yeah. Do you have any details to fill in there? I mean, should we go into this in more

detail here? Or --

MR. CAMPER: It would be helpful.

DR. STITT: Well, Barry, do you want to reconsider some of our little discussions?

For wrong sites, some of the discussions that are going on in AAPM, ACMP, and ASTRO have to do with misadministration means. I'm on 35.2. It involves a delivery of radioactive material to the wrong treatment site, situations in which the resulting excess dose to the wrong treatment site must be at least 20 Centigrade.

This is a proposed suggestion that you might look at in this next group you're talking about working with.

Migration of permanently implanted seeds outside the treatment site would be excluded.

DR. HOLAHAN: It currently is.

DR. STITT: Okay. Then, the change would be using a 200 Centigrade, 200 rad, as a threshold. That is, wrong site has to have a dose that exceeds 200 to be a misadministration, 200 Centigrade.

MEMBER FLYNN: Judith, can I ask you where you are? On what --

DR. STITT: Oh, I'm making this up. These are some suggestions from a --

MEMBER FLYNN: You're reading something, and I

thought maybe it was --

DR. STITT: Oh, I am. This is a draft proposal that's not ready for -- it was written in response to revisions of Part 35, and this is the Physics Committee of ASTRO.

DR. HOLAHAN: Now, this is, though, looking at a threshold for wrong treatment.

DR. STITT: Wrong site.

DR. HOLAHAN: It is not within --

DR. STITT: That's correct.

DR. HOLAHAN: -- the treatment volume.

DR. STITT: That's correct.

DR. HOLAHAN: So is there anything in there on what is the treatment site?

DR. STITT: No.

DR. HOLAHAN: Okay.

DR. STITT: There is also a comment that we're looking at where the calculated total administered dose includes the sum of external beam treatments and brachytherapy procedures as specified in the written directive differs from the prescribed dose by more than 20 percent. So it's basically using a 20 percent, but it's combining with the external beam therapy plus the fractionated high dose rate brachytherapy.

So that's where we've gotten so far on wrong

site. That's our suggestion at this point for a threshold.

MR. CAMPER: Why 200 R?

DR. STITT: Because it's a commonly -- I mean, it's a dose that would do nothing to any tissue, including the lens which is the most radiation-sensitive organ in the body. I mean, we're talking about sites not organs, when you're talking about brachytherapy treatment. And it shouldn't cause harm. And, in fact, you probably wouldn't see any visible effect if it were on the skin.

Anything below that, it's kind of where we currently are, which is low doses that are requiring a lot of people's time and a lot of paperwork. We can keep working on treatment site, though.

DR. HOLAHAN: Yes. Treatment site is one that I think we perhaps -- because I think to get in a threshold on wrong treatment site, it's probably going to require rulemaking. But if we can get a working definition of treatment site that we can at least have as a working model, it gives us something to go on, because currently there is no threshold for wrong treatment site.

MEMBER NELP: Is that a commonly referred to number in the radiation therapy domain, 200? Is that something that people talk about all the time as overtreatment or mistreatment?

DR. STITT: No. It's just a very low number in

our business. I mean, some of the people in these discussions wanted to use the following beyond normal tissue tolerance. I mean, then you'd be talking about thousands of -- several thousand rad. I mean, the 200 is --

MEMBER NELP: What about one-half of expected normal tissue tolerance? Because that seems like a very low number to me.

DR. STITT: 200?

MEMBER NELP: Yeah.

DR. STITT: Oh, I agree with you. It is.

MEMBER NELP: That's far below one-half of tissue tolerance.

DR. STITT: Yes.

MEMBER NELP: If you say one-half of tissue tolerance, you're still going to be -- have a 50 percent margin of harm, theoretically. I'm wondering -- again, I don't think the NRC wants to know -- both of those particular small variations -- like, if you said 200, we don't -- with radiopharmaceutical therapy, of course, we treat with millicuries. We do treat with rad. Many people don't even both to calculate.

Two hundred rads Centigrade, or so forth, in therapy for thyroid cancer would be inconsequential, less than one percent. I think half of the tissue tolerance

would get you more into the real world.

DR. STITT: It does. It's a considerably higher dose. Even the 200 rad or Centigrade would actually be very helpful in a lot of stuff that the NRC has seen pass by them. That would eliminate quite a number of things.

MEMBER FLYNN: With all of the various normal tissue tolerances there are out there, plus the disagreement as to what the normal tissue tolerances would be, you'd be creating basically a nightmare out there to decide what that should be.

MEMBER NELP: Well, then you could say 500 or estimated normal half tolerance.

MEMBER FLYNN: You've got tissue tolerance for all of the liver, for part of the liver. You've got for all of the bowel, for part of the bowel, you've got --

MEMBER NELP: I'm talking about the treatment site.

MEMBER FLYNN: Well, whatever the treatment site might be.

MEMBER NELP: Yeah.

MEMBER FLYNN: I know you could have hypothetical complications in trying to come up with this. My concern is it's an unrealistically low number. It's well below anything. I don't know --

MEMBER NELP: Well, one way --

MEMBER FLYNN: The most sensitive tissue is the bone marrow, right?

MEMBER NELP: Well, if the source was --

MEMBER FLYNN: You'd have to treat the whole organ.

DR. STITT: Right.

MEMBER FLYNN: Let's say, for example, a male was being treated for cancer of the anus or the rectum, and let's say the scrotum, the testicles got an extra 200 or 500 rads. It may be of concern to him.

MEMBER NELP: So that would be a -- don't most people think that that's a significant dose?

MEMBER FLYNN: Yes.

MEMBER NELP: That's not a problem.

MEMBER FLYNN: It's not a problem?

MEMBER NELP: It's not a problem in defining that it is half of a significant dose.

MEMBER FLYNN: I know that you get aspermia when you get 20 or 30 rads to your testicles. All I'm saying is I'm -- I don't think there is -- that would cause, really, too much controversy in trying to define what half of a tissue tolerance is.

DR. STITT: Yes, sir?

CHAIRMAN SIEGEL: Well, I guess one -- you can

partially get around this by having both a threshold and linking it to what the dose to that tissue would have been if the therapy had gone off without any hitches, and then making it a percentage of that dose.

So like 20 percent of what the tissue would have gotten if everything had gone according to Hoyle, or 200 rems.

DR. STITT: Yeah. But the problem is the tissue should have gotten zero; 20 percent of zero is still zero. That's what I --

CHAIRMAN SIEGEL: Then you put in "or."

DR. STITT: Oh, or is --

CHAIRMAN SIEGEL: Whichever is greater.

DR. STITT: Okay.

CHAIRMAN SIEGEL: Whichever is greater. So if a tissue was supposed to get 5,000 rads, and you were off by 200 rems, you wouldn't report it. If it was supposed to get 5,000 and it was off by 2,000, you'd report it. If it was a tissue that was supposed to get zero, and it got 10, you wouldn't report it, but if it got 200, if we use that as the number, then you would report it.

DR. HOLAHAN: Why would you want to report it?

CHAIRMAN SIEGEL: Because -- once again, please understand the disconnect that we agree with you on between what needs to initiate the whole inspection and patient

notification stuff versus the NRC's need to know if devices are malfunctioning or if systems are otherwise failing. And I support that completely --

MEMBER NELP: But I would say that if my system works within 200 MR --

CHAIRMAN SIEGEL: This time.

MEMBER NELP: -- and I propose to give that tissue nothing, my system is working extremely well.

CHAIRMAN SIEGEL: That's this time. This time it -- no, that's this time it worked within 200 MR. The next time it fails it might fail --

MEMBER NELP: That's not what I'm saying. I realize you have an argument about failure, identifying future failure. I'm saying if my system works within 200 rads to normal tissue, and I didn't plan to give anything to that tissue, my system worked very well indeed. There is no one that would argue.

DR. HOLAHAN: But I think we're also looking at an error in the delivery process. If it was because the sources had been placed in the wrong location --

MEMBER NELP: Do you realize the error in the estimates of these rad doses? 200 rads of error is nothing. I Imagine the errors in some of these doses are multiples of that. You're well beyond the projected error of estimate. You're well below that. There's no way in

God's green earth you know that if you give 5,000 rads to tissue that you're plus or minus -- I think if you're plus or minus 10 percent, as a radiotherapist you would feel that you're very much on the ball. Is that correct?

DR. STITT: He keeps looking at me when he asks these questions.

(Laugher.)

MEMBER NELP: No, I'm talking generically. Isn't that true?

MEMBER FLYNN: We talked about it more in terms of the calculated administered dose, not the pure dose that -- we're not taking into account the errors in calibrating the cobalt machine or --

MEMBER NELP: No. We're talking about what you estimate, your best estimate of the dose is based on the anatomical variances and the physical factors, and the locations of the doses, and I would -- who is the top-notch dosimetrist in this bunch? You?

If you calculate a dose --

DR. WAGNER: That's why we need the other physicist.

(Laughter.)

MEMBER NELP: But if you calculate a dose and you get within 10 percent, I imagine you feel you've done a -- and if you never --

CHAIRMAN SIEGEL: I think with current 3D treatment planning, I think the doses are --

MEMBER NELP: You never know what the reality is because you rarely measure the dose that you deliver. Isn't th correct?

CHAIRMAN SIEGEL: I think you're ascribing a little too much slop to the current practice of modern radiation oncology. I think --

MEMBER NELP: For manually implanted brachytherapy, for low level brachytherapy where you have --

MEMBER FLYNN: Well, all of the systematic errors that go into a dose in, let's say, in a teletherapy patient, including calibrating that cobalt source, the uncertainty of the exact source activity, a lot of things -- plus or minus five percent, you ask any radiation oncology physicist, is not an unreasonable number. But we're not talking about that plus or minus five percent. We're talking about the errors above that.

MEMBER NELP: No. You're talking -- no. I'm sorry. I thought we were talking about 200 millirem to tissue that would ordinarily get zero in a procedure where if you're within plus or minus 500 millirem you're happy.

DR. HOLAHAN: At 200 rads, wasn't it?

DR. STITT: Getting back to that, I think we

ought to think some more about what was just said in the discussions. That is, a threshold and then the -- we've discussed this percentage issue, and it may -- it may be worth getting back to -- to that, and possibly, Tricia, this will help a bit with treatment site versus wrong treatment site.

I mean, maybe we just want to do some more thinking on this and leave treatment site hanging out for a while, because wrong -- if we can define wrong treatment site, maybe treatment site becomes intuitive possibly.

MR. CAMPER: A comment on wrong treatment site. The International Commission on Radiation Units and Measurements, in report number 29, talks about some definitions for treatment planning. It talks about target volume, it talks about treatment volume, and they talk about irradiated volume.

It would be helpful if we could make copies of this article that I have here and let you look at these definitions that ICRU uses, and see if there is any utility in them in terms of treatment site, one of them being acceptable as a treatment site.

And when we break, I can make copies of this. I don't think you have this. I just got this yesterday afternoon myself. And it would be interesting to -- to have you look at these definitions and at least give us

some quick preliminary feedback as to whether or not any of those might work.

It is also published in Khan's Book of Radiation Therapy Physics, the same definitions are in --

DR. STITT: Yeah. I mean, those are pretty common things that we're all accustomed to using in therapy. And, in fact, one of the cases I was an advisor on -- and I think it was a nasopharynx case -- the folks trying to plead their case were pleading that this was part of the target volume. And I think they were right on that, and so this would be another way to focus on treatment site.

MR. CAMPER: Correct. From a regulator standpoint, they would appear to have the right pedigree. The question is --

DR. STITT: The ICRU?

MR. CAMPER: Yeah.

DR. STITT: I would hope so.

MR. CAMPER: I'm saying it has the right pedigree.

DR. STITT: Yeah.

MR. CAMPER: Therefore, can one of them work for us as the treatment site?

DR. STITT: Well, I would think it would be -- yeah, let's look at those. We'll take care of it when we

start making up our own in-house definitions.

MR. CAMPER: Yeah. Precisely my point.

CHAIRMAN SIEGEL: Why don't we get those copied, and maybe people can look at them overnight. We can spend a few more minutes on this particular issue tomorrow morning.

Let's go on to your last question.

(Laughter.)

Your last multi-part question.

(Laughter.)

How about just "no"?

DR. HOLAHAN: I ran out of space. Then you have to go to the if not, why not.

CHAIRMAN SIEGEL: I know it.

(Laughter.)

DR. HOLAHAN: Basically, the recent findings that we've had, some of the problems with the HDR, the question of -- that we are currently imposing requirements on HDR licensees through licensing guidance and license commitments, with the policy and guidance directive.

Also, and Janet will get more into the issue tomorrow about a possible delay of a revision of Part 35, but if that also occurs where we're looking further down the line, do you believe it's appropriate that we need to proceed with some type of rulemaking of the brachytherapy

issues -- first of all, to incorporate the HDR licensing guidance into real space, which includes physical presence of -- you know, the issues that were addressed in the bulletin as well as some of the other --

CHAIRMAN SIEGEL: Stop. Yes. I mean, because right now you're rulemaking by license condition, and therefore it's not subject to public comment; it's only subject to whatever individual licensees can negotiate if they can negotiate anything. And the better way to do that is by following the Administrative Procedures Act and doing it the right way.

And I think we've said before that we thought this was an area that needed your attention because it was a regulatory gap.

DR. HOLAHAN: Okay. Yes.

CHAIRMAN SIEGEL: So unless I hear substantial demurs from the rest of the table, I'll answer for us "yes."

MEMBER FLYNN: The only question I have is you wanted to gather information on HDR brachytherapy fractionation. If you gather information that may alter what the rulemaking might be a year from now, you can modify the rulemaking?

CHAIRMAN SIEGEL: The rulemaking won't go that quickly.

(Laughter.)

MR. CAMPER: All right. That's a good point. I mean, when we say "expedited rulemaking," remember that we have this major revision to Part 35 planned.

(Laughter.)

I mean, even if we expedite it, you're looking at a couple of years -- an oxymoron.

DR. HOLAHAN: And I'm going to sort of do these a little bit out of order.

The modification 35.400 is -- about two years ago, staff had started to look at the list of uses for brachytherapy sources that were currently in 35.400, but they're very specific as to what each source can be listed for. And there were some efforts on the part of maybe just modifying that to basically say that you can use a source that is being -- has undergone the source and device registration and for the purposes that it is authorized for under that source and device registration.

Should we include that type of effort within this rulemaking effort? And then the --

CHAIRMAN SIEGEL: So that would be like a radiopharmacy rule for sources?

DR. GLENN: It would be somewhat that way. But there still would be a requirement that the -- from the NRC's point of view, that it be reviewed for safety for

that particular type of use. In other words, there might be a different environment for intracavitary versus interstitial, and so there might be some restrictions that come from the construction of the device of the source itself.

MR. CAMPER: That's correct; 32.210 requires that they would, in their submittal, describe for what purpose the device is going to be used and present data as to the safety of the device for that environment.

CHAIRMAN SIEGEL: So right now if a licensee wants to use a particular device source combination for therapy for which it was not intended in its FDA labeling?

DR. HOLAHAN: No, in its --

CHAIRMAN SIEGEL: Isn't that correct?

DR. GLENN: For the use that's in the regulation is the current --

DR. HOLAHAN: Yeah. If they wanted to use it for something other than is currently listed in 35.400, they would need to come in for an exemption to the regulations in order to use it.

CHAIRMAN SIEGEL: As a license amendment.

DR. HOLAHAN: Although it could have been approved for that use since the original source and device registration to include it as that use.

MR. CAMPER: Or the manufacturer, of course,

could seek approval for a change. But they don't do it; the licensees end up doing it.

CHAIRMAN SIEGEL: And how many of those are you getting a year?

DR. HOLAHAN: I don't --

MR. CAMPER: Not very many. We did go through a flurry of activity requests, and then a couple were withdrawn as it turned out because I think it was going nowhere. Not many.

DR. STITT: What are the nature of those requests? To do what with what?

MR. CAMPER: I don't recall.

DR. STITT: I mean, I'm having trouble thinking of them; that's why I -- I simply don't know.

MR. CAMPER: Oh, let's see.

DR. HOLAHAN: I mean, I think we've seen some uses where they've come in. In fact, we did put out a policy and guidance that you could use -- I think it was at I-125 infalladium for in -- for one of the uses not listed. I believe it's interstitial, but --

DR. GLENN: There's one where interstitial and intracavitary -- but they wanted to use it for the other.

MR. CAMPER: Yeah, it's the interstitial, intracavitary, interluminal distinction.

DR. HOLAHAN: Right.

MR. CAMPER: They wanted to use a source for a method that's not specifically listed in Part 35.

CHAIRMAN SIEGEL: And you would propose doing something with Part 35 that would make it easier to achieve that?

DR. HOLAHAN: Correct.

MR. CAMPER: Yes.

DR. GLENN: Something less than a rule change?

DR. HOLAHAN: But it could be done as -- yes, we would.

CHAIRMAN SIEGEL: Please try it. How could we be opposed?

DR. HOLAHAN: Okay. Then the next -- let me go back up, then. The quality assurance checks -- oh, first of all, with the HDR issue, one of the things I'll mention -- and I think it was mentioned earlier in the licensing guidance -- there are some specific requirements for medical physicists doing HDR procedures, and that would also be addressed.

And then, quality assurance checks for brachytherapy similar to teletherapy -- and I did provide you with the excerpt from 35.600. I know you have the overall Part 35, but specifically 35.632 has requirements for full calibration measurements. There are also requirements for periodic spotchecks and safety checks and

whether we should consider something like --

CHAIRMAN SIEGEL: Didn't we --

DR. HOLAHAN: Pardon me?

CHAIRMAN SIEGEL: Didn't we already at a previous meeting tell you that we thought that you probably needed to do something like that?

DR. HOLAHAN: That's right. And I guess our question is, do you think we should go ahead? The question is, should we wait until the overall revision, or is it significant enough that we should address it all at once now?

CHAIRMAN SIEGEL: I'm going to defer to Judith and --

DR. STITT: I think addressing it now would make a lot of sense.

DR. HOLAHAN: Okay. And, I mean, it would be addressed in the public meeting. And then, finally, the revision of brachytherapy definitions, which we discussed before.

CHAIRMAN SIEGEL: It seems clear that that needs some work, too, and sooner rather than later.

DR. HOLAHAN: Well, that was the easiest question of all.

CHAIRMAN SIEGEL: All right. Any other points or questions for Trish? We've worked you very hard.

Bob?

MR. QUILLIN: We touched on gamma knife issues very briefly in this presentation. But most of the issue was about the HDR. Do you have any plans in the gamma knife area?

DR. GLENN: Maybe I should respond to that. We certainly do, but we're a lot further along in our thinking about what we need to do with HDR than what we need to do with gamma knife.

The NRC currently only has, what, four gamma knife licensees, and we've got --

DR. HOLAHAN: That's correct.

DR. GLENN: -- hundreds of HDR letters and --

MR. CAMPER: We are doing something currently in updating our licensing guidance for the gamma stereotactic devices, but we're certainly nowhere along the way, as John said, with regards to any considerations or rulings yet.

CHAIRMAN SIEGEL: Okay. Let's take a 15-minute break. We are 45 minutes behind schedule, but that's life.

(Off the record for a break from 3:46 p.m. until 4:01 p.m.)

CHAIRMAN SIEGEL: Moving right along, we are back on the record.

And now we are going to hear about the

revisions in the abnormal occurrence reporting criteria, and Bob Prato from the Office of Analysis and Evaluation of Operational Data, otherwise known as AEOD.

MR. PRATO: Again, my name is Bob Prato. I work in the Office for the Analysis and Evaluation of Operational Data, Nuclear Materials Assessment Section.

I'm going to be giving an overview on the ongoing effort by the staff to revise the abnormal occurrence criteria. But before I get into the actual presentation, I would like to make a couple of brief comments.

First of all, any information that's covered today is predecisional. The present status of the paper is that it is in the Commission's hands for the first time, and it was signed by the EDO last week, and they have not seen it. So all of this information that's going to be presented in this meeting is predecisional.

The second item is about two months ago, in an effort to get early input from this committee and from the agreement states, we sent out an early draft of the staff's proposed revision to the criteria. And as a result, we received comments from a number of the agreement states, approximately 12 of them.

Those comments that we received affected some changes in the copy of the draft that you received. So if

you're going to comment on the revised criteria, we ask that you please wait until the Commission signs the present version and issues it for public comment. Okay?

A little background on the abnormal occurrence process -- in 1974, the Energy Reorganization Act was promulgated, and as part of the Energy Reorganization Act, Section 208 was -- became law, which required the Commission to report any occurrences that were significant, from the standpoint of public health and safety, to Congress in a quarterly report.

In response to that, in 1977, the Commission published its first set of abnormal occurrence criteria. In 1980, we issued the misadministration reporting requirement, and as a result of that reporting requirement, in 1981, we issued some interim reporting guidance for misadministration reporting to Congress.

That interim guidance was intended to only be in effect for about two years, until we got a feel for what we felt was appropriate to report to Congress and what we felt was not appropriate to report to Congress. So in 1984, we actually issued and developed misadministration reporting criteria, and we've been using that criteria ever since.

In May -- on May 19, 1994, the staff received a memorandum from the Commission requiring us to initiate an

effort to revise the criteria.

A number of factors went into the direction in which the revision took, so there are three major items that shaped the revision as it exists right now in the Commission's hand. The first one is the May 19, 1994, staff requirement memorandum which initiated this effort.

In that memorandum from the Commission, the Commission were very specific on a number of items. Okay? The first item was the medical misadministration criteria. They actually gave us a specific criteria which right now is in the revision. They also gave us some very specific guidance on the overexposures.

They asked us to update the criteria to the revised Part 20 requirements, which became mandatory in January 1, 1994, and they told us to come up with some official guidelines for reporting other events of interest.

Other than the Commission memorandum of May 19th, on May 15th we received another Commission memorandum which commented on the abnormal occurrence criteria report. In that memorandum, one of the Commissioners stated that we needed to revise the lost and stolen abandoned source criteria because it was too vague, and there wasn't enough guidance out there for us to select appropriate events to report to Congress.

Finally, there were a number of ongoing

regulatory efforts that we felt that should be considered as we developed the criteria to make sure that we added or did not add certain aspects of the criteria so it wouldn't require revision any time in the near future.

Some of the highlights of the changes include the overexposure criteria. This is a relatively general change in philosophy. Typically, in the past, occupational exposure was treated as less important, less significant than normal exposure to individuals in the general public. But for Section 208 of the Energy Reorganization Act, Congress was very specific to state that we should only report those events that were significant from the standpoint of public health and safety.

And the Commission took the position that the exposed individual status as a member of the general public, occupational worker, or wrong patient, was indifferent to whether or not the event was significant. So as a result, they asked us to combine all of the overexposure requirements into one criteria.

At the same time, they also told us to go back and ensure that the threshold that they recommended, which was 25 rems TEDE, was appropriate for all of the categories, and we did that. As a result, we came up with a second criteria for minors, fetuses, and embryos. Okay? And that criteria is set at 5 rems TEDE, because of the

increased radiosensitivity.

Criterion 6 is lost or abandoned sources. I don't believe that we need to cover that in this meeting, so I'll move on.

Medical misadministration criteria -- as prescribed by the Commission, the criteria, that table that exists right now in back of each of the abnormal occurrence reports no longer will be effective once the policy becomes effective. Instead, the criteria will look more like theirs, where a misadministration -- and it has to be a misadministration that results in 100 rads to a critical organ -- and a critical organ in this case is bone marrow, gonads, and the lens of the eye. Okay? Or, 1,000 rads to any other organ.

And on top of that, it has to be greater than 50 percent, the prescribed dose, or -- and it has to be the wrong radiopharmaceutical, the wrong route of administration, the wrong treatment site, the wrong treatment mode, and leaking sources, or leaking sources.

In addition, the Commission also gave us some specific requirements on other events of interest. Those requirements, as prescribed by the Commission, or as recommended by the Commission, included recurring events or conditions with generic implications, multiple misadministration with common causes, reactivity addition

-- again, that's reactor oriented -- and they also asked us to add the 5 rems unintended radiation exposure to an adult, other than a radiation worker.

CHAIRMAN SIEGEL: Where does wrong patient fit with that last item?

MR. PRATO: We defined "unintended radiation exposure" as any exposure to an -- how did we word that? I have it right here. We defined an unintended radiation exposure as any exposure for the purpose of reporting as an AO includes any occupational exposure, exposure to the general public, or exposure as a result of a misadministration involving the wrong patient, that exceeds the reporting values established in the regulations, and all other reported misadministrations will be considered for reporting as an AO under the criteria for medical licensees.

So the only one that gets captured, the only place that really gets captured, is -- it's under Criterion 1 and Criterion 2. It's -- sir?

CHAIRMAN SIEGEL: I'm just trying to follow this. You said --

MEMBER NELP: In Criterion 1, could you define TEDE?

CHAIRMAN SIEGEL: Total effective dose equivalent.

MEMBER NELP: Thank you.

MR. PRATO: Okay. This is the actual wording in Criterion 1 right now, any unintended radiation exposure to an adult. And there is a footnote on unintended radiation exposure, and that is the footnote, how it reads. So wrong patient falls under overexposure, not under the medical misadministration.

CHAIRMAN SIEGEL: Well, then, go back to the one that's medical. Does this -- so the threshold, therefore, here would be the 25 rem TEDE threshold, right, or not? That's where I'm getting lost, because my concern is -- the only reason I'm perseverating on this is it sounds like the wrong patient reporting for an abnormal occurrence conceivably is going to be less than the wrong patient reporting for misadministration.

Okay. Let me make sure --

MR. PRATO: Okay. It has to exceed at least 100 rems for it to be reported as an abnormal occurrence under, okay?

CHAIRMAN SIEGEL: Correct. But then, what's --

MR. PRATO: Now, it's 25 --

CHAIRMAN SIEGEL: But then, what's this 5 rems unintended -- give me an example of that item, 5 rems unintended exposure to an adult.

MR. PRATO: To an adult, okay, other than the

radiation worker.

CHAIRMAN SIEGEL: Is that wrong patient? Are we talking about patients here? I'm still confused.

MR. PRATO: To an adult, other than a radiation worker.

CHAIRMAN SIEGEL: Well, then, that's what I'm trying to say is that if, as we will probably --

MR. PRATO: That's correct. But there's a difference between being reported as an abnormal occurrence and an other event of interest. So it is possible that an adult -- an adult wrong patient received 20 rads, it would be reportable as another event of interest. But if he receives 30 rads, it would be reported as an abnormal occurrence.

CHAIRMAN SIEGEL: My only question is, I'm -- depending on how -- depending on where the criteria for reporting of wrong patient events is set under the misadministration reporting requirements, how are you going to know about these? You're not going to be told about these. Wrong patient events that result in 5 rads exposure, if they're reported, if they were to have been reported under Part 20 requirements, we would know about them. If as intended, they are going to be reported under Part 35 requirements, you're not going to know about them.

Am I correct, John? Am I reading that right?

MR. PRATO: Again, this -- the existence and especially the normal reporting activity, I've looked at all of the abnormal occurrence reports since --

MEMBER FLYNN: I've looked at all of the abnormal occurrence reports since 1977 for brachytherapy and teletherapy. There were quite a few patients where the abnormal occurrence reports were treating the right hip versus the left hip, the right side of the neck versus the left side of the neck, the right eye versus the left eye.

But my problem is it says here the word, "50 percent are greater than prescribed, or -- or, wrong treatment site, like left hip versus right hip."

But it seems to me that the way this is written, if you gave 10 rads to the wrong patient, Mrs. Smith rather than Mrs. Jones, you wouldn't have to report it because it's less than -- I mean, four rads. It doesn't make any sense, but you --

MR. PRATO: -- Part 35 -- any administration to the wrong patient is reportable.

MEMBER FLYNN: Okay. Because of the abnormal occurrence reports. There were six people who were the wrong patient.

MR. PRATO: The hierarchy is that the licensees report regardless --

MEMBER FLYNN: All right. That's fine.

MR. PRATO: And then, we evaluate each event to determine whether it falls in the abnormal occurrence or the other --

CHAIRMAN SIEGEL: I guess what's missing there, to be absolutely clear, is that that needs to be 5 rems TEDE, to be absolutely clear.

MR. PRATO: That's right.

CHAIRMAN SIEGEL: Okay. I'm sorry. I apologize.

MR. PRATO: Okay.

CHAIRMAN SIEGEL: I am with it now. So that would be captured as a misadministration.

MR. PRATO: That's right.

CHAIRMAN SIEGEL: Okay.

MR. PRATO: Okay. While we were developing the abnormal occurrence criteria, we initiated a separate effort to determine whether or not we were developing effective criteria. To do that, we took a look at the last three years worth of abnormal occurrence reports, and those that we remembered that we were seriously considering to report as an abnormal occurrence report, and we compared those against the new criteria -- the criteria under development.

As a result of that evaluation, we found out that 30 of the 51 misadministrations previously reported as

an AO would not be reported under the new revised criteria. Along with that, unintended exposures, wrong, lost, stolen and abandoned source, uncontamination event, and two other events that didn't fall into any category, previously reported as an AO, would not have been reported under the new criteria.

Two misadministrations, one fuel cycle and one training reactor, one contamination, and again, one other event reported as other events of interest would not have been reported under the new criteria as well. Along with that, we found that two events not previously reported as an abnormal occurrence would have been reported under the new criteria.

In short, what that -- what the results of all of this means is that there is a 52 percent reduction in abnormal occurrences expected and a 60 percent reduction in other events of interest as a result of this new criteria.

Finally, presently, the paper is in to the Commission, and we expect it to be published within the next couple of weeks. Once it is published, it goes through a 90-day public review comment period, and after that it goes to a 120-day comment resolution period. And then it goes back to the Commission for review and approval, and we expect this criteria to become policy in the early summer of 1995. Right now, the tentative

schedule is for the beginning of June.

Sir?

MEMBER FLYNN: Could you -- when you're done, can you put the slide on the wrong -- I mean, the lost or abandoned source --

MR. PRATO: Sure.

MEMBER FLYNN: It said one percent of the initial activity of the source, is that what that said?

MR. PRATO: Yes.

MEMBER FLYNN: Does it say non-disbursable source?

MR. PRATO: Yes, sir.

The lost, stolen, and abandoned source criteria is based on Tab A1 in Appendix A of Part 571, which is the packaging requirements.

MEMBER FLYNN: This is A? This could be a solid source like is used in radiotherapy?

MR. PRATO: Yes. The 0.1 times A_1 value for non-disbursables are sealed sources if you will.

MEMBER FLYNN: I'm sorry. I can't see that. If it's less than 0.1, then it's not a criteria for reporting thresholds?

MR. PRATO: That's right, less than. If it's equal to or greater than 0.1 times the A_1 value --

MEMBER FLYNN: So if you had a 10 curie iridium

source, and --

MR. PRATO: I'm not sure what that value is in 10 CFR Part 71. I can look it up, look at it and --

DR. PAPERIELLO: I think it is 10 curie. In fact, the limit on cesium sources or iridium sources is the maximum amount you can ship without using a type B package, and I think that's where the A_1 value -- the A_2's I believe are your --

MEMBER FLYNN: What you're saying is, sir, if you have a 10 curie iridium source, if it's decayed to be 90 millicuries and you lose it, you don't have to report it? Am I understanding that right?

MR. PRATO: I think it has to be reported, but we don't have to report it to Congress.

MR. CAMPER: These are the reporting requirements to Congress, not to the NRC.

MR. PRATO: That's right. Again, these do not affect 10C FAR requirements.

MR. SWANSON: Can I ask a general question? What has Congress typically done with these reports in the past?

MR. PRATO: I'm not sure anybody knows that answer except for the Congressmen. We have received very few, if any, comments on them.

MEMBER BROWN: How does the new Congress affect

-- do you think they still want it?

(Laughter.)

MR. PRATO: We aren't on the scheduled reduction effort. We've evaluated the abnormal occurrence as well as the process. It's not going to go away. What will probably happen is that we will make it less than a quarterly report; maybe semi-annual or maybe annual.

MR. SWANSON: So you don't have a suspicion that they will be upset that they'll only get 30 reports instead of 52 reports now, right?

(Laughter.)

MR. PRATO: No.

CHAIRMAN SIEGEL: No.

MR. SWANSON: Okay.

MEMBER NELP: I think the Commission directed -- to revise the criteria. NRC directed the revision staff.

MR. PRATO: I mean, I know Congress is informed of the change in policy, and they know that the criteria is going to change. And if they have any problem with it, I'm sure Mr. Siegel will hear about it.

CHAIRMAN SIEGEL: A couple of just procedural -- not procedural questions but specifics. The document that we received on -- in August that was the document that was going to go forward to the Commission, or at least in

draft form, is the basis for the proposed changes.

Will most of this information appear in the Federal Register notice? Because there were some things that I found quite unclear that --

MR. PRATO: That's very easily explained. Part of that -- the first part of that is the FRN.

CHAIRMAN SIEGEL: Okay.

MR. PRATO: That package that we sent you included the Federal Register notice itself, it included a basis document, it included an analysis for lost, stolen, and abandoned sources, and it included the analysis that we did, the tables in the back with the analysis.

So what is going to be published in the Federal Register notice is the FRN itself, and that's all. The rest of it becomes part of the public document room, and it's accessible to anybody who wants it. And as we get calls for inquiries and they have questions -- and the agreement states received a similar package -- all of that information will be made available to them.

CHAIRMAN SIEGEL: Will most of the basis document be the Federal Register notice?

MR. PRATO: That's not our intent right now. Typically, that's not done for rulemaking, and this is just a policy statement.

CHAIRMAN SIEGEL: Okay.

MR. PRATO: It's not even required to be put in the Federal Register notice -- the policy statement -- but the Commission, as well as the staff, feels it's important enough to get public comment on it. Therefore, we're going to publish it.

CHAIRMAN SIEGEL: Okay. Then, I won't necessarily worry about these issues. There are some things that I just thought were relatively unclear, that if this was going to appear in the Federal Register, I was going to offer suggestions to help you from writing something that was embarrassing.

MEMBER NELP: It is going to appear is what I heard.

CHAIRMAN SIEGEL: It changes from --

MR. PRATO: Just the Federal Register notice. Just the actual policy changes itself.

MEMBER NELP: That's fine.

MR. PRATO: The basis document is not going to be in the FRN, but if there is something in there that you feel, we would -- I would seriously appreciate --

MEMBER BROWN: What oversight committees do you report this to?

MR. PRATO: I don't know. The first one appears to -- I really don't know. Sorry. We can find that out for you, though.

MEMBER BROWN: It's not that important. If you knew, I'd be interested. Thanks.

MR. PRATO: It's really not hard to find that out. I'll find that out and let you --

MEMBER BROWN: Okay. Thank you.

MR. PRATO: Anybody else?

CHAIRMAN SIEGEL: Well, I will get my few minor comments on the basis document back to you directly.

MR. PRATO: Okay.

CHAIRMAN SIEGEL: Rather than waste the Committee's time doing it.

MR. PRATO: We will also be, once we get it signed by the Commission, you'll receive an updated copy. Okay?

CHAIRMAN SIEGEL: Good. Thank you.

Let me just -- since there are a number of people in this room who were not in Reston, was it two years ago that we talked about this last? This -- what?

MR. PRATO: A little bit more than that.

CHAIRMAN SIEGEL: A little bit more than that? This is a whole lot better than what we looked at in Reston at that previous meeting where we thought it was going to be an hour report and we spent about four hours discussing it.

This is clear, straightforward, logical, and

really an improvement.

MR. PRATO: The intent was to come up with discreet criteria, something that you can look at and understand clearly. And the other thing was to raise that to that level -- that threshold to a high degree of gray, so that we get rid of more than the not-so-serious report.

CHAIRMAN SIEGEL: Good. Super. Thanks.

MR. PRATO: Thank you.

CHAIRMAN SIEGEL: All right. Next, we're going to hear about some issues relating to administration of radioactive materials to individuals -- a carefully chosen word, I understand.

(Laughter.)

And Steve McGuire from Nuclear Regulatory Research will present.

MR. McGUIRE: Good afternoon. I have to admire your fortitude, starting at 8:00 in the morning and still being here at 5:00, close to 5:00.

I'm Steve McGuire. I'm with the Office of Research in the NRC, and I'm going to talk about -- it's basically administration of radiation and radioactive materials to patients, but in particular this rule change concerns the administration to the wrong patient.

Now, what brings us to this situation? There was a case a while back where a radiopharmaceutical was

administered to the wrong patient, but the dose was less than the 5 rems in Part 35 for misadministration. But it was greater than the .1 rem maximum to -- dose to a member of the public that's in Part 20.

So the question was asked, okay, this is admittedly not a misadministration under Part 35, but is it a violation of Part 20? And the Commission took up this issue, and they decided, no, we wanted all of these medical administrations to be covered under the regulations in Part 35, and they were not to be considered subject to the dose limits in Part 20.

There was a section in Part 35 that dealt very explicitly with misadministrations. There was a rulemaking on the subject, and that was what was going to regulate it.

So they sent us down, it says, an SRM there, that stands for staff requirements memo, and that's how the Commission tells the staff what to do, and they said, "Just tweak Part 20 a little bit so that it's quite clear what we mean now on this subject."

So we have prepared a proposed rule. That package has now been prepared, and we will -- unless you people this afternoon have any strenuous objections or point out any problems that we have, we will send it on to the Commission promptly.

What we're going to do in this proposed rule is

attempt to make it clear that all medical administrations to any individual is regulated by Part 35. Now, this would not affect sort of other things which are non-misadministration, such as dose to -- for example, scattered X-rays, where you're not intentionally attempting to give that individual some radiation, and it wouldn't affect the occupational dose limits for the nurses and doctors and everything like that; just the person to whom the radiation is administered to.

There was one other issue that the Commission was a little bit uncertain, though, and there was some -- they asked us to seek comment on it. In Part 35, under misadministrations, it says that if you exceed the misadministration threshold for the wrong patient, that above that threshold the patient must be notified, as well as the NRC must be notified. But there is no NRC regulatory requirement for notification below that threshold.

And the Commission kind of had a little bit of uncertainty about this kind of gray area, you might say, between the public dose limit of .1 rem and the 5 rem misadministration threshold. They wondered, well, there was some thought that perhaps there ought to be a requirement in there. They weren't sure about that, but they asked us in the Federal Register notice to

specifically request comment on that particular issue.

Now, the change that we are proposing is in Part 20 to essentially use the same words in four different locations, to be kind of consistent throughout on what is regulated in Part 20. The four places are the scope, the definition of public dose, the definition of occupational dose, and the public dose limit in 20.1301.

The words that would appear identical in all four places are shown on the slide there. It would exclude doses due to any medical administration the individual has received. And we chose to use the word "individual" rather than "patient" because in this particular case that I -- the enforcement action that I just told you about, there is the question, well, there was a patient of this one doctor but not the patient of the other doctor, and there was maybe a patient for this procedure but it wasn't a patient for the procedure he got.

So we kind of thought about it, and we said, "Well, the intent, really, is that medical administrations are supposed to be covered under Part 35." And using the word "individual" puts them all under there. It doesn't worry about the problem of who -- is this a patient for this particular procedure, or so on. The patient also is -- it's a little bit -- it's used in many places in Part 35, and the doctors have a certain definition of what

they consider it is.

So when you try to define it to meet everyone's expectations of what the term means in all of these different uses, it ends up rather complicated, and we didn't think we needed to really get into that issue at all.

Really, in conclusion, as I said, the proposed rule is ready to go to the Commission, assuming you don't have major problems with this. And if the Commission approves it, it would be published in the Federal Register some time close to the end of the year.

CHAIRMAN SIEGEL: We've got the language -- the proposed language in our packages. How do you plan to handle the issue of the reporting gray area? Is there going to be something in the PRM about -- a comment about whether that should require individual notification?

MR. McGUIRE: Yes, exactly. We're just asking the question.

CHAIRMAN SIEGEL: If the public comment were in favor of notification of those individuals, would that then become the basis of another proposed rulemaking, or would that likely appear as an addition to the final rule?

MR. McGUIRE: No, it would go right into the final rule.

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CHAIRMAN SIEGEL: Without the world -- so --

but you won't have any draft language.

MR. McGUIRE: That's correct. That's permissible and --

CHAIRMAN SIEGEL: It may be permissible. The question is is whether it's optimal.

(Laughter.)

MR. McGUIRE: Well, certainly, it's not optimal.

CHAIRMAN SIEGEL: I think it was Richard Nixon who said we could do it, but it would be wrong.

(Laughter.)

And I'm just wondering whether it's a good idea because it potentially is a bigger paperwork requirement than you might realize.

MR. McGUIRE: That's a little bit of a problem with this approach. We didn't really want to propose wording I think for a couple of reasons. One, we didn't know what the wording would say, and I guess our inclination is kind of against it.

CHAIRMAN SIEGEL: Against the notification.

MR. McGUIRE: Yeah. Or the Commission kind of dealt with that issue in the misadministration rulemaking, and it was a hard-fought battle, and perhaps -- perhaps one can consider it a definitive battle.

CHAIRMAN SIEGEL: Well, I think -- I mean,

we're on record and we could go back on -- go on record again as I think we told you at the last meeting, that we did not think that there was need for a notification in the event of these kinds of exposures that exceeded the Part 20 limits but were below the Part 35 limits.

And I think Judy may have demurred at the last meeting on that point and dissented, but we pointed out to Judy I think that there was a medical obligation to tell the patient you had made a mistake, but there was no reason why that had to be a matter of NRC jurisdiction because the radiation exposure per se was not a reason for NRC to mix in as it were. I think it was Dr. Wagner who made that point quite eloquently last time.

And so I guess unless anyone around the table wants to disagree, we would reemphasize that point one more time as an additional take-home message. And, Judy, you can dissent again if you'd like to.

MEMBER BROWN: That's okay.

CHAIRMAN SIEGEL: Thank you.

MR. McGUIRE: I think, if I can remember the Federal Register notice exactly, what it does say is that it recognizes that it is standard medical practice that in errors involving radiation or anything else that the patient would be notified, that the medical profession considers that they should be notified and that it would be

standard practice to do so. And we say that the question is, is it necessary that in addition to this, that there be a federal requirement?

CHAIRMAN SIEGEL: I suspect you'll get a resounding "no" of the commentary.

MEMBER NELP: I don't want to comment on that. I presume it's implicit, but I presume the rems are total estimated total body doses. I presume that's -- I presume that's defined in the proposed rule, in the regulation, so you know what you're --

MR. McGUIRE: It's defined in the misadministration rule in Part 35.

MEMBER NELP: I just -- it wasn't stated in here, this excerpt.

MR. McGUIRE: No.

CHAIRMAN SIEGEL: Well, the parts that are in Part 20 are defined in Part 20. These are total effective dose equivalents. Okay.

Any other comments? Questions?

I guess you'd like a recommendation from us, right?

The Chair would entertain a motion that you send this to the Commission. Is there a so moved here?

MR. SWANSON: So moved.

CHAIRMAN SIEGEL: Is there a second?

DR. WAGNER: Second.

CHAIRMAN SIEGEL: All in favor? Opposed? Let it show that we have unanimously recommended that you do what you were planning on doing.

MR. McGUIRE: Well, I appreciate that. Thank you very much.

CHAIRMAN SIEGEL: Thank you.

God, we finished ahead of time. Do we have any other business this afternoon? Well, we played catchup ball. Wonderful.

Let's see, I had something. But I can't remember what it is. Oh, that's it. We are I think finished with today's business, unless Tori has any housekeeping announcements to be made.

For those of you who need taxis, you'll likely find them by the metro stop. For those of you who need the metro, it's in the metro.

MEMBER BROWN: May we leave our books here for tomorrow?

CHAIRMAN SIEGEL: Is the room going to be locked? Yes, we may.

(Whereupon, at 4:40 p.m., the meeting was adjourned.)

C E R T I F I C A T E

This is to certify that the attached proceedings before the United States Nuclear Regulatory Commission in the matter of:

Name of Proceeding: ADVISORY COMMITTEE FCR THE MEDICAL USE OF ISOTOPES (ACMUI) MEETING

Docket Number: N/A

Place of Proceeding: ROCKVILLE, MARYLAND

were held as herein appears, and that this is the original transcript thereof for the file of the United States Nuclear Regulatory Commission taken by me and, thereafter reduced to typewriting by me or under the direction of the court reporting company, and that the transcript is a true and accurate record of the foregoing proceedings.

Corbett Riner

CORBETT RINER
Official Reporter
Neal R. Gross and Co., Inc.