UNITED STATES OF AMERICA
NUCLEAR REGULATORY COMMISSION

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BRIEFING ON PROPOSED RULEMAKING FOR
PREPARATION AND USE OF RADIOPHARMACEUTICALS

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PUBLIC MEETING

Nuclear Regulatory Commission
One White Flint North
Rockville, Maryland

Tuesday, March 9, 1993

The Commission met in open session, pursuant to notice, at 2:00 p.m., Ivan Selin, Chairman, presiding.

COMMISSIONERS PRESENT:

IVAN SELIN, Chairman of the Commission
KENNETH C. ROGERS, Commissioner
JAMES R. CURTISS, Commissioner
FORREST J. REMICK, Commissioner
E. GAIL de PLANQUE, Commissioner

STAFF SEATED AT THE COMMISSION TABLE:

SAMUEL J. CHILK, Secretary

MARTIN MALSCH, Deputy General Counsel

HUGH THOMPSON, Deputy Executive Director for Operations

ROBERT BERNERO, Director, NMSS

BILL MORRIS, Director, Division of Regulatory Applications, RES

JOHN TELFORD, Reg. Dev. Br., Division of Regulatory Applications, RES

JOHN GLENN, Chief, Medical Licensing Branch, NMSS

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

2:00 p.m.

CHAIRMAN SELIN: Good afternoon, ladies and gentlemen.

The Commission is here to receive a briefing from the NRC staff on a proposed rulemaking concerning the preparation and use of pharmaceuticals and related matters. The staff's recommendation and its rulemaking were provided to the Commission in a staff paper from March 2nd, from last week, copies of which are supposed to be available in the room. This rulemaking responds to and largely is intended to grant a petition for rulemaking submitted by the American College of Nuclear Physicians and by the Society of Nuclear Medicine. There are some other changes that the staff proposes as well.

This meeting serves as a means for the staff to explain directly to the Commission and through us to the public what changes are being recommended for proposal on the basis of these changes. In this regard, the Commission is concerned to hear what the staff has to say about one issue.

By substantially granting the petition, the proposed rules, if made final -- and I'd like to stress that all that's being asked is permission to

print the rule for comment, but that the proposed rule would provide much greater flexibility for qualified individuals to prepare and use radioactive drugs by eliminating certain restrictions. The staff states that it believes these changes are consistent with the Commission's policy on medical use of isotopes and that the additional safeguards being recommended will ensure adequate protection. The Commission clearly needs to fully understand the staff's thinking in this regard.

Commissioners, do you have any other opening comments?

Mr. Thompson, you may proceed.

MR. THOMPSON: Thank you, Mr. Chairman.

Commissioners, today the staff will brief you on the proposed rule. It is a proposed rule developed in response to a petition submitted by the Society of Nuclear Medicine and the American College of Nuclear Physicians in June of 1989. This petition did call for NRC to relax some of the current NRC regulatory requirements and to fully recognize the activities that licensed nuclear pharmacists and physicians are permitted to conduct under state law.

When the regulation of radioactive drugs shifted from the NRC to the FDA in 1976, the NRC made

FDA approved labeling a regulation by requiring our licensees to follow the package inserts or to get specific license approval for deviations. The revision of Part 35 in April of 1987 and the subsequent inspection and enforcement actions that followed that regulation has resulted in this request to the Commission that we are proposing today.

This proposed rulemaking is the result of almost four long years of evolutionary and sometimes controversial effort. We've met with the regulated community, the academic institutions, the professional societies, the state regulators, including the agreement states, the advisory committee, and the FDA. I would also like to note that considerable input was received from NRC's medical visiting fellows and their input was very helpful in preparing the proposed rule.

This proposed rule will decouple NRC regulations from the FDA package inserts, but it is not intended to diminish the responsibilities of NRC licensees to follow all applicable state and federal regulations and in particular the FDA regulations. This decoupling will modify certain restrictions on our licensees, thus allowing greater flexibility within existing FDA and state regulations for the use of radioactive drugs prepared by a licensed nuclear

pharmacist or under the direct supervision of an authorized user physician.

It is our belief that this proposed regulation will allow greater flexibility without compromising public health and safety. It will only be permitted under the supervision of medical professions, physicians and licensed radiopharmacists who meet the training requirements in the proposed rule.

With that, Mr. Chairman, I'd like to turn the briefing over to Doctor Morris of the Office of Research, and we also have with us today John Telford from the Office of Research, Bob Bernero and John Glenn from the Office of Nuclear Material Safety and Safeguards.

CHAIRMAN SELIN: Thank you.

DOCTOR MORRIS: Thank you, Hugh.

Before moving on with the discussion in the handout, I did want to acknowledge the efforts of all those staff members who have contributed to the development of the rulemaking that is proposed to you here today. In addition to John Glenn and John Telford here at the table, behind us are Sher Bahadur, Tony Tse and Sam Jones of the Office of Research, and Larry Camper and Josie Piccone from NMSS. Stu Treby

and Marjorie Rothschild from the Office of the General Counsel were also part of the team to develop this package. All those individuals spent a lot of hours working on this project and their efforts are appreciated for the outstanding job they did.

(Slide) Moving on to the handouts, the first page is simply an outline of the presentation.

(Slide) And therefore, moving on to page 3, Hugh has essentially given you the big picture as to why this petition was submitted and the thinking of the petitioners.

Just to get to the point, let's look at the first bullet and I will indicate there that what the petitioners are requesting is the relaxation of Part 35 which currently limits use of byproduct material to cases where the Food and Drug Administration has accepted a claimed exemption for an investigation of a new drug, an IND, or has approved a new drug application, NDA.

When the petition was submitted, 35 also required compliance with the package insert instructions regarding indications for use and methods for administration. Of course the interim final rule has now provided temporary relief from these restrictions, but that relief would expire next

August. The petitioners describe several situations where these restrictions would impede physicians in providing treatment which in the physicians' judgment would be in the best interest of patients, however they asserted that such modes of treatment would not violate any regulations or requirements of any regulatory agency, state or federal, other than the NRC.

The petitioners asserted also that the restrictive nature of the NRC's regulations which require that drugs containing byproduct material only be prepared in accordance with the manufacturers' instructions have the effect of disenfranchising radiopharmacists, nuclear pharmacy as a profession. They requested that the NRC regulations recognize the profession of radiopharmacy and the traditional activities of these professions and they specifically cited compounded should be permitted.

The petitioners describe several examples of medical research in different settings that provide important new methods and information for treating patients. They point out that there are modes of oversight such as institutional review boards and radioactive drug research committees for assuring the safety of such research, but that NRC's regulations do

not provide a general license for conducting such activities.

I might point out that currently research may be carried out by NRC licensees provided they've got an exemption from the NDA and IND restrictions and have a specific entry on their license to allow research.

The petition pointed out that the expanded use of, for instance, radiobiologics is an example of the potential benefits of research. Radiobiologics are essentially substances that would be developed in-vitro from animal cellular material which also would contain a radioisotope. They're using specific kinds of cells to grow the biologic. There would be a high affinity for certain target cells in the body of a patient, for instance, and by attaching the radioisotope you would provide the capability for high resolution imaging and, in the case of treatment for cancer, high localized doses to the infected cells.

CHAIRMAN SELIN: Do the monoclonal antibodies fall under that?

DOCTOR MORRIS: Monoclonal antibodies is one of the radiobiologics.

(Slide) Moving on to the next page of the handout, we took the NRC's Medical Use Policy as the

foundation for our review. These principles were used with the objective to grant the flexibility sought by the petitioners to the extent possible while continuing to ensure an adequate level of radiation safety. To achieve this goal, as Hugh mentioned, staff sought input from a number of sources as indicated on page 5 of the handout.

On hearing and learning what the petitioners had in mind and hearing of their concern that the NRC's regulations might be, in fact, having a negative impact on providing patient care, a series of consultations with the Food and Drug Administration was begun and as a result of that we were able to develop the interim final rule. That would have allowed -- that did allow the physician-directed deviation from package inserts stated in SECY-93-050. The rule would be extended now until December 31st, 1993 and this has been done, again, after the continued consultation with the Food and Drug Administration. Also, we were able to arrive at a decision last year to remove the documentation requirements that went with the interim final rule that required the physicians to state their rationale for these departures.

After issuance of the interim final rule,

the staff began to develop a succession of straw man versions of the proposed amendments which were generally responsive to the petition. These proposals were discussed at several meetings. At the meeting with the agreement states which was held in Atlanta last July, the straw man rule language was discussed and, in addition, the issue of compatibility was a major concern to the agreement states and we'll come back to that issue later on.

The meetings with the series of groups mentioned at the bottom of page 5 and on the next page of the handout, the focus of the discussion was to define the responsibilities of those professional radiopharmacists to be formally recognized in the NRC's regulations and to develop proposed training and experience criteria to be met by these individuals. The concept under consideration was to establish in the regulations the position of the authorized nuclear pharmacists as the analogue to the physician authorized user.

(Slide) Moving on to the next page, on page 7, I just wanted to mention again the valuable advice we've received from Doctor Polycove and Mark Rottman. They assisted in evaluating the petition and developing the proposed amendments. And again

mentioning the presence of the advisory committee as a resource of expertise to the staff through meetings in May and October of 1992, we were able to come to arrive at the proposed amendments that we've developed and proposed to you in the SECY paper. Those are discussed in some detail on page 8 now.

(Slide) Although we didn't adopt the rule language that was proposed by the petitioners, we believe that these proposed amendments fully have the practical effect of fully granting the petition.

The first bullet here refers to the fact that we would now no longer refer in our regulations to the concept of the new drug application and the investigation of new drug processes that the FDA has established and licensees would be able to administer unsealed byproduct material to patients provided that the material was prepared by or under the supervision of qualified individuals and the doses administered are measured using properly calibrated instruments. Those measures are essentially focused on the radiation safety issue and are intended to be that and only that and not to interfere with the judgment or the professional expertise of physicians and pharmacists.

To avoid any confusion about the Agency's

intentions in taking this step, the amendments do include a statement that nothing in NRC's regulations relieves licensees from complying with the applicable FDA, federal or state requirements.

The third item on page 8 refers to the staff's proposal to permanently grant the relaxation of the interim final rule. This is being accomplished by simply eliminating reference to package inserts in the revised regulation.

Regarding the final bullet on this page, as I discussed earlier, licensees will now be able to administer byproduct material prepared by or under the supervision of properly qualified individuals. One group of such qualified individuals would be those with the title "authorized nuclear pharmacist." Authorized nuclear pharmacist would work under either a Part 32 or a Part 35 license and would be either board certified by the Board of Pharmaceutical Specialties or would meet the specified training and experience criteria contained in a new paragraph, Paragraph 35.980.

COMMISSIONER REMICK: I have a question. Would they be certified as nuclear pharmacists or certified as pharmacists?

MR. TELFORD: The former. They'd be board

certified as nuclear pharmacists by the Board of Pharmaceutical Specialties.

COMMISSIONER REMICK: I see.

CHAIRMAN SELIN: Is this procedure comparable to the way we recognize nuclear physicians or other professionals? In other words, the idea is that in most cases there's a board that's properly constituted to recognize a specialty and that this gives us an out. It says that even if somebody is not recognized by a Board for some reason or other, there's an alternative way to become certified.

DOCTOR GLENN: It's completely parallel to the system that we set up for the nuclear physicians.

CHAIRMAN SELIN: So that reading the language about what it takes to satisfy us outside the board, there's nothing to be read into that about further requirements to what a board has to be satisfied with to certify a pharmacist? That's a pretty poorly put question.

If the board decides somebody is certified, that person is certified, right?

DOCTOR GLENN: That's correct. We would not have an additional requirement on top of the certification.

CHAIRMAN SELIN: Okay. Thank you.

MR. MORRIS: I started to mention that there would be an alternative grandfathering clause that would state that a licensed or registered pharmacist who is designated now as an authorized user on a nuclear pharmacy license, this is different from a physician authorized user, could be grandfathered now as an authorized nuclear pharmacist.

(Slide) Moving on now to page 9, continuing with the proposal.

COMMISSIONER REMICK: What would that person have to do to grandfathered?

MR. MORRIS: I believe we just notify --

COMMISSIONER REMICK: Has to request?

MR. THOMPSON: You mean what was his qualifications to be an authorized --

COMMISSIONER REMICK: No, if we are going to grandfather somebody, is there anything that person has to do or is it automatic?

DOCTOR GLENN: I would say if they're listed on the license, it is automatic.

MR. TELFORD: They are currently listed on a license, on a commercial nuclear pharmacy's license. They're currently listed. We know they have a state license to practice pharmacy. The assumption is that they already meet the training and experience criteria

that we have specified in 35.980. Therefore, there's nothing else they need to do. They're already on the license, as Doctor Glenn said.

COMMISSIONER REMICK: So, they can just assume then if they're listed on their license, if this rule goes into effect that they are --

MR. TELFORD: If they have a state license to practice pharmacy.

MR. THOMPSON: But we should clarify the statement of considerations to make that clear if it's not very clear now.

COMMISSIONER REMICK: Because I think in some cases in the past we've asked people to do something to get that into effect. I'm thinking back when senior reactor operators came into effect. People had to initiate something.

MR. THOMPSON: You're probably the only one here that can remember that.

COMMISSIONER de PLANQUE: Perhaps you're going to mention this later and if so fine, but you also mentioned considering the individual's character for this. Is this something new and how are you going to do that?

MR. MORRIS: I think this is new because in the past we had to have a licensing action to enter

the person onto the license. Now, the staff wanted to have the option after hearing through a notification of a proposal that a person is going to become an authorized nuclear pharmacist, to be able to look at whether there had been any problems with that person's record.

COMMISSIONER de PLANQUE: Are you going to have written criteria for making this determination or how will this go?

DOCTOR GLENN: This determination, as I see it, is made on the basis of has an action been taken against this person, either by the Commission through an order or if we become aware of a criminal action taken against the person. But certainly we will maintain lists of those who, based on our deliberate misconduct rule, have been issued an order suspending them from practicing at another facility.

MR. MALSCH: I should add, this is not different from any other category of licensees and would have been an issue even without this regulation change if a character issue were raised before we granted authorized user status. The reason we find it here is because we're sort of raising it automatically and are providing a reason for NRC staff to step in after they're already authorized. But the issue is a

longstanding one. It's not been very prominent at this stage, but it's a prominent area of legal regulation.

For example, we have had cases where people have been, let's say, convicted of misusing drugs, had local licenses -- still be an NRC user --

COMMISSIONER de PLANQUE: But you feel that in this particular application the criteria are pretty clear-cut?

MR. THOMPSON: I think I agree with Marty. We probably don't have any specific criteria written down, but it has been a practice where we look at the case by case circumstances and there may be convictions or they may have willful violations of NRC regulations and we take all those factors into consideration in making our judgments as to whether this is an individual that you can rely on to follow NRC rules and regulations or, in this case, just to rely on to carry out the functions that they are proposed to do under the nuclear pharmacy.

COMMISSIONER ROGERS: Well, do we use the term "character" elsewhere in our regulations or do we specify the kinds of deficiencies that we look for rather than character defects?

MR. MALSCH: I think we've used the word

"character" and it may even appear in the statutes, but I don't think we have any place in the regulations any further specificity about this. I mean it's left to be a case by case judgment.

MR. MORRIS: I might mention in the access authorization area we have established access authorization criteria to try to make sure that we have trustworthy and reliable individuals having access to the equipment in nuclear plants. That comes close to the character issue, but I don't recall the word "character" having been used there.

COMMISSIONER ROGERS: Well, I think the concern that I have, and maybe Commissioner de Planque also, is the broad interpretation of the word "character." If we're looking for certain specific problems and that those are really pretty much the extent to which we've looked, then I don't know that you'd want to characterize that as a character examination. Character involves an awful lot. It's another possible area of great sensitivity because if you specify what it is you're looking for, that's one thing. That's all very well and good. But a character defect in one person's eyes is a character plus in another person's eyes.

I occasionally say that I have a character

defect because I like to be a regulator and some of my former colleagues think that is a character defect. I'm not sure it is. But I think the point is that the word "character" itself really encompasses a very broad sweep and if you don't have to use it, I don't see any reason why we should. If we could be more specific by example --

MR. THOMPSON: We'll take a look at that, Commissioner. I think, as I remember, it is a part of the statute which is where we derived it from, but I think we could probably give some better articulation of what it is that we are really looking for in the statement of consideration. And if we need to make some modification, we'll work with the General Counsel on that.

COMMISSIONER ROGERS: I think that the language in the material here really sort of raises a red flag in some people's eyes.

MR. THOMPSON: In the traditional use of the word "character," I think it probably does. I think we just really went back to the Atomic Energy Act to select that word.

CHAIRMAN SELIN: Mr. Morris?

MR. MORRIS: Again on page 9, the regulations would now simply state that qualified

individuals may prepare or supervise preparation of radioactive drugs. This would be understood according to the traditional interpretation of that term "prepared drugs" to include compounding. That's one of the traditional functions of the pharmacist. The current restrictions that drugs be prepared only in accordance with the manufacturer's instructions would now be eliminated. This would allow the full practice of pharmacy as a profession.

Similarly, this broad interpretation of what drug preparation entails would encompass preparation and use of radiobiologics. Many of these radiobiologics would be anticipated to involve alpha and beta emitters. The proposed amendments include new requirements to measure alpha and beta doses to be administered to patients using calibrated instruments. These requirements supplement similar provisions for gamma emitters already included in the regulations and this is one of the quid pro quos for the new mode of freedom that we're granting.

Finally, the revised regulations would provide a general license under Part 35 to conduct research using byproduct material involving human subjects. The conditions of this general license would be first that all the provisions of Part 35 now

afforded to patents would also be applicable to human subjects of research. This would include, for example, requirements to measure and administer doses using properly calibrated instruments and the provisions of the quality management rule to prevent misadministrations and for reporting misadministrations.

Second, the key provisions of the federal policy on human research must be followed. Specifically, licensees would need to obtain the informed consent of the human subject in the prior review and approval of an institutional review board. This to flesh out this issue of this federal policy on human research. We included on page 10 some information about that policy.

(Slide) The policy has been adopted in regulations of 15 agencies and departments, including the Food and Drug Administration, specifically in Part 21 -- I'm sorry, 21 CFR Parts 50 and 56 of the FDA regulations. The policy includes criteria for the approval by an institutional review board for research that address risk to issues such as the minimization of risk to subjects, that these risks are reasonable in relation in relation to the anticipated benefits of the research, provisions for collecting data to ensure

safety of subjects, provisions for informed consent and measures to achieve compliance, such as written assurances to the agency heads and reports of any anticipated problems involving risk to subjects or continuing noncompliance or any suspension of IRB approval. So, this policy goes quite far, we believe, in protecting human subjects during research and would now be through the coverage of the other agencies, for the most part, cover the research that we conducted under the new regulations.

CHAIRMAN SELIN: But again, generally speaking, it says if the research is consistent with FDA guidelines, we will not add further restrictions to that?

MR. MORRIS: That essentially is it.

CHAIRMAN SELIN: And it gives us a case by case way of dealing with research which for some reason or another falls outside of FDA guidance?

MR. MORRIS: Yes.

CHAIRMAN SELIN: So, all of these complicated conditions are really supplementary -- not additional. They're ors in Boolean logic, not ands. You can either have an IND or any type of FDA approval or meet these conditions and be allowed to carry out the research.

MR. MORRIS: Yes. The idea is that if you are now conducting research under one of these other agencies, including the FDA's implementing the regulations for the policy, the proposal envisions no need to do anything other than just have a solid compliance with that, including the IRB approvals and the informed consent. That would be the focus of any inspections we might conduct.

CHAIRMAN SELIN: Apart from things like technician safety and calibration.

MR. MORRIS: Those things already come under our Part 20 --

CHAIRMAN SELIN: Exactly.

MR. MORRIS: -- or the existing Part 35.

CHAIRMAN SELIN: Okay.

COMMISSIONER REMICK: Are those 15 agencies that have endorsed those guidelines all research-granting agencies?

MR. MORRIS: That was the intent of the federal policy, that all research granting agencies would endorse them and the policy states that as its objective. The FDA is not primarily a research granting agency, it's more of a regulatory agency. But all the research under the Department of Health and Human Services would come under this heading.

COMMISSIONER REMICK: What are the pros and cons of the NRC specifically endorsing those guidelines? You indicate that we have not specifically endorsed them, but you're asking for comment. What are the pros and cons of the NRC adopting those also?

DOCTOR MORRIS: Well, the approach we're taking here in my mind was taken to some extent to avoid some of the resource implications of trying to implement a very complicated policy that involves a lot of issues that go beyond radiation safety, such as the make-up of the board needs to include advocates for different types of individuals who might be the subject of research. Many issues that seem new and complex for us would, if we tried to, essentially adopt the policy through a rulemaking, for instance. That would be part of the baggage that would come with that. So, to me, that seems to be one issue that has to be kept in line. So, our approach has been to avoid that extra work and effort when we can have confidence. For the most part, the other federal agencies are doing a responsible job in taking care of that.

COMMISSIONER REMICK: One of the observations I had in reading that, I was wondering if

you're asking for public comment. Do you think in general the people who might provide comments will understand what that federal policy is? Eventually the IRBs and so forth, but --

DOCTOR MORRIS: Well, what we're trying to gauge here to some extent is just where and under what circumstances research might be conducted that is not currently under the federal policy. If we learned that for the most part we find that there are just hardly any exceptions, we would wonder whether we need to even bother. We'd just rely on the federal policy completely. So, that was one reason that we thought it would be worthwhile exploring that area.

COMMISSIONER ROGERS: How are you going to explore that? How are you going to get the answer to that question?

DOCTOR MORRIS: Well, we're going to assess the comments that come in. But I agree --

COMMISSIONER ROGERS: That isn't going to give you the answer to the question necessarily.

DOCTOR MORRIS: I understand that we cannot be sure that those comments will be dispositive as to whether there are exceptions and a number to be placed on the institutions or clinics or hospitals

which do research that don't fall under one or more of those agencies' regulations.

COMMISSIONER ROGERS: It's certainly conceivable to me that there could be a significant amount of research that's not federally funded at all, wouldn't fall under those agencies that could use byproduct materials in private hospitals or something of this sort. Why should they respond to this and why should they tell you that they would like to be under the same federal policy? They'd just remain silent on it. Then you'd never even know that they exist.

MR. THOMPSON: Well, we would know when they existed because we'd have a requirement if they wanted to conduct those activities, now to get a specific license from us that would permit them to do that. So, they would either have to --

COMMISSIONER ROGERS: Well, do they need a specific license to do research?

MR. THOMPSON: I think if they were using humans involved in the research, we have a requirement that they get a specific license from us.

Is that right, John?

COMMISSIONER ROGERS: There is a special license for -- I mean a licensee who already has a license but hasn't done any research now contemplates

doing some research using human subjects has to get a special license or a license amendment?

DOCTOR GLENN: Well, they don't have to get a special license, they would have to get a license amendment --

COMMISSIONER ROGERS: A license amendment.

DOCTOR GLENN: -- and it would be a specific authorization on the license to do research.

COMMISSIONER ROGERS: I see.

DOCTOR GLENN: Currently that is a condition that is on almost all of our broad scope medical licenses.

COMMISSIONER ROGERS: Excuse me. I don't understand what you said.

DOCTOR GLENN: Currently we have --

COMMISSIONER ROGERS: Is it on the license explicitly now? They have it but it says that they have to apply?

DOCTOR GLENN: The authorized use as specified on most of our license is a broad scope for the large teaching institutions. It will say "medical diagnosis therapy and research on humans."

COMMISSIONER ROGERS: So they've already got it then?

DOCTOR GLENN: The large teaching

institutions already have it.

COMMISSIONER ROGERS: Well, then your answer to my question won't give you -- you won't get any additional information from them on this federal policy.

MR. TELFORD: However, we're saying in the Federal Register notice that these are the conditions under which we would allow all licensees, in particularly the licensees that Doctor Glenn are talking about, the ones that we call the specific licensee. This is the notice to them that these are the conditions under which we would allow research and we're asking the question, "If you are not federally funded, et cetera, and don't fall under the policy, please let us know that you're outside of that area and you would like --"

COMMISSIONER ROGERS: That would be a specific requirement that they do it?

MR. TELFORD: That's a specific question in the FRN currently, which is to try to gauge the amount of activity that's outside of the sphere that we're creating.

COMMISSIONER ROGERS: Okay. But you still don't have any way of knowing how responsive those people will be to that request.

MR. TELFORD: Well, that's true except that we're going to give a copy to all the licensees and if they anticipate doing research -- if I were a licensee and I anticipated doing research in the future, I would certainly speak up. Of course there's no guarantee that they would have to, but --

COMMISSIONER ROGERS: Or if they're already doing it but don't fall under any federal guidelines or federal support.

MR. BERNERO: But this would be a new constraint on them. This would be a notice by the Commission that there would be a new constraint or set of constraints. If they would want to avert those constraints, they'd have to comment.

COMMISSIONER ROGERS: Okay.

COMMISSIONER REMICK: My guess is -- one time I had responsibility for implementing that and if I recall I think it applies to institutions that accept any kind of federal funds. It does not have to be federal funds for that specific research. But if you accept a dollar here, you're obligated. The drug-free work place was like that and I think the human subjects was also. So, the chances are that almost any institution would receive some federal funds, that presumably be -- but what I was worried about is if

what you have in the document is clear enough for people to make comment. It seems like you're assuming that everybody would know what that federal policy is. You outline it very briefly, but I don't know if you even give them a federal register reference to track it down.

MR. THOMPSON: We can certainly modify this to be much more specific than the previous Federal Register notice and we'll be glad to do that.

DOCTOR MORRIS: (Slide) I think we can move on now to the issue of compatibility on page 12 of the handout.

Currently most provisions of Part 35 are Division 3 items of compatibility. The agreement states have expressed their view that these amendments not be a matter of compatibility or in any case the lowest level of compatibility possible, Division 3. We based our proposal to you on the current criteria for compatibility determinations used by the Office of State Programs and our judgment about how to interpret that policy. We understand that this compatibility policy is currently under review and could change, but this is the current practice.

The staff believes that definitions, as according to that policy, which are the basic mode and

the basis for effective communication between regulated agencies and the regulated community should be Division 1 and that certain new provisions, which in this case are those that address basic principles of radiation safety, should be Division 2 items of compatibility. That's the way we've sorted this out.

For example, manufacturer and preparation of transfer of byproduct material, drugs, provisions for research, radiation safety committee provisions, supervision, possession, use, calibration of dose calibrators, possession, use and calibration of instruments to measure doses, measurement of doses, training of physician authorized user and authorized user nuclear pharmacist, and their recentness of training are all under the umbrella in our proposal for Division 2 compatibility at this time.

CHAIRMAN SELIN: Could you -- please, Commissioner Curtiss.

COMMISSIONER CURTISS: You may have the same question I do.

CHAIRMAN SELIN: We'll see if I get the same answer.

COMMISSIONER CURTISS: Maybe we'll ask it twice.

I guess at least at this point there's not

a meeting of the minds on the question of how compatibility ought to be -- how these provisions ought to be treated in the context of compatibility. Do you attribute the states' position to a disagreement or lack of understanding on the substance of what you're proposing here or is it attributed more generally just to the state's desire to have as much flexibility as possible? Why is it that we seem to have on their behalf such a strong consensus that these not be matters of compatibility and on our behalf a different view?

DOCTOR GLENN: Let me answer --

DOCTOR MORRIS: Because I was not at the meeting, John. Go ahead.

DOCTOR GLENN: I was going to refer to the specific meeting we had in Atlanta last summer where we did discuss the issue of compatibility with the agreement states and where they did express their strong preference that it be as low a level of compatibility as possible. I think one thing that they were very clear about is they didn't necessarily disagree with where we wanted to end up, but they didn't like us specifying how they got there.

There was a considerable amount of comment that they would prefer to accomplish the same end

through license conditions, through licensing guidance rather than through regulations. They also impressed upon us the difficulty they have in getting their regulations changed and to get them to come into full compatibility with our regulations.

So, to a large degree, the discussion was on practical -- how hard it was for them to come into the level of compatibility that we might request.

MR. THOMPSON: That's my understanding. I wasn't at the meeting, but clearly some states have to go to the legislation to get new regulations in place and it's a very long and complicated process. They may prefer to just each new license come in, place those conditions on the license and achieve the same level of "protection" that you would through our regulation. It kind of leaves you with a bit of uneasiness in knowing precisely that the state has every license with this same amount of regulatory oversight that you would if they had regulations that covered all of their licensees.

COMMISSIONER CURTISS: I guess I'm generally comfortable with this approach as a starting point. It would be useful, as I'm sure you will, to solicit comment and continue to interact with the states for the purpose of determining whether there

are approaches that can be taken that will achieve the same health and safety objective that we're desiring here without, on our side, unduly straining resources to evaluate all those individual approaches as well as on their side not requiring them to undertake an approach that may be difficult in terms of legislative enactment of new regulations or unduly strain already limited resources in some of these states and perhaps with an eye on what the objective here is from the health and safety standpoint, see if we can't reach some consensus or meeting of the minds here on the state compatibility question.

MR. TELFORD: I would like to emphasize in response to your first question that we did spend the better part of a day discussing this rule language. So, I'm sure that they understand exactly what we want to achieve.

COMMISSIONER CURTISS: Okay.

MR. TELFORD: And as Doctor Glenn said, depending upon the state, there are different ways that the state would like to achieve compatibility. And perhaps that might rest in how the Commission would define how the states can achieve compatibility. Some states will simply adopt our regulations verbatim because they have small staffs and they don't want to

do anything else. Other states will want to have an umbrella type of regulation, as Doctor Glenn was saying, that's a very broad thing, like he shall have procedures and practices which bring about radiation safety and then basically exercise that through the licensing conditions or regulatory guides. Other states will want to write their own regulations and go through their own process. But it seems to me that it's more of a Commission decision as to how you will allow the states to achieve compatibility.

At this point the staff would have to say, "Given the current guideline, this is what we propose."

COMMISSIONER CURTISS: I think it's an appropriate starting point.

MR. THOMPSON: And we are going to be working on the compatibility issue with agreement states.

CHAIRMAN SELIN: That's a key point. I did have the same question as Commissioner Curtiss, but I won't rephrase it to see if I get the same answer. I was impressed with the answer because it was neither of the two alternatives. It wasn't a substantive disagreement and it wasn't just a knee-jerk reaction that says less is better and more is

worse, but some specific problem.

Before I comment on that, I'd like to ask you a question, Mr. Thompson. What is the generic situation when we require something to be Division 1 compatibility? What happens if the state doesn't get the legislation through their legislature or what have you? They could be in --

MR. THOMPSON: First they have a period of time for which they are allowed to get their regulations in. After that, when we do our evaluations, we do not find their regulations compatible and we will basically meet with them and understand their plans to go about achieving that level of compatibility. If it continues, we will elevate within the state governmental organization the concern that the Commission has and eventually it would come up to you.

CHAIRMAN SELIN: In that event, I would like to follow up on our comment, Mr. Thompson. The question of whether this is Division 1 compatibility or not is no different here from many other areas. It's a subject that's being discussed in the general consideration of compatibility that the staff and the Commission are discussing. So, I personally would suggest that you consider some kind of language in the

statement of considerations or the introduction that says -- I mean this is just a suggestion. You have to decide this. The Commission might decide that it's not a good idea, but that somehow you just make it clear that by the draft rule requiring that this be Division 1, what we intend is, number one, we hope that you the staff will have an answer on compatibility in general before the rule goes final, and that of course would be reflected in the rule. And the second, that this does not mean that the staff has disregarded the agreement states' discussion that, in fact, both in the specific case and the generic case of different ways of achieving the same objectives that you'd be open to comment from the states on how the substantive compatibility be achieved. I personally don't feel comfortable at this point in effect rejecting the states' arguments and saying that's done because that's an issue that's generally before us, but neither would I like to hold up the publication of the rule in order for the Commission to answer what is a thorny question. It's not such a difficult question, it's just go so many different special cases that we have to make sure that we carry it out in a way that we intend to.

MR. THOMPSON: Well, as you might remember

from the Commission's regulations they put in place after the Riverside misadministration, we did not make that amount of compatibility. Some states actually imposed or adopted regulations very similar to ours and others --

CHAIRMAN SELIN: But this is different. You really feel strongly, and as far as I can see you're probably right, that one way or another the states need to have the functional equivalent of Division 1 compatibility. But as they point out, in many cases just flat out saying it that way causes them some problems and on a general basis we're trying to see if there are other ways of achieving this compatibility. So, I personally don't want to hold you up and I don't want to second guess for now that these are issues that require the equivalent of Division 1 or Division 2 compatibility as appropriate, but nor do I want to go out with a message that says to the states, "We've considered your arguments and we have definitively rejected them."

So, if you can fudge on that, if you can leave the option open --

MR. THOMPSON: We will certainly explain the circumstances in the statement of consideration.

MR. MALSCH: Mr. Chairman, I just want to

add something to what Mr. Telford said, which makes this an especially sensitive compatibility issue. That is if you literally made every word and phrase of the regulation a matter of strict compatibility Division 1, the effect would be that states would be forced to issue general licenses where they would prefer to issue licenses on a case specific basis and that could be a sensitive issue for agreement states.

CHAIRMAN SELIN: I sort of lost track, Doctor Morris. Have you finished your presentation?

DOCTOR MORRIS: Well, I just wanted to just summarize and bring us back to the point that you had addressed earlier. We believe that with the promulgation of these amendments the NRC regulations would no longer include unnecessary restrictions on the use of byproduct material which might limit physicians and pharmacists in using their knowledge and skills and treatment of patients or in conducting research to develop new techniques or knowledge to improve treatment.

The new provisions for calibration of instruments and for measurement of doses, for training and experience for personnel involved in the preparation of drugs containing byproduct material and the proposals for safe conduct of research on human

subjects we believe will assure that the adequate level of protection will continue. I think that addresses a key question that was raised earlier and those are the kinds of things, those radiation safety requirements, that we've put in here we believe buy that assurance.

COMMISSIONER REMICK: Those are the additional safeguards you refer to? You have a statement in there that there are some restrictions being relieved, but you feel they're additional safeguards. Are those the ones you had in mind?

DOCTOR MORRIS: Yes. Yes. Training requirements, calibration requirements, protection of human subjects, those kinds of things.

CHAIRMAN SELIN: Commissioner Rogers?

DOCTOR MORRIS: That's all.

COMMISSIONER ROGERS: In looking over your Table 1 in the SECY, the summary of the comparison between the petition requests and our response, I notice that in three of the items the term used is greater discretion in each of our responses. That really doesn't say very much by itself. A very small amount of additional discretion is greater discretion. A wide degree of discretion is greater discretion. There's a fuzziness there that I really couldn't get

very much from. So, I looked to see how you dealt with, in particular, Section 35.100 compared to the petition. I must say I didn't understand -- I saw differences in the wording and I couldn't tell whether there was a substantive difference here or not or whether this was a rewriting of the language of the petition, but basically adopting it, or whether there was something else. It seemed to me that there was a difference, a significant difference in the wording proposed in the petition for that text and what the proposed rule has.

I wonder if you could say something about that. Do you -- what is your view? Were there significant differences in your thinking between what you saw emerging from the requests in the petition and what you felt was appropriate language in the new rule, or was this really just simply a different way of expressing the same thing using somewhat different terms?

I saw it in this particular case as perhaps something substantially different. I wonder if you could respond to that.

DOCTOR GLENN: Okay. My view is that we, in fact, granted what the petitioners requested. But the wording that we ended up with was a very

evolutionary process. We received quite a bit of criticism the first time around when we attempted to draft language where we essentially said what was and what was not permitted. I will give credit to the agreement states that at the Atlanta meeting they are the ones who opened our eyes to the particular approach that we used here, which was to avoid using FDA terms in order to say what could or could not be done, but to say, "You may use byproduct material without any excuse from any other pharmacy or FDA regulation, but with certain additional radiation safety standards applied over the existing regulatory scheme." So, out of that meeting I think is where the approach that you see here developed. So, there is a change in the way we approach the task. I think the end result though is very responsive to the petition.

CHAIRMAN SELIN: Do I hear you saying that it wasn't the pride of authorship, your language has evolved from a process whereby each change in this case away from the petition was to carry out some specific objective and that would seem to you to be --

DOCTOR GLENN: That's correct. As we tried things out, we got input from the different groups about what was good or bad about what we were doing and this was the end of that evolutionary

process.

COMMISSIONER ROGERS: Well, I was trying to understand what this greater discretion meant really and just tried to pick one example to see and I ran into a little bit of difficulty. I don't want to prolong this unduly, but the petition on page 10 had certain language and in the rule on page 60, the notice, I guess, on page 67, the same section addresses this issue. In the petition, the wording was, "A licensee may use for medical use," and it seems to me that's a statement by itself right there, "any byproduct material in a radiopharmaceutical and for a diagnostic use involving measurements of uptake, dilution or excretion in which," and then there are certain things. The proposed language here is simply, "A licensee may use for uptake, dilution or excretion studies any unsealed byproduct material prepared for medical use that is either," and then there are certain conditions.

It seems to me there's a big difference between those two statements because the one in the petition says a licensee may use for medical use. It doesn't say what that medical use is, and then gives an example of uptake, dilution or excretion, whereas your statement just simply says a licensee may use for

uptake, dilution or excretion studies. So, their language, it would seem to me, was much broader because there was, in a sense, any medical use but in particular and for a diagnostic use involving measurements of uptake, dilution or excretion. So, you see, I would see a very big difference between those two, the application of those two sections. I was wondering whether that was in your mind or whether that's just the way it came out or whether that was the intent.

DOCTOR GLENN: I think if you look at the existing setup of Part 35, you will in fact see that the 100, 200, 300 sections in their titles include those terms which we have maintained here. So, there was not an attempt to, I think, limit the uses. We think we provided for more discretion in the kinds of uses that were already being permitted in --

COMMISSIONER ROGERS: Well, I may have just picked, you know, one part of it to focus on. My question is really what the greater discretion really amounts to in each of those cases. Perhaps it would be easier if you could spell that out in each of those three responses where you've indicated greater discretion has been afforded exactly what that greater discretion is.

MR. BERNERO: If I could volunteer an opinion here, I think we're saying greater discretion than past permitted practice rather than greater discretion than requested by the user or by the petitioners. In pages 34 and 35 of the discussion of the regulation, on 35.100, we tried to make the point of how to achieve the objective requested and achieve it to give the discretion for the use of unsealed material and avoiding the word "pharmaceutical."

CHAIRMAN SELIN: Let me make a suggestion. There are three specific instances that Commissioner Rogers has brought up. There's no obligation that we should take the petition language and start with that, but it would be useful. I perhaps might suggest that if you would in each of those cases prepare a note that suggests either what you read is the difference between the petition language and what you're proposing to grant or a reason that you didn't follow petition language. In this case I gather you're saying that your recommended language is closer to the structure of Part 35 than the petition language and there's no reason to get out of the structure. So, if it's something like that, that would be --

COMMISSIONER ROGERS: I was just looking to see whether here was something in the minds of the

petitioners that they were requesting that you address that you decided you would not address and something that you decided you would address, and just to get that clear so that we understand how far we've gone and maybe no further than somebody else requested, but where we stop short of that. I would be helpful, I think. So, I'd appreciate very much your responding as the Chairman suggested.

The other point that troubled me a little bit as the use of the word "patient" as a subject in research. I can understand why you did it, because it just sweeps the regulations right over that and you don't have to worry about it anymore. But I don't know, I don't really like applying terms that aren't exactly the common term and a subject of research is not necessarily a patient. It might be, it might not be.

DOCTOR MORRIS: Yes. I could mention that we stand prepared if that is a problem to change it. We would just use patient and human subject everywhere that patient now occurs pretty much is what we would have to do if we took that step.

COMMISSIONER ROGERS: Yes. Okay.

DOCTOR MORRIS: So, it was just a device and we could change it.

COMMISSIONER ROGERS: I think it's just a little too much of a corner cut.

DOCTOR GLENN: We anticipated some criticism for that. We did check it out with Doctor Seigel who is chairman of the committee. At first he had the same reservations. He did come around eventually to saying he thought it might be a very useful mechanism in this particular case.

COMMISSIONER ROGERS: Okay. That's all I have.

CHAIRMAN SELIN: Commissioner Curtiss?

COMMISSIONER CURTISS: No questions.

CHAIRMAN SELIN: Commissioner Remick?

COMMISSIONER REMICK: On page 1 of the SECY document, the footnote I thought was kind of interesting. Are we setting people up for litigation? We say that we're now permitting people to digress from the package inserts, but we immediately point out that some people have been taken to court --

MR. MALSCH: It's quite possible that licensees operating under these regulations would be violating FDA requirements. That's the effect in some cases of eliminating restrictions currently in the regulations.

Now, in most cases, that's probably not

going to be the case because the FDA would have no jurisdiction. But in cases where the FDA would have jurisdiction, then we would be authorizing something which the FDA would be prohibiting. That's why it's necessary to have something that says, "This doesn't relieve you from those other requirements."

CHAIRMAN SELIN: Is that answering Commissioner Remick's question about the footnote?

MR. MALSCH: The footnote points out that --

CHAIRMAN SELIN: People have ignored the inserts and gotten zapped.

MR. MALSCH: In general, the FDA has no jurisdiction to force physicians treating patients to follow the package inserts.

CHAIRMAN SELIN: Right.

MR. MALSCH: So, they ordinarily don't have jurisdiction directly over the practice of medicine as such. They wouldn't exercise jurisdiction there. But in some cases where physicians have gone beyond just the practice of medicine, and for example advertise a certain product for a use not approved by the FDA or engaged in some sort of interstate commerce in the product, then they have been prosecuted not for practicing medicine, but for engaging in an activity

subject to FDA jurisdiction. Now, those cases are kind of unusual and I think that's all the footnote was pointing out.

COMMISSIONER ROGERS: Well, it says though, "Due to certain practices in which drugs were not prepared or used in accordance with the package insert."

MR. MALSCH: Right. The emphasis on practices, and the practices would normally involve not just preparing or using in accordance with the insert, but something else, like advertising or distribution of interstate commerce or something else. It's usually, as a general rule, merely using not in accordance with the insert would not violate any FDA requirement.

In fact, that's why our provisions that we're now eliminating from the regulations actually had a substantial impact on our licensees because they would otherwise be authorized to depart from package insert instructions. It was only the NRC at the federal level which was prohibiting them from doing so. That's why this whole regulation relaxation is so meaningful.

COMMISSIONER REMICK: Well, if you hadn't explained it, Marty, I'm not sure I would have read

into certain practices what you just told me it means. I'm not sure others would either.

MR. MALSCH: It is a little vague.

COMMISSIONER REMICK: One other question. The staff certainly feels, I think, that this is the right way to go. At least that's the impression one gets from the presentation. Are there any downsides that we should know of of the proposed rule of the potential downsides, if there are --

MR. MALSCH: I'll identify a downside and it's the policy issue. That is generally whether our relaxation is here, what you are doing is replacing a requirement for case specific licensing with a general license. So, as with any general license, you're removing from yourself the discretion to do case by case reviews. So, outliers might be missed.

COMMISSIONER REMICK: I see. Okay. Any others come to mind?

CHAIRMAN SELIN: Well, you already identified the fact that this might put some of the agreement states into a bind unintendedly.

MR. BERNERO: Yes. Certainly the implementation of it there. That's a very real difficulty with the agreement states. But as was discussed a little while ago, that is a characteristic

difficulty not unique to this rulemaking. The administrative burden of implementing a consistent national program is a generic problem.

COMMISSIONER REMICK: Thank you.

CHAIRMAN SELIN: Commissioner de Planque?

COMMISSIONER de PLANQUE: No further questions.

CHAIRMAN SELIN: Okay. I'd like to thank you on behalf of the Commission for really quite a lucid discussion of a complex issue. It seems pretty clear that there's no very strong opposition to going forth with the statement. But as you listen to the different Commissioners, we have some reservations and we would like to make sure that one way or another these reservations are reflected in the material to say that in some of these cases the fact that the Commission is permitted -- but assuming the Commission permits the publication, that this doesn't mean that we consider these closed issues.

MR. THOMPSON: I understand.

CHAIRMAN SELIN: We understand that there's a comment period from here on in, that the petition does not replace the comment period on the proposed rule and we want to make sure that that's clear in the instructions.

Okay. Thank you very much.

MR. THOMPSON: Thank you, Mr. Chairman.

(Whereupon, at 3:04 p.m., the above-entitled matter was concluded.)

CERTIFICATE OF TRANSCRIBER

This is to certify that the attached events of a meeting of the United States Nuclear Regulatory Commission entitled:

TITLE OF MEETING: BRIEFING ON PROPOSED RULEMAKING FOR PREPARATION AND USE OF RADIOPHARMACEUTICALS

PLACE OF MEETING: ROCKVILLE, MARYLAND

DATE OF MEETING: MARCH 9, 1993

were transcribed by me. I further certify that said transcription is accurate and complete, to the best of my ability, and that the transcript is a true and accurate record of the foregoing events.

Carol Lynch

Reporter's name: Peter Lynch

STAFF BRIEFING ON PROPOSED RULEMAKING FOR PREPARATION AND USE OF RADIOPHARMACEUTICALS

MARCH 9, 1993

BILL M. MORRIS

CONTACT: BILL M. MORRIS
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OUTLINE OF PRESENTATION

- PETITION SUBMITTED BY ACNP AND SNM
- NRC MEDICAL USE POLICY
- PARTICIPATION OF OUTSIDE GROUPS
- EXPERTISE WITHIN THE AGENCY
- THE PROPOSED AMENDMENTS
- FEDERAL POLICY ON HUMAN RESEARCH
- COMPATIBILITY

THE ACNP-SNM PETITION REQUESTED NRC TO

- PERMIT PHYSICIAN AUTHORIZED USERS GREATER FLEXIBILITY IN MEDICAL USE OF BYPRODUCT MATERIAL
- FORMALLY RECOGNIZE THE PRACTICE OF NUCLEAR PHARMACY
- PERMIT GREATER FLEXIBILITY IN PREPARING RADIOPHARMACEUTICALS
- PERMIT BROADER CATEGORIES OF RESEARCH
- PERMIT THE USE OF RADIO-LABELED BIOLOGICS

NRC'S MEDICAL USE POLICY

- CONTINUE TO REGULATE THE MEDICAL USES OF RADIOISOTOPES TO PROVIDE FOR THE RADIATION SAFETY OF WORKERS AND THE GENERAL PUBLIC

- REGULATE THE RADIATION SAFETY OF PATIENTS WHERE JUSTIFIED BY THE RISK TO PATIENTS AND WHERE VOLUNTARY STANDARDS, OR COMPLIANCE WITH THESE STANDARDS, ARE INADEQUATE

- MINIMIZE INTRUSION INTO MEDICAL JUDGMENTS AFFECTING PATIENTS AND INTO OTHER AREAS TRADITIONALLY CONSIDERED TO BE A PART OF THE PRACTICE OF MEDICINE

PARTICIPATION OF OUTSIDE GROUPS

- Food and Drug Administration (FDA)
- Agreement States
- National Association of Boards of Pharmacy
- American Board of Science In Nuclear Medicine
- American Pharmaceutical Association - Board of Pharmaceutical Specialties

PARTICIPATION OF OUTSIDE GROUPS (CONTINUED)

- AMERICAN SOCIETY OF HOSPITAL PHARMACISTS
- COMMITTEE ON RADIONUCLIDES AND RADIOPHARMACEUTICALS OF U. S. COUNCIL OF ENERGY AWARENESS (USCEA)

EXPERTISE WITHIN THE AGENCY

- Advisory Committee for the Medical Use of Isotopes (ACMUI)
- Visiting medical fellows

THE PROPOSED AMENDMENTS

- ELIMINATE REFERENCE IN NRC REGULATIONS TO FDA REGULATORY FRAMEWORK
- STATE THAT NOTHING IN NRC'S REGULATIONS RELIEVES LICENSEES FROM COMPLYING WITH APPLICABLE FDA, OTHER FEDERAL, AND STATE REQUIREMENTS
- ALLOW DEPARTURES FROM PACKAGE INSERTS UNDER THE DIRECTION OF PHYSICIAN AUTHORIZED USERS
- ESTABLISH CONCEPT OF AUTHORIZED NUCLEAR PHARMACISTS AND SPECIFY TRAINING AND EXPERIENCE REQUIREMENTS

THE PROPOSED AMENDMENTS (CONTINUED)

- ALLOW COMPOUNDING OF RADIOACTIVE DRUGS BY PROPERLY QUALIFIED OR SUPERVISED INDIVIDUALS
- ALLOW USE OF BYPRODUCT MATERIALS IN RESEARCH INVOLVING HUMAN SUBJECTS PROVIDED FEDERAL POLICY IS FOLLOWED
- ALLOW USE OF RADIOLABELED BIOLOGICS GIVEN NEW REQUIREMENTS FOR MEASUREMENT OF DOSAGES

FEDERAL POLICY ON HUMAN RESEARCH

- FEDERAL POLICY FOR THE PROTECTION OF HUMAN SUBJECTS PUBLISHED JUNE 18, 1991
- ADOPTED IN CONFORMING REGULATIONS BY 15 AGENCIES AND DEPARTMENTS INCLUDING FDA
- FEDERAL POLICY REQUIRED
  - INSTITUTIONAL REVIEW BOARD (IRB)
  - INFORMED CONSENT
  - MEASURES TO ACHIEVE COMPLIANCE (E.G., WRITTEN ASSURANCES, REPORTS)

FEDERAL POLICY ON HUMAN RESEARCH (CONTINUED)

- NRC WILL LICENSE RESEARCH ACTIVITIES NOT COVERED BY THIS FEDERAL POLICY ON A CASE-BY-CASE BASIS (EXPECTED TO BE RARE)

- FRN REQUESTS COMMENTS ON THE NECESSITY OF REFERENCING THE POLICY IN NRC'S REGULATIONS

COMPATIBILITY

- CURRENTLY MOST PROVISIONS OF PART 35 ARE DIVISION 3 ITEMS OF COMPATIBILITY
- AGREEMENT STATES EXPRESSED VIEWS THAT THESE AMENDMENTS NOT BE A MATTER OF COMPATIBILITY OR THE LOWEST LEVEL OF COMPATIBILITY POSSIBLE (DIVISION 3)
- STAFF BELIEVES THAT DEFINITIONS SHOULD BE DIVISION 1 AND CERTAIN NEW PROVISIONS DIVISION 2 ITEMS OF COMPATIBILITY

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TORRANCE, CALIFORNIA 90509

March 8, 1993

Hugh L. Thompson, Jr.
Deputy Executive Director for
Nuclear Materials, Safety, Safeguards
and Operation Support
U.S. Nuclear Regulatory Commission
Washington, DC 20555

Dear Mr. Thompson:

This letter is written as a member of the general public, and not as a member of NRC's Advisory Committee on Medical Uses of Isotopes.

I wish to comment on NRC's 2 Mar. 91 documents pertaining to Proposed Amendments on Preparation, Transfer, and Use of Byproduct Material for Medical Use, Secy-93-050. The documents are flawed and should not be published in their presently inaccurate state. Doing so would be dangerous to NRC, as it would appear from these documents that NRC is permitting hazardous behavior to go unchecked.

These documents refer to the ACNP/SNM Petition of June, 1989. However, the reason for the ACNP/SNM Petition was not, as stated by NRC, to "provide greater flexibility". The reason for the Petition was that NRC regulations and license conditions had become incompatible with State Medicine and Pharmacy Law, and were incompatible with the efficient and effective delivery of healthcare services by professional practitioners of nuclear medicine and nuclear pharmacy. These professionals were being forced by NRC to subject patients to unnecessary risks, unnecessary costs, and dangerous alternate procedures. In some cases, potentially life-saving therapy was being denied. Professionals were jeopardizing their ability to practice their profession in order to act in the best interests of their patients. NRC had loomed as a bigger danger to patients and professionals than the radioactive material being regulated. Clearly, this was a remarkable aberration of regulatory behavior that required immediate corrective action on NRC's part.

The rest of the Commission document is misleading in terms of what we "asked for", what the Immediately Effective Interim Final Rule "gives" us (actually, essentially nothing), and what this Proposed Rule "gives" us.

The most important failing in this document, and in the Federal Register notice as well, is that NRC completely missed the major point of the Petition. Once a physician is licensed to practice nuclear medicine, he must be free to use everything he knows or can learn to help his patient. The same is true for nuclear pharmacists. If NRC is licensing physicians who are really not capable of intelligently handling byproduct material and not intelligently directing and managing its uses, then NRC is guilty of criminal negligence, having not fulfilled its responsibility to the public. If NRC licenses a physician (or a pharmacist) and then restricts him from using his best judgment, he is essentially an "impaired physician", and his patients are at risk. Patients do not do well if their physician has had a "regulatory lobotomy".

If you do not understand this, let me try a military analogy. Let us assume that a group of Marines is undergoing basic training, and some of them miss a lot of target practice for some reason or other. Nevertheless, the platoon later lands on a hostile beach to fight an enemy. At the last minute, the platoon leader takes the guns away from the guys who missed target practice, but expects them to fight anyway. Now, the leader could presumably have required extra target practice and refused to let them join their platoon at that time. However, <u>once they hit the beach, they need a gun</u>. NRC is behaving like this foolish platoon leader.

The other, really malevolent thing about this document is that in deciding which nuclear physicians and which nuclear pharmacists will be permitted to practice their profession according to State Law, "NRC can consider an individual's character in addition to credentials in determining whether the individual should be approved as an authorized user or authorized nuclear pharmacist, such as verifying that the individual has not committed or caused others to commit any willful violations of the Commissions regulations". This is a "Catch-22". Every nuclear physician and nuclear pharmacist worth his salt has willfully violated NRC's regulations in order to provide appropriate services and patient care. <u>That is why we wrote the Petition!</u> Indeed, NRC is actually encouraging physicians to violate the Interim Final Rule by removing the recordkeeping requirement. I would argue that not a single legitimate package insert departure is permitted according to the dastardly definition in that Rule, which was never made available for public comment beforehand, and was not changed despite the requests of SNM and ACNP.

There are other problems with this Proposed Rule, such as the fact that a byproduct drug is presently going through FDA review

as a device, and the manufacturer will most likely be listed as a device manufacturer, not a drug manufacturer. Your Proposed Rule, which did not pay attention to the Petition, will cause a problem here. NRC also does not understand the Federal Policy for the Protection of Human Subjects, and I cannot concur with the concept of considering "human subjects" (for research purposes) as "patients". Separate laws and considerations apply to them. This is an inadvisable regulatory "convenience" that is a set-up for trouble with things like procedure manuals and the so-called "Quality Management" Program. There are problems with labeling, something NRC should avoid completely and leave in the competent hands of others such as FDA and Boards of Pharmacy. NRC is overly prescriptive with "time and date" of dose calibration. If NRC left it to professional judgment, it would be done right. Indeed, NRC has never shown that there was any need for a regulation here at all. When it comes to C-14, I do not care about the time, date, week, month, year, or decade. The nearest century will do just fine.

Some items in the Federal Register notice are not only wrong, but dangerous. The Petition never asked that we "compound radiopharmaceuticals whose manufacture and distribution are not regulated by the State or FDA". I can't think of anything not regulated by the State Board of Medicine, the State Board of Pharmacy, the State FDA, or the Federal FDA. The problem is that I believe this document is a "set up". I'll bet it is already in the hands of the Cleveland Plain Dealer, all ready for an "expose" as ugly as the last. However, you will have no defense, because your defense is that you made untrue statements in the Federal Register, and you can never admit to that.

Think about the following facts. Why did an NRC informer lie to the Plain Dealer about the writing of this Petition? Why is one of the reporters bragging that he has an uncensored version of the I-G report on McElroy and this Petition? (This is a security violation that calls for an FBI investigation). This Petition had nothing to do with the Plain Dealer articles. Yet. The reporter argues that he has nothing against medicine, but is presenting the views of an employee of NRC who feels that NRC is dangerously lax. Then, NRC publishes material suggesting that NRC is perfectly happy to let physicians and pharmacists do dangerous things. The connection is obvious. I'll bet the Plain Dealer even has old FDA letters relating to the Interim Final Rule and Syncor's lawsuit. This is going to be very unfortunate. Print this material in the Federal Register, and the Rule is going to become politically difficult to sustain.

March 8, 1993
Hugh Thompson, Jr.
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Therefore, I urge you most strongly to cancel publication of this material. Please correct it, and think of it as a press release to the Plain Dealer as you do so.

Sincerely,

Carol Marcus

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RULEMAKING ISSUE
(Notation Vote)

March 2, 1993 SECY-93-050

For: The Commissioners

From: James M. Taylor
Executive Director for Operations

Subject: PROPOSED AMENDMENTS ON PREPARATION, TRANSFER, AND USE OF BYPRODUCT MATERIAL FOR MEDICAL USE

Purpose: To obtain the Commission's approval for the publication of the proposed rule.

Summary: The proposed rule has been developed in response to a petition for rulemaking. This amendment would provide greater flexibility for properly qualified nuclear pharmacists and physicians to prepare and use radioactive drugs containing byproduct material. Other miscellaneous amendments to clarify or update the current regulations are also being proposed. In addition, the staff is proposing that certain provisions in this amendment be items of compatibility for Agreement States.

Background: Radioactive drugs containing byproduct material are used in nuclear medicine to diagnose or treat certain diseases. Until the publication of the Interim Final Rule (discussed below), NRC regulations restricted medical use licensees to using or preparing certain radioactive drugs in accordance with the U.S. Food and Drug Administration (FDA) approved package inserts. The FDA does not generally require[1] physicians or pharmacists to follow these inserts. In

[1] However, there have been cases upheld on judicial review, in which physicians and pharmacists have been prosecuted for violating the Federal Food, Drug, and Cosmetic Act due to certain practices in which drugs were not prepared or used in accordance with the package insert.

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NOTE TO BE MADE PUBLICLY AVAILABLE AT COMMISSION MEETING ON MARCH 9

addition, current NRC regulations do not specifically allow medical use licensees to use byproduct material in research involving human subjects, in certain radiolabeled biologics, and in compounding radioactive drugs.

The American College of Nuclear Physicians (ACNP) and the Society of Nuclear Medicine (SNM) submitted a petition for rulemaking in 1989. The petitioners requested that the Commission amend its regulations to fully recognize the role of licensed nuclear pharmacists and physicians. In response to a Federal Register Notice requesting public comments on the receipt of the petition, the NRC received 466 comment letters. About 99 percent of the commenters supported and agreed with the petition.

The staff is disclosing that during the development of the ACNP-SNM petition, one NMSS staff member provided substantial assistance in the preparation of the petition, but has not participated in the staff's resolution of the petition or in the development of this proposed rule. Another individual reviewed the petition prior to its formal submittal to the Commission and participated, to a limited extent at an early stage, in the staff's resolution of the petition and in the development of the proposed rule. To assure that this does not happen again, I have recently reissued instructions to the staff on the appropriate role of the staff in dealing with petitioners.

To promptly address some patient care issues raised in the ACNP-SNM petition, the NRC published an Interim Final Rule on August 23, 1990 (55 FR 34513). This interim rule allows, for a period of 3 years, specific departures from the package inserts under the direction of an authorized user who is a physician (physician authorized user), provided certain records were kept. Subsequently, NRC and FDA staff reviewed records on departures and determined that additional recordkeeping was unnecessary. The NRC published a rule to eliminate these recordkeeping requirements (57 FR 45566; October 2, 1992). The staff plans to extend the termination date of the Interim Final Rule to December 30, 1994, via a specific Federal Register Notice.

Discussion: At various stages in the development of this rulemaking, the staff has consulted with the FDA staff, Advisory Committee on the Medical Uses of Isotopes (ACMUI), Board of Pharmaceutical Specialties, American Pharmaceutical Association, American Board of Science in Nuclear Medicine, National Association of Boards of Pharmacy, Committee on Radionuclides and Radiopharmaceuticals of the U.S. Council

for Energy Awareness, American Society of Hospital Pharmacists, and three graduate schools of pharmacy.

Based on these discussions and the Commission's policy statement on the medical uses of radioisotopes (44 FR 8242; February 9, 1979), the staff proposes to eliminate certain restrictions regarding the medical use of byproduct material without compromising the level of protection of public health and safety against radiological hazards. The staff believes that the adoption of these proposed amendments will achieve these objectives and would not be in conflict with the Commission's policy statement on medical uses of radioisotopes.

The staff is proposing to grant the substance of the petition for rulemaking by the publication of the proposed rule. The major features of the proposed rule include: (1) allowing departures from package inserts as directed by physician authorized users; (2) creating the concept of an "authorized nuclear pharmacist" and specifying training and experience requirements; (3) allowing physician authorized users and authorized nuclear pharmacists to use byproduct material to compound radioactive drugs; (4) allowing the use of byproduct material in research involving human subjects[2]; and (5) allowing the use of radiolabeled biologics[3].

In addition, the proposed rule contains other miscellaneous amendments that include: (1) revising the definitions of "medical use" and "authorized user"; (2) requiring measurements of dosages of alpha- or beta-emitting radionuclides; (3) deleting nonradioactive reagent kits from the regulations; (4) allowing licensees to permit an authorized user or authorized nuclear pharmacist, who meets certain requirements, to work without submitting a license amendment provided NRC is notified; (5) deleting the provisions on visiting authorized users; (6) clarifying requirements that are applicable to a Type A specific licensee of broad scope; (7) recognizing additional

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[2] The Commission should note that the proposed regulations would permit research, without a license amendment, involving human subjects even though NRC has not adopted the uniform Federal Policy for the Protection of Human Subjects because NRC was not required to do so. Also, the Federal Register Notice will specifically request comments on the necessity of requiring compliance with the Federal Policy.

[3] Recently, the FDA has approved a radiolabeled biologic containing indium-111.

professional society or board certifications, such as the certification in nuclear medicine by the Royal College of Physicians and Surgeons of Canada; (8) changing the requirements for recentness of training; (9) requiring supervision by a physician authorized user regarding preparation of byproduct material for medical use and to provide comparable requirements regarding the supervisory responsibilities of authorized nuclear pharmacists; (10) adding responsibilities for the Radiation Safety Committee regarding additional activities which the proposed changes to Part 35 would authorize; and (10) adding a definition for "patient" to include an individual who is undergoing a diagnostic or therapeutic procedure or participating as a human subject in a research procedure for the purpose of obtaining scientific information (thus, requirements for misadministration reporting and for the quality management program also apply to human subjects).

As the Commission may note, some features of the proposed rule, as described above, may involve deleting or moving certain requirements of the regulations.

On July 15 and 16, 1992, the staff held a workshop with representatives of 23 Agreement States to discuss the draft rule language for the proposed rulemaking. The Agreement States participants expressed a clear consensus that this proposed rulemaking be either not an item of compatibility or the lowest level of compatibility possible.

However, because this amendment has safety significance for Agreement State licensees, as well as NRC licensees, this proposed amendment would be an item of compatibility for the Agreement States. All definitions contained in §§ 30.4 and 35.2 would be Division 1 items of compatibility. The definitions contained in this rulemaking must be the same for all NRC and Agreement State licensees so that consistency will be maintained.

Additionally, the staff believes that §§ 32.72, 35.6, 35.22(b)(2), 35.25, 35.50, 35.52, 35.53, 35.920, 35.972 and 35.980 should be Division 2 items of compatibility, because these requirements are necessary to ensure adequate protection of the public health and safety. For example, §§ 35.920 and 35.980 provide the radiation safety training and experience criteria for authorized users and authorized nuclear pharmacists that are important prerequisites for ensuring that byproduct material is handled safely. It should be noted that changing § 35.920 to a Division 2 item of compatibility would impact those authorized users who

want to compound radioactive drugs as well as those authorized users who want to perform imaging procedures currently allowed under § 35.200. The Agreement States would be allowed to establish requirements that are more stringent than NRC's requirements, but not less stringent.

For comparison with the proposed rulemaking, the definitions in § 30.4 are currently Division 1 items of compatibility. Section 32.72 is currently a Division 2 item of compatibility. Also, in Part 35, the definitions associated with the quality management rule and misadministrations are currently Division 1 items of compatibility. Sections 35.32 and 35.33 are currently Division 2 items of compatibility. All other sections of Part 35, except § 35.8, are currently Division 3 items of compatibility, including those sections on training and experience for authorized users and radiation safety officers, supervision, and surveys for contamination.

It would be appropriate for Agreement States to adopt the remaining sections of Part 35 in this proposed rulemaking, but it is not necessary to require any degree of uniformity between NRC and the States. Therefore, a Division 3 item of compatibility would be appropriate for those sections.

At the Commission's direction (SRM, January 22, 1993), the staff is currently re-evaluating NRC practices concerning the implementation of the provision in the Atomic Energy Act which provides that the Agreement States' regulatory programs are to be compatible with NRC's. This re-evaluation will include early and significant involvement of the Agreement States. At the conclusion of this effort, the staff will recommend to the Commission generic guidance on the application of compatibility.

The staff recognizes that the Commission's medical use program is currently under review. Some of this proposed rule would eliminate certain restrictions related to the practice of medicine and pharmacy and thereby provide greater flexibility in medical use of byproduct material. However, the staff believes that additional safeguards against radiological hazards are included in the proposed amendments that will continue to ensure adequate protection of public health and safety. Therefore, the staff recommends that the proposed rule be published for comment.

The resources needed to promulgate this rulemaking are included in the FY1993-1997 Five-Year Plan. Resources to implement this rule may require a review and reassignment of

resources in NMSS and in the regions.

Coordination: The Office of the General Counsel has no legal objection to this paper.

Recommendations: That the Commission:

1. Approve publication of the Notice of Proposed Rulemaking (Enclosure 1).

2. Certify that this rule, if promulgated, will not have a negative economic impact on a substantial number of small entities in order to satisfy requirements of the Regulatory Flexibility Act, 5 U.S.C. 605(b).

3. Note:

   a. The rulemaking would be published in the Federal Register for a 120-day public comment period;

   b. A draft regulatory analysis (Enclosure 2) will be available in the Public Document Room;

   c. A draft environmental assessment and a finding of no significant impact (Enclosure 3) will be available in the Public Document Room;

   d. The appropriate Congressional committees will be informed (Enclosure 4);

   e. A public announcement (Enclosure 5) will be issued;

   f. Copies of the Federal Register Notice will be distributed to each affected licensee and other interested parties;

   g. The Chief Counsel for Advocacy of the Small Business Administration will be informed of the certification regarding economic impact on small entities and the reasons for it as required by the Regulatory Flexibility Act; and

h. The proposed rule contains information collection requirements that are subject to review by OMB. Upon Commission approval, formal request for OMB review and clearance will be initiated.

James M. Taylor
Executive Director
for Operations

Enclosures:
1. Federal Register Notice
2. Draft Regulatory Analysis
3. Draft Environmental Assessment
4. Congressional Letters
5. Public Announcement

Commissioners' comments or consent should be provided directly to the Office of the Secretary by COB Tuesday, March 16, 1993.

Commission Staff Office comments, if any, should be submitted to the Commissioners NLT Tuesday, March 9, 1993, with an information copy to the Office of the Secretary. If the paper is of such a nature that it requires additional review and comment, the Commissioners and the Secretariat should be apprised of when comments may be expected.

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Enclosure 1

Federal Register Notice

[7590-01]

NUCLEAR REGULATORY COMMISSION

10 CFR Parts 30, 32, and 35

RIN: 3150 - AD69

Preparation, Transfer for Commercial Distribution, and Use of Byproduct Material for Medical Use

AGENCY: Nuclear Regulatory Commission.

ACTION: Proposed rule.

SUMMARY: The Nuclear Regulatory Commission (NRC) is proposing to amend its regulations for the medical use of byproduct material. This action is being taken in response to a petition for rulemaking. The proposed rule is intended to provide greater flexibility by allowing properly qualified nuclear pharmacists and authorized users who are physicians greater discretion to prepare radioactive drugs containing byproduct material for medical use. The proposed rule would also allow research involving human subjects using byproduct material and the medical use of radiolabeled biologics. In addition, the proposed rule also contains other miscellaneous and conforming amendments necessary to clarify or update the current regulations.

DATE: The comment period expires _____ (120 days following publication in the Federal Register). Comments received after this date will be considered if it is practical to do so, but the Commission is able to assure consideration only for comments received on or before this date.

ADDRESSES: Mail written comments to the Secretary, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Attention: Docketing and Service Branch.

Hand deliver comments to 11555 Rockville Pike, Rockville, Maryland, between 7:45 a.m., and 4:15 p.m. on Federal workdays.

Copies of the draft regulatory analysis and any public comments received on the proposed rule may be examined at: the NRC Public Document Room, 2120 L Street, NW. (Lower Level), Washington, DC.

FOR FURTHER INFORMATION CONTACT: Samuel Z. Jones or Anthony N. Tse, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC 20555, telephone (301) 492-3738 for Mr. Jones, or (301) 492-3797 for Mr. Tse.

SUPPLEMENTARY INFORMATION:

BACKGROUND

The Petition for Rulemaking

On June 5, 1989, the American College of Nuclear Physicians (ACNP) and the Society of Nuclear Medicine (SNM) submitted a petition for rulemaking requesting the Commission to amend its regulations to fully recognize the role of licensed nuclear pharmacists and physicians. On September 15, 1989 (54 FR 38239), the Commission published in the Federal Register a notice of receipt of a petition for rulemaking for public comment (PRM-35-9).

During the development of the ACNP-SNM petition, one NRC staff member provided substantial assistance in the preparation of the petition, but has not participated in the NRC's resolution of the petition or in the development of this proposed rule. Another NRC staff member reviewed the petition prior to its formal submittal to the Commission and participated, to a limited extent at an early stage, in the NRC's resolution of the petition and in the development of the proposed rule.

The NRC reviewed the petition and identified the following issues:

A. The petitioners requested that authorized users who are physicians (physician authorized users) be given greater flexibility regarding the medical use of radiopharmaceuticals containing byproduct material. Specifically, the petitioners requested that these physicians be permitted to: (1) use radiopharmaceuticals to treat diseases that are not listed in the U.S. Food and Drug Administration (FDA) approved package insert; (2) use methods of administration of radiopharmaceuticals for therapy that are not listed in the package insert; (3) use radiopharmaceuticals other than those for which the FDA has accepted an Investigational New Drug (IND) or an approved New Drug Application (NDA); (4) prepare radiopharmaceuticals using radionuclide generators and reagent kits in a manner other than in accordance with the manufacturer's instructions; and (5) compound radiopharmaceuticals in accordance with State law.

B. The petitioners requested that the NRC recognize the practice of nuclear pharmacy by nuclear pharmacists and the certification of nuclear pharmacists by the Board of Pharmaceutical Specialties. Specifically, the petitioners requested that nuclear pharmacists be permitted to: (1) compound

radiopharmaceuticals as described in State or FDA regulations; (2) compound radiopharmaceuticals whose manufacture and distribution are not regulated by the State or FDA; (3) prepare radiopharmaceuticals using radionuclide generators and reagent kits in a manner other than in accordance with the manufacturer's instructions; (4) produce reagent kits; and (5) distribute radiopharmaceuticals that are not regulated by the FDA.

C. Additionally, the petitioners requested that the NRC: (1) permit categories of research using radioactive drugs that do not require an IND, such as research approved by a Radioactive Drug Research Committee (RDRC); (2) permit the use of radiolabeled biologics for which the FDA has issued a license in response to a product license application (PLA); and (3) clarify its regulations pertaining to specific licenses of broad scope.

In response to the Federal Register Notice that announced the receipt of the petition, 466 comment letters were received. About 99 percent of the commenters supported and agreed with the petition. After consideration of the public comment letters and consultation with the FDA staff, the Commission determined that some issues should be addressed promptly.

On August 23, 1990 (55 FR 34513), the Commission published an Interim Final Rule to allow, for a period of 3 years, the use of therapeutic radiopharmaceuticals for indications not listed in the package insert and to allow departures from the manufacturer's instructions for preparing diagnostic radiopharmaceuticals using radionuclide generators and reagent kits. In response to the Commission's request for public comments associated with the Interim Final Rule, eight comment letters were received. Seven letters supported the intent of the rule but disagreed with the recordkeeping requirements contained in the rule. One comment letter sought clarification

of the rule. The Interim Final Rule permitted specific departures only at the written direction of a physician authorized user, and it does not permit pharmacy-directed departures.

On September 20, 1990, NRC received a "Petition for Reconsideration and for Stay of Action" (Petition for Reconsideration) from Syncor International Corporation (Syncor) regarding NRC's Interim Final Rule. Among other objections, the petition asserted that the rule violates the Atomic Energy Act, the Administrative Procedure Act, and NRC's implementing regulations, and that the recordkeeping requirements of the Interim Final Rule have a direct and negative impact on nuclear pharmacies.

On October 19, 1990, Syncor also filed a "Petition for Review" with the U.S. Court of Appeals for the District of Columbia Circuit (Syncor International Corp. v. NRC, NO 90-1495). The petition asked the court to review and set aside portions of the "Interim Final Rule," especially the recordkeeping requirements in 10 CFR 30.34(i)(1)(i-ii).

Also, Syncor requested NRC to amend its nuclear pharmacy license to permit certain pharmacy-directed departures in addition to the Interim Final Rule's physician-directed departures. Syncor and NRC staff agreed to hold the court action in abeyance for a period of several months to give NRC an opportunity to respond to Syncor's request. After considerable interaction among the NRC, Syncor, and the FDA, the requested license amendments for pharmacy-directed departures were granted. Because of the generic interest this licensing action might have had for other commercial nuclear pharmacy licensees, the NRC, on June 26, 1991, sent each of these licensees a letter informing them of NRC's action in issuing Syncor's amendments. Until the amendments contemplated in this proposed rulemaking are adopted through the

issuance of a final rule, the NRC stands ready to consider similar license amendment requests from other commercial nuclear pharmacies.

Meanwhile, to provide relief from the recordkeeping requirements contained in the Interim Final Rule, the Commission published a final rule entitled "Departure From Manufacturer's Instructions; Elimination of Recordkeeping Requirements" (57 FR 45566; October 2, 1992). This rule eliminated all the recordkeeping requirements. Based on the information collected under the Interim Final Rule, both the NRC and FDA staff agreed that the major trends in departures that could be identified by the recordkeeping were already discernible. Thus, additional recordkeeping was not necessary.

In a parallel effort, the NRC continued to work on the remaining issues in the ACNP-SNM petition. On August 7, 1991, the NRC conducted a public workshop in Rosemont, Illinois, to present "strawman" language on the training and experience criteria for authorized nuclear pharmacists to representatives of the following organizations: Board of Pharmaceutical Specialties, American Board of Science in Nuclear Medicine, National Association of Boards of Pharmacy, Committee on Radionuclides and Radiopharmaceuticals of the U.S. Council for Energy Awareness, American Pharmaceutical Association, American Society of Hospital Pharmacists, and three graduate schools of pharmacy. Subsequently, the NRC also discussed the proposed resolution of these issues in meetings with the FDA, the NRC's Advisory Committee on the Medical Uses of Isotopes (ACMUI), and the Agreement States. This proposed rulemaking is the evolutionary result of numerous meetings with the aforementioned groups.

THE PROPOSED MODIFICATIONS

In a policy statement published on February 9, 1979 (44 FR 8242), entitled "Regulation of the Medical Uses of Radioisotopes; Statement of General Policy," the NRC stated:

1. The NRC will continue to regulate the medical uses of radioisotopes as necessary to provide for the radiation safety of workers and the general public.

2. The NRC will regulate the radiation safety of patients where justified by the risk to patients and where voluntary standards, or compliance with these standards, are inadequate.

3. The NRC will minimize intrusion into medical judgments affecting patients and into other areas traditionally considered to be a part of the practice of medicine.

In conformance with this policy, the Commission proposes to eliminate certain restrictions in the NRC regulations on the practice of medicine and pharmacy (e.g., compounding), and provide the authority for research involving human subjects and the use of radiolabeled biologics. The Commission believes that these restrictions can be eliminated without compromising the level of protection of public health and safety against radiological hazards. The Commission recognizes that physicians have the primary responsibility for the diagnosis and treatment of their patients and recognizes that the nuclear pharmacists have the primary responsibility for the preparation of radioactive drugs. NRC regulations are predicated on the assumption that properly trained and adequately informed physicians and pharmacists will make decisions that are in the best interest of patients. Furthermore, the pharmacological

aspects of radioactive drugs, including drug safety and efficacy, are regulated by the FDA or the States.

The Commission believes that the proposed amendments would provide greater discretion for physician authorized users to use byproduct material in the practice of medicine. Also, the proposed amendments would incorporate into the regulations the concept of an authorized nuclear pharmacist to allow properly qualified pharmacists greater discretion to prepare (including compound) radioactive drugs containing byproduct material for medical use.

In response to the petition for rulemaking, the Commission is proposing to:

1. Allow physician authorized users to use therapeutic radioactive drugs containing byproduct material for indications or methods of administration not listed in the FDA-approved package insert;

2. Allow physician authorized users to use radioactive drugs containing byproduct material for research involving human subjects;

3. Allow physician authorized users to use radiolabeled biologics containing byproduct material;

4. Allow medical use licensees and commercial nuclear pharmacies to depart from the manufacturer's instructions for preparing radioactive drugs using radionuclide generators and reagent kits;

5. Allow medical use licensees and commercial nuclear pharmacies to compound radioactive drugs using byproduct material;

6. Delete the existing regulations related to the nonradioactive reagent kits; and

7. Clarify regulatory requirements for specific licenses of broad scope.

Table 1 summarizes the requests made in the petition and the Commission's responses.

In addition to the proposed amendments in response to the issues raised in the petition, the Commission is proposing related or miscellaneous amendments to Parts 32 and 35. In general, the objective of these proposed amendments is to clarify, update, and simplify the current regulations. Specifically, these proposed amendments include:

1. In Part 32, the Commission is proposing to replace the word "radiopharmaceutical" with the term "radioactive drug" in proposed § 32.72. This change is necessary to include both radiopharmaceuticals and radiolabeled biologics in Part 32.

2. In Part 35, whenever applicable, the Commission is proposing to use the term "unsealed byproduct material for medical use" instead of "radiopharmaceutical" or "radioactive drug." This proposed change is intended to indicate that the Commission's regulations regarding the medical use of byproduct material are focused on radiation safety and are separate from FDA's regulations regarding radioactive drugs. However, to prevent massive changes in Part 35, the word "radiopharmaceutical" will continue to be used in the sections for which modifications are not proposed. Thus, the word "radiopharmaceutical" would be equivalent to "unsealed byproduct material for medical use" in the sections that are not modified by this proposed rule.

3. The Commission is proposing to modify the definition of "medical use" in Parts 30 and 35 by using the term "patient," which by its definition would include the administration of byproduct material to human subjects for

Table 1

Summary of Requests in the Petition and the Commission's Responses

Request	Response
Permit authorized users to use radiopharmaceuticals for therapeutic uses not covered in the package insert.	Permit physician authorized users who are qualified for therapeutic administration greater discretion to use radioactive drugs for therapeutic uses.
Permit authorized users to use radioactive drugs for research involving human subjects.	Permit physician authorized users to use radioactive drugs for research provided that human subjects are protected.
Permit authorized users to use radiolabeled biologics.	Permit physician authorized users greater discretion to use radiolabeled biologics.
Permit medical use licensees and pharmacies to depart from package inserts when using generators and kits.	Permit physician authorized users and authorized nuclear pharmacists who meet certain training and experience criteria greater discretion to use generators and kits.
Permit medical use licensees and pharmacies to use byproduct material to compound radioactive drugs.	Permit physician authorized users and authorized nuclear pharmacists who meet certain training and experience criteria to prepare (including compound) radioactive drugs.
Permit nuclear pharmacists to prepare reagent kits.	Delete NRC regulations on reagent kits which do not contain byproduct material. Thus, nuclear pharmacists would be able to prepare reagent kits under applicable law.
Clarify requirements on licenses of broad scope.	Clarify the requirements by adding two exemptions in Part 35.

the purpose of obtaining scientific information (i.e., research). In addition, the Commission proposes to delete the language in the definition of "medical use" that the administration of byproduct material be in the practice of medicine in accordance with a license to practice medicine. The definition of other terms in Part 35 (e.g., physician) include this licensing concept.

Also, the Commission is proposing to add a definition for "patient" in Part 35 to include an individual who is participating in a research procedure as a human subject. With this proposed new definition, applicable requirements in Part 35, such as misadministration reporting and quality management program, would also apply to human subjects; thus, an equivalent level of protection would be provided for both patients and human subjects.

4. In Part 32, the Commission is proposing to clarify the existing regulations regarding the labeling of syringes, vials, generators, or other containers of radioactive drugs. This proposed change is necessary to avoid confusion over the types of information to be submitted.

5. In Part 32, the Commission is proposing to delete the text in 32.72(b) because it is out of date.

6. In discussing the proposed regulations concerning transfer of radioactive drugs, the Commission has noted later in this preamble that it is sometimes necessary to transfer a dosage of a radioactive drug on a case-by-case basis from one medical use licensee to another medical use licensee. These case-specific transfers would not be considered commercial transfers by the NRC and, therefore, would not require a Part 32 license.

7. In Part 35, the Commission is proposing to change the lower limit for testing dose calibrators for linearity from 0.37 Megabecquerel

(10 microcuries) to 1.1 Megabecquerels (30 microcuries) for consistency with 10 CFR 35.32, "Quality Management Program."

8. In regard to the accuracy, linearity, and geometry tests of dose calibrators, the Commission is proposing to replace the requirement for the Radiation Safety Officer's (RSO) signature with the requirement for the identity of the individual actually performing these tests. This proposed change is necessary to identify the individual who actually performed these tests. Furthermore, this change would provide additional time for the RSO to devote to other radiation safety issues. However, this change would not affect the responsibilities of the RSO that are defined in existing 10 CFR 35.21.

9. The Commission is proposing to update the regulations by recognizing several certification boards in the training and experience requirements.

10. The Commission is proposing that licensees may allow authorized users and authorized nuclear pharmacists who meet certain requirements to use byproduct material without the licensee first obtaining a license amendment from the NRC. Therefore, the Commission is proposing to delete the provisions in Part 35 addressing visiting authorized users.

11. The Commission is proposing to modify the requirements for recentness of training of certain authorized users.

12. The Commission is proposing to add requirements regarding the preparation of byproduct material for medical use under the supervision of a physician authorized user and to provide comparable requirements regarding the supervisory responsibilities of authorized nuclear pharmacists.

13. The responsibilities of the Radiation Safety Committee would be modified under the proposed rule to reflect the activities which the proposed changes to Part 35 would authorize.

DISCUSSION OF PROPOSED REGULATORY TEXT

Section 30.4. Definitions.

The definition of "medical use" would be modified to conform to the corresponding definition proposed for 10 CFR 35.2. This definition would be modified by using the term "patient," which by its definition would include the administration of byproduct material to human subjects.

In addition, the modifications would delete the current statement in this definition that the byproduct material be administered in the practice of medicine in accordance with a license issued by a State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico. This change is being made because (1) this aspect of the definition is included in other existing definitions in Part 35 (e.g., authorized user and physician) and (2) the definition of "medical use" would include research involving human subjects.

Section 30.34 Terms and conditions of licenses.

Section 30.34(i) provided interim relief from the restrictions that licensees follow the manufacturer's instructions when preparing radiopharmaceuticals using radionuclide generators and reagent kits. This

proposed rulemaking would eliminate these restrictions. Therefore, the Commission proposes to delete § 30.34(i) in its entirety.

Section 32.72 Manufacture, preparation, or transfer for commercial distribution of radioactive drugs containing byproduct material for medical use under 10 CFR Part 35.

The Commission proposes to retitle this section to more accurately reflect the operations of licensees (i.e., manufacturers and commercial nuclear pharmacies) regulated under this section.

Section 32.72(a).

This paragraph is being modified to add the word "prepare" and the phrase "transfer for commercial distribution" to more accurately reflect the operations of licensees regulated under this section.

Section 32.72(a)(1).

The proposed amendment to this paragraph is an editorial change to replace "§ 30.33 of this chapter" with "10 CFR 30.33."

Section 32.72(a)(2).

The Commission proposes to modify this paragraph to recognize radioactive drug manufacturers holding registration by the FDA, or appropriate

State agencies, as well as commercial nuclear pharmacies licensed by State Boards of Pharmacy (SBPs) and nuclear pharmacies operating in Federal facilities. The intent of this paragraph is to make clear that commercial nuclear pharmacies are covered under this section.

Radioactive drugs transferred from a commercial nuclear pharmacy to another licensee in the normal course of business are considered commercial transfers by the NRC and require a Part 32 license. However, the Commission recognizes that in the course of patient care, it is sometimes necessary for licensees to transfer a dosage of a radioactive drug on a case-by-case basis from one medical use licensee to another medical use licensee. These case-specific transfers would not be considered commercial transfers by the NRC and, therefore, would not require a Part 32 license.

Section 32.72(a)(3).

The Commission proposes to modify this paragraph to clarify the type of information that should be submitted to the NRC. The words "packaging" and "package" in the existing § 32.72(a)(3) could be interpreted as referring only to the external transportation package (e.g., cardboard box). In the proposed § 32.72(a)(3), the words "... per vial, syringe, generator, or other container ..." would be used to clearly indicate the types of information to be submitted. In addition, the phrase "group licensees" would be replaced with the phrase "medical use licensees."

Section 32.72(a)(4).

The Commission proposes to modify § 32.72(a)(4)(i) to clarify the types of information that should be contained on the label to be affixed to each container of a radioactive drug. This action is proposed to ensure that the information on the label would include information specified in existing 10 CFR 35.60(b) and 35.61(b).

Also, the Commission proposes to replace the phrase "each package" by the phrase "labels to be applied to containers of radioactive drugs, as specified in 10 CFR 35.60(b) and 35.61(b) ..." for the same reason as for the proposed changes in § 32.72(a)(3), discussed above.

In addition, the Commission is also proposing to delete the last sentence of § 32.72(a)(4)(i) because it is out of date.

Furthermore, "time of assay" would be added to the existing "date of assay." This information is necessary for determining the dosage, at the time of administration, for radioactive drugs containing radionuclides with short half-lives.

The Commission also proposes to delete the provision in § 32.72(a)(4)(ii) that required FDA approval before combining labeling information. In addition, the remaining phrase of the existing § 32.72(a)(4)(ii) "the labels, leaflets or brochures required by this paragraph are in addition to the labeling required by the Food and Drug Administration (FDA)" would be replaced by a sentence "NRC's labeling requirements are independent of requirements of the U.S. Food and Drug Administration (FDA)." This proposed sentence would be moved to the existing § 32.72(a)(4)(i) which would be renamed § 32.72(a)(4). This proposed

amendment would not preclude use of one label if it contains all the required information.

Section 32.72(b).

The Commission proposes to replace this paragraph because the existing text is obsolete.

The Commission proposes new text that would allow an "authorized nuclear pharmacist" (or individual working under the supervision of the "authorized nuclear pharmacist") working in a commercial nuclear pharmacy to prepare (including compound) radioactive drugs. The NRC is using the phrase "prepare radioactive drugs" in a general sense, which includes: (1) using radionuclide generators and nonradioactive reagent kits to produce radioactive drugs; and (2) using byproduct material and other basic ingredients to compound radioactive drugs.

Current regulations require that a Part 32 licensee may not depart from manufacturer's instructions when preparing radioactive drugs unless: (1) a license amendment has been granted permitting the departure; or (2) the departure has been requested by a physician authorized user. This requirement restricts the ability of qualified nuclear pharmacists to practice their profession which could otherwise include, but for NRC restrictions, compounding radioactive drugs. NRC believes that this restriction can be eliminated provided that the pharmacist meets the training and experience requirements in proposed 10 CFR 35.980.

The Commission is proposing to define the terms "medical use" and "authorized nuclear pharmacist" in Part 32 by referencing the definition of

these terms in proposed 10 CFR 35.2. The definition of "medical use" would be modified to use the term "patient," which by its definition would include the administration of byproduct material to an individual who is participating in a research procedure as a human subject. It is necessary to define an "authorized nuclear pharmacist" because the proposed amendments would provide pharmacists with the authority to possess and use byproduct material in the practice of nuclear pharmacy.

For purposes of Part 32, an authorized nuclear pharmacist also includes those individuals who are currently licensed or registered by a state as a pharmacist and who are also designated, as of the effective date of the final rule, as an "authorized user" on a nuclear pharmacy license issued by the Commission under 10 CFR Part 32 to work as an authorized nuclear pharmacist. The Commission believes that this limited "grandfathering" is justified because: (1) currently these "authorized users" essentially meet the training and experience criteria for an authorized nuclear pharmacist as specified in proposed 10 CFR 35.980(b)(1); and (2) these "authorized users" are currently working in a nuclear pharmacy.

A Part 32 "authorized user" who does not currently possess a valid state pharmacy licensure or registration would not be grandfathered as an authorized nuclear pharmacist because, under state law, this individual is not qualified to be a pharmacist. However, such an individual may work in a nuclear pharmacy under the supervision of an authorized nuclear pharmacist.

The Commission proposes to require licensees to submit a copy of the individual's board certification, the license, or the permit, and the state pharmacy licensure or registration to the NRC within 30 days of the date that the licensee permits the individual to work as an authorized nuclear

pharmacist. This proposal would reduce licensees' burden because such a notification would replace the currently required license amendment and the associated amendment fee which are currently necessary before a licensee may allow an authorized nuclear pharmacist to work in its facility. In addition, the proposed action would also eliminate the delay associated with the license amendment process. The NRC will review the notifications upon receipt to verify that the requirements of proposed § 32.72(b) have been met. During the review process, the NRC can consider an individual's character in addition to credentials in determining whether the individual should be approved as an authorized user or authorized nuclear pharmacist, such as verifying that the individual has not committed or caused others to commit any willful violations of the Commission's regulations. At the time of the next licensing action, the names of approved individuals would be listed on the license, without fee, as an authorized nuclear pharmacist.

Section 32.72(c).

The Commission proposes to add this paragraph to explicitly require Part 32 licensees to measure and record each dosage of radioactive drugs before transferring these drugs to a medical use licensee. This proposed change is necessary so that the proposed relief to 10 CFR Part 35 medical use licensees with respect to measurements can be granted. In proposed § 35.53, medical use licensees would not be required to measure unit dosages of alpha- and beta-emitting radioactive drugs obtained from Part 32 licensees before administering such unit dosages to patients. Thus, it is necessary for the Part 32 licensees to make these measurements.

Section 32.72(d).

This paragraph is necessary to remind Part 32 licensees to comply with applicable FDA, other Federal, and State requirements in addition to applicable NRC requirements. Compliance with NRC requirements does not eliminate the need to comply with other lawful requirements. However, it is not the intent of the Commission to perform inspections to ensure compliance with FDA or State requirements nor to enforce those regulations.

Section 32.73 Manufacture and distribution of generators or reagent kits for preparation of radiopharmaceuticals containing byproduct material.

The Commission proposes to delete this section in its entirety. Since radionuclide generators would be included as a radioactive drug in proposed § 32.72, it is no longer necessary to include the generators in § 32.73. In addition, the Commission is proposing to discontinue regulating reagent kits because they do not contain byproduct material.

Section 35.2 Definitions.

Authorized nuclear pharmacist. The Commission proposes to add this new definition. It is necessary to define an authorized nuclear pharmacist because the proposed amendments would provide pharmacists the authority to possess and use byproduct material in the practice of nuclear pharmacy independent of the supervision of a physician authorized user.

The definition would specify three groups of individuals that would be qualified as authorized nuclear pharmacists: (1) individuals certified by the Board of Pharmaceutical Specialties (BPS) as a board certified nuclear pharmacist (BCNP), (2) individuals identified as authorized nuclear pharmacists on a Commission or Agreement State license, or (3) individuals identified as authorized nuclear pharmacists on a permit issued by a Commission or Agreement State specific licensee of broad scope. The individuals in the second and third groups must meet the training and experience requirements specified in the proposed § 35.980(b).

Authorized user. The Commission is proposing to modify the definition of "authorized user" to include those individuals who are: (1) board certified by at least one of the boards listed in Paragraph (a) of §§ 35.910, 35.920, 35.930, 35.940, 35.950, or 35.960; (2) identified as an authorized user on a Commission or Agreement State license, or (3) identified as an authorized user on a permit issued by a Commission or Agreement State specific licensee of broad scope. The individuals in the second and third groups must meet the training and experience requirements specified in paragraphs (b) or (c) of §§ 35.910 or 35.920, or paragraph (b) of §§ 35.930, 35.940, 35.950, or 35.960.

Proposed § 35.13 would eliminate, under certain conditions, the requirement for a licensee to submit an amendment to list an authorized user on its license. Instead, proposed § 35.14 would require specific licensees of limited scope to provide a copy of the individual's board certification, the license, or the permit to the Commission within 30 days of the date that the licensee permits the individual to work as an authorized user.

However, before allowing a physician who does not have board certification (or is not listed on a license or a permit) to work as an authorized user, the specific licensee of limited scope must continue to submit a license amendment and obtain NRC approval. The NRC will review the notifications upon receipt to verify that the requirements of proposed § 32.72(b) have been met. During the review process, the NRC can consider character in addition to credentials in determining whether the individual should be approved as an authorized user or authorized nuclear pharmacist, such as to verify that the individual has not committed or caused others to commit any willful violations of the Commission's regulations.

Medical use. The Commission is proposing to modify the definition of "medical use" by using the term "patient," which by its definition would include the administration of byproduct material to human subjects.

Currently, NRC allows by license condition specific medical use licensees of broad scope to perform research involving human subjects using byproduct material. Because Part 35 is silent on research involving human subjects using byproduct material, Part 35 specific medical use licensees of limited scope may only conduct such research if NRC grants a license amendment to do so. The effects of the current regulatory framework are to inhibit or delay research activities by specific medical use licensees of limited scope.

Medical research involving human subjects not using radioactive material is currently conducted by large medical institutions and community hospitals through, for example, their participation in regional and national research programs. Such research may lead to better understanding of diseases, improved diagnostic and therapeutic methods, new or better drug products or medical devices, or essential basic scientific information.

Current regulations require all medical institutions to have a Radiation Safety Committee whose responsibilities include oversight of all uses of licensed material. Other Part 35 licensees are required to have a Radiation Safety Officer who has such responsibility. The Commission believes that restrictions on research can be reduced provided there are certain additional protections of human subjects as described in proposed § 35.6.

The proposed provisions include requiring a licensee who conducts research involving human subjects to: (a) possess a Part 35 license authorizing medical use, (b) implement the Federal Policy for the Protection of Human Subjects or comply with specific NRC licensing requirements, and (c) have a physician authorized user who will supervise the administration of the byproduct material.

The Commission believes that information gathered through research, although it may not benefit the individual subject of the research, has the potential to benefit the society at large. Therefore, given adequate protection of the rights and radiological safety of human subjects, it is appropriate to permit this activity.

The Commission is also proposing to delete the current statement in this definition that the byproduct material be administered in the practice of medicine in accordance with a license issued by a State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico. This change is being made because this aspect of the definition is included in other existing definitions in Part 35 (e.g., authorized user and physician).

Patient. The Commission is proposing to add this new definition. The term "patient," for the purposes of this part, would include an individual who is: (1) undergoing a diagnostic or therapeutic procedure; or

(2) participating in a research procedure as a human subject. With the addition of this definition, the applicable provisions of Part 35, such as requirements related to misadministrations and the quality management program, also apply to a human subject. Thus, an equivalent level of protection would be provided for both patients and human subjects.

Pharmacist. The Commission is proposing to add this new term to define a pharmacist in Part 35 to complement another new definition "authorized nuclear pharmacist."

Section 35.6 Provisions for research involving human subjects.

The Commission is proposing to add this section to address the protection of the rights of human subjects who would be involved in research using byproduct material. The Commission believes that most research involving human subjects using byproduct material is currently conducted, funded, supported, or regulated by another federal agency which has implemented the Federal Policy for the Protection of Human Subjects (56 FR 28002; June 18, 1991). Therefore, the rights of human subjects involved in such research activities would be protected by the other federal agency funding the research under the provisions of the Federal Policy. The Federal Policy has been implemented by 15 Federal departments or agencies (not including NRC) and includes provisions, among others, for obtaining Institutional Review Board (IRB) review and approval of the research activities and informed consent from the human subjects. NRC understands that compliance with the Federal Policy by institutions conducting research

involving human subjects is achieved through the use of letters of assurance of compliance and certain reporting requirements.

This section proposes to allow the licensees covered by the Federal Policy as adopted by another federal agency to conduct human research without prior NRC approval. If a licensee's activities are not funded by another federal agency which has adopted the Federal Policy, the licensee would need to apply for and obtain approval of a specific amendment to its NRC license prior to conducting research involving human subjects using byproduct material. During the review of the license amendment application, the NRC would ensure that the proposed research would receive approval of the Institutional Review Board and obtain the human subject's informed consent. The Commission is soliciting public comment on the number and type of research activities which would not be funded by another federal agency which has adopted the Federal Policy and, thus under the proposed rule, would require a license amendment.

The focus of NRC inspections would be to confirm that both types of licensees have obtained prior IRB review and approval of the research activities and informed consent of the human subjects.

The Commission is soliciting public comment on whether it should broaden or narrow its focus to require compliance with all or none of the provisions of the Federal Policy or equivalent license conditions. In making comments, consideration should be given to the fact that all the radiation safety provisions of 10 CFR Part 35 are proposed to be made applicable to research involving human subjects.

Section 35.7 FDA, other Federal, and State requirements.

The section is necessary to remind medical use licensees to comply with applicable FDA, other Federal, and State requirements. However, it is not the intent of the Commission to perform inspections to ensure compliance with FDA or State requirements nor to enforce those regulations.

Section 35.11 License required.

The Commission is proposing to add paragraph (c), in parallel with the existing paragraph (b), to this section. The new paragraph (c) would permit an individual to prepare unsealed byproduct material for medical use under the supervision of an authorized nuclear pharmacist or authorized user who is a physician. Also, the existing paragraph (a) would be revised by replacing the phrase "paragraph (b)" with "paragraphs (b) or (c)."

Section 35.12 Application for license, amendment, or renewal.

The Commission is proposing to add paragraph (e) to this section. This paragraph would remind Part 35 medical use licensees that they may apply for a Type A specific license of broad scope under 10 CFR Part 33.

Section 35.13 License amendments.

The Commission proposes to modify paragraph (b) of this section to delete the term "visiting authorized user." Instead, under the proposed

provisions, the licensees could allow, without a license amendment, an individual to work as an authorized user provided that the individual is: (1) certified by a board listed in Subpart J, (2) identified as an authorized user on a Commission or Agreement State license, or (3) identified as an authorized user on a permit issued by a Commission or Agreement State specific licensee of broad scope. However, the licensee would be required to provide a copy of an individual's board certification, the license, or the permit to the Commission within 30 days of the date that the licensee permits the individual to work as an authorized user (See proposed § 35.14).

The Commission also proposes to add an exception for authorized nuclear pharmacists to this section like the exception for authorized users.

Section 35.14 Notification.

In addition to the existing notification requirement, the Commission proposes to amend this section to require specific licensees of limited scope to submit a copy of an individual's board certification, the license, or the permit as discussed in § 35.13. This proposal would reduce licensees' burden because such a notification would replace the currently required license amendment and the associated amendment fee which are currently necessary before a specific licensee of limited scope may allow an authorized user to work in its facility. In addition, the proposed action would also eliminate the delay associated with the license amendment process. The NRC will review the notifications upon receipt to verify that the requirements of this section have been met. In addition, the NRC would verify at that time that this individual has not committed or caused another individual to commit any

willful violations of the Commission's regulations. At the time of the next licensing action, the name of this individual would be listed on the license, without fee, as an authorized user. The Commission also proposes to apply this section to authorized nuclear pharmacists in the same manner as for authorized users.

Section 35.15 Exemptions regarding Type A specific licenses of broad scope.

The Commission is proposing to clarify requirements on Type A specific licenses of broad scope by adding the proposed exemptions. This proposed section would specify that an application for and receipt of a license amendment would not be necessary for the following actions: (1) permit a new authorized user or authorized nuclear pharmacist to work under the license and (2) permit a change of the area of use of byproduct material within the address identified in the license. Also, specific licensees of broad scope would be exempt from certain notification requirements specified in proposed § 35.14.

These changes are being made to ensure that the proposed rule conforms with the current practice regarding Type A specific licensees of broad scope. Under current practice, the other prescriptive and performance requirements of Part 35 apply to Type A specific licensees of broad scope. Because a Part 33 specific licensee of broad scope is required to establish more complete administrative procedures and controls to ensure radiation safety than a Part 35 licensee, the exemptions would not reduce protection of public health and safety.

Section 35.22 Radiation Safety Committee.

The Commission is proposing to amend paragraph (b)(2) to apply this section to authorized nuclear pharmacists in the same manner as for authorized users.

The Commission also proposes to require the Radiation Safety Committee to review an individual's certification, license, or permit, and determine, based on the proposed § 35.13(b)(1) through (b)(4), whether to allow the individual to work as an authorized user or authorized nuclear pharmacist without submitting a license amendment for NRC approval.

Section 35.25 Supervision.

Existing paragraph (b) would be redesignated as paragraph (c).

The Commission is proposing to add a new paragraph (b) to address the supervisory responsibilities of the licensee, the authorized nuclear pharmacist, and the physician authorized user who prepare unsealed byproduct material for medical use. Specifically, under the proposed paragraph, an authorized nuclear pharmacist or a physician authorized user would be able to permit individuals to prepare unsealed byproduct material for medical use, provided that the individuals are adequately supervised. This section describes the level of supervision that an authorized nuclear pharmacist or a physician authorized user would be required to provide to individuals who are preparing unsealed byproduct material for medical use under their supervision.

Section 35.27 Visiting authorized user.

The Commission is proposing to delete this section which permits a visiting authorized user to work for a period of 60 days each year without a license amendment. Under proposed § 35.13(b), the concept of a visiting authorized user would no longer be necessary. Any individual who meets § 35.13(b)(1) through (b)(4) would be permitted to work in a licensee's facility either temporarily or permanently. However, under proposed § 35.14, the licensee would be required to provide a copy of the individual's board certification, the license, or the permit to the NRC.

Section 35.49 Supplier for sealed sources or devices for medical use.

The Commission is proposing to modify this section as follows:

The title of this section would be modified to indicate that this section would only apply to sealed sources or devices for medical use.

The Commission is proposing to delete the reference to §§ 32.72 and 32.73 in the proposed § 35.49(a) because, under the proposed rule, the requirements applicable to unsealed byproduct material for medical use would be incorporated into the proposed §§ 35.100, 35.200, and 35.300. Furthermore, the proposed rule would allow medical use licensees to prepare (including compound) radioactive drugs. Therefore, limiting suppliers of radioactive drugs to manufacturers or commercial nuclear pharmacies would no longer be necessary. However, the requirements applicable to sealed sources or devices as specified in § 32.74 will remain in the proposed § 35.49(a).

In addition, the Commission is proposing to delete existing § 35.49(b). Under the proposed rule, all the requirements applicable to reagent kits would be deleted because the reagent kits do not contain byproduct material. Therefore, this paragraph would no longer be necessary.

The existing § 35.49(c) would be redesignated as § 35.49(b).

Section 35.50 Possession, use, calibration, and checks of dose calibrators.

The Commission is proposing the following modifications to this section.

(1) In paragraph (a), the phrase "photon-emitting" would be inserted to clarify that this section is applicable only to photon-emitting radionuclides. This modification would avoid confusion between this section and proposed § 35.52 pertaining to instruments to measure dosages of alpha- or beta-emitting radionuclides.

(2) The Commission is proposing to use the term "radionuclides" instead of the term "radiopharmaceuticals." The new term is broader and would include radiolabeled biologics as well as radiopharmaceuticals.

(3) In paragraph (b)(3) regarding the linearity test of the dose calibrator, the lower limit for the test would be changed from 0.37 megabecquerel (10 microcuries) to 1.1 megabecquerel (30 microcuries). This modification is necessary for consistency with the requirements of the Quality Management Program (§ 35.32) and proposed § 35.53 (c)(3).

(4) In paragraphs (e)(2) through (e)(4) regarding records on the accuracy, linearity, and geometry tests of dose calibrators, the Commission is proposing to require the identity of the individual actually performing these tests rather than the Radiation Safety Officer's (RSO) signature. This

proposed change is necessary to identify the individual who actually performed these tests. Furthermore, this change would provide additional time for the RSO to devote to other radiation safety issues.

Section 35.52 Possession, use, calibration, and checks of instrumentation to measure dosages of alpha- and beta-emitting radionuclides.

The Commission is proposing to require medical use licensees to possess and use instrumentation to measure alpha- or beta-emitting radionuclides. New radiolabeled biologics are being developed which have potential benefits for diagnosis and treatment in medicine. Some of these biologics may contain alpha- or beta-emitting radionuclides that do not emit photons of sufficient energy or frequency to be detected or quantified in a dose calibrator. Thus, this section is proposed so that medical use licensees would be able to determine that the correct dosages will be administered to patients.

The measurement requirements of this section would not apply to unit dosages obtained from a manufacturer or a commercial nuclear pharmacy for the following reasons: (1) the instrumentation for measuring activity of alpha- or beta-emitters is expensive and not commonly available in a medical use licensee's facility; (2) the frequency of using alpha- or beta-emitters for most medical use licensees is very low; and (3) the manufacturer or the commercial nuclear pharmacy would be required, pursuant to proposed § 32.72(c), to measure each dosage of a radioactive drug prior to transfer for commercial distribution.

Section 35.53 Measurement of dosages of unsealed byproduct material for medical use.

The Commission is proposing to modify this section as follows:

(1) In the title, the term "radiopharmaceutical dosages" would be replaced by the phrase "dosages of unsealed byproduct material for medical use." This is proposed to avoid the connotation that the Commission is regulating drug safety and efficacy. The word "unsealed" is proposed to emphasize that this section applies only to unsealed byproduct material for medical use. This section does not apply to sealed sources such as teletherapy or brachytherapy sources.

(2) Existing paragraphs (a) and (b) have been combined as proposed paragraph (a). However, the measurement requirements are the same.

(3) The new text of paragraph (b) would require medical use licensees to measure dosages of alpha- or beta-emitting radionuclides, except for unit dosages obtained from a manufacturer or a commercial nuclear pharmacy. Medical use licensees would be required to measure dosages that will be administered to patients.

The measurement requirements of this section would not apply to unit dosages of alpha- or beta-emitting radionuclides because the manufacturer or the commercial nuclear pharmacy must measure the dosage before distributing it to a medical use licensee. Also, the proposed rule would allow a licensee to use the combination of several measurements and calculations to determine the dosage because it may not be possible to measure alpha- or beta-emitting radionuclides by a single measurement.

(4) In paragraph (c)(3), 0.37 megabecquerel (10 microcuries) would be changed to 1.1 megabecquerels (30 microcuries). This modification is necessary for consistency with the requirements of the Quality Management Program (§ 35.32). Also, since the radiological risk associated with a dosage of 1.1 megabecquerels (30 microcuries) is small, it is unnecessary to require more than just recording that the dosage is less than 1.1 megabecquerels (30 microcuries).

Section 35.100 Use of unsealed byproduct material for uptake, dilution, and excretion.

The current § 35.100 requires medical use licensees to use only byproduct material in a radiopharmaceutical for uptake, dilution and excretion for which the FDA has accepted a "Notice of Claimed Investigational Exemption for a New Drug" (IND) or approved a New Drug Application (NDA). The effect of this restriction is to prohibit a licensee from using other types of radioactive drugs such as those approved by a Radioactive Drug Research Committee (RDRC), unless a license amendment is received authorizing such use.

The Commission believes that these restrictions can be eased without compromising the level of protection of public health and safety against radiological hazards because of certain conditions which must be met (discussed below). In addition, the Commission recognizes that physicians have the primary responsibility for the diagnosis and treatment of their patients. Commission regulations are predicated on the assumption that properly trained and adequately informed physicians will make decisions that are in the best interest of their patients. Furthermore, the pharmacological

aspects of radioactive drugs, including drug safety and efficacy, are regulated by the FDA.

Detailed discussions of proposed changes are presented below.

The Commission is proposing to use the term "unsealed byproduct material" instead of the term "radiopharmaceutical" in this proposed section. This is proposed to avoid the connotation that the Commission is regulating drug safety and efficacy. The word "unsealed" is proposed to emphasize that this section applies only to unsealed byproduct material for medical use and does not apply to sealed sources such as teletherapy or brachytherapy sources.

This proposed modification would provide medical use licensees with the maximum flexibility to use any byproduct material for medical use provided that the material is: (1) obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or (2) prepared by an authorized nuclear pharmacist, a physician authorized user who meets the training requirements specified in § 35.920, or an individual under supervision of either, as specified in proposed § 35.25.

In addition, the Commission is proposing to modify this section as follows:

(1) The phrase "unsealed byproduct material prepared for medical use" would be used. This phrase includes "IND" and "NDA," as specified in the existing § 35.100, and other radioactive drugs containing byproduct material that are not specified in the existing § 35.100.

(2) The supplier or preparer of unsealed byproduct material for medical use would be specified under this section. A licensee may obtain byproduct material from a manufacturer or a commercial nuclear pharmacy.

(3) This proposed section would allow licensees to use unsealed byproduct material to prepare (including compound) radioactive drugs by physician authorized users who meet § 35.920, authorized nuclear pharmacists, or individuals under their supervision. The NRC is using the phrase "prepare radioactive drugs" in a general sense to include: (a) using radionuclide generators and nonradioactive reagent kits to produce radioactive drugs and (b) using byproduct material and other basic ingredients to compound radioactive drugs.

(4) This proposed section would require a physician authorized user who wants to prepare radioactive drugs to meet the requirements specified in existing § 35.920. Training and experience requirements specified in existing §§ 35.910 and 35.930, although adequate to administer byproduct material, would not be sufficient for preparing radioactive drugs. Similar training and experience requirements for authorized nuclear pharmacists are proposed in § 35.980.

(5) This proposed section would also allow an individual under the supervision of a physician authorized user or an authorized nuclear pharmacist to use byproduct material to prepare (including compound) radioactive drugs. A Part 35 medical use licensee operating a nuclear pharmacy to prepare radioactive drugs for use within the licensee's facility would not be required to obtain a Part 32 license, unless the nuclear pharmacy transfers radioactive drugs for commercial distribution. The proposed rule language in § 35.25 would require the supervising physician authorized user or authorized nuclear pharmacist to instruct the individual on radiation safety principles and procedures and would require the individual to follow the procedures.

(6) The Commission recognizes that, in the course of patient care, it is sometimes necessary to transfer a dosage of a radioactive drug, on a case-by-case basis, from one medical use licensee to another medical use licensee. These case-specific transfers would not be considered commercial transfers by the NRC and, therefore, would not require a Part 32 license. Licensees should be aware that other than infrequent transfers may require a license for commercial transfer of byproduct material.

Section 35.200 Use of unsealed byproduct material for imaging and localization studies.

Paragraph (a) of the current § 35.200 restricts medical use licensees to use byproduct material in a radiopharmaceutical for which the FDA has accepted an IND or approved an NDA. The effect of this restriction is to prohibit a licensee from using other types of radioactive drugs such as those approved by a Radioactive Drug Research Committee (RDRC), unless a license amendment is received that authorizes such use. Furthermore, paragraphs (b) and (c) of the current section require licensees to follow the manufacturer's instructions for eluting radionuclide generators and preparing reagent kits unless a departure is directed by a physician authorized user.

The Commission believes that these restrictions can be eased without compromising the level of protection of public health and safety against radiological hazards because of certain conditions which must be met (discussed below). In addition, the Commission recognizes that physicians have the primary responsibility for the diagnosis and treatment of their patients and recognizes that the nuclear pharmacists have the primary

responsibility for the preparation of radioactive drugs. Commission regulations are predicated on the assumption that properly trained and adequately informed physicians and pharmacists will make decisions that are in the best interest of their patients. Furthermore, the pharmacological aspects of radioactive drugs, including drug safety and efficacy, are regulated by the FDA.

Detailed discussions of proposed changes are presented below.

(1) The Commission is proposing to use the term "unsealed byproduct material" instead of the term "radiopharmaceutical" in this proposed section to avoid the connotation that the Commission is regulating drug safety and efficacy. Also, this phrase includes "IND" and "NDA," as specified in the existing § 35.200, and other radioactive drugs containing byproduct material that are not specified in the existing § 35.200.

(2) This proposed modification would provide medical use licensees with the maximum flexibility to use any byproduct material for medical use provided that the material is: (a) obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or (b) prepared by an authorized nuclear pharmacist, a physician authorized user who meets the training requirements specified in § 35.920, or an individual under supervision of either, as specified in proposed § 35.25.

(3) The supplier or preparer of unsealed byproduct material for medical use would be specified under this section. A licensee may obtain byproduct material from a manufacturer or a commercial nuclear pharmacy.

(4) This proposed section would allow licensees to use unsealed byproduct material to prepare (including compound) radioactive drugs by physician authorized users who meet § 35.920, authorized nuclear pharmacists,

or individuals under their supervision. The NRC is using the phrase "prepare radioactive drugs" in a general sense to include: (a) using radionuclide generators and nonradioactive reagent kits to produce radioactive drugs and (b) using byproduct material and other basic ingredients to compound radioactive drugs.

(5) This proposed section would also allow an individual under the supervision of a physician authorized user or an authorized nuclear pharmacist to use byproduct material to prepare (including compound) radioactive drugs. The proposed rule language in § 35.25 would require the supervising physician authorized user or authorized nuclear pharmacist to instruct the individual on radiation safety principles and procedures and would require the individual to follow the procedures.

(6) The Commission recognizes that, in the course of patient care, it is sometimes necessary to transfer a dosage of a radioactive drug, on a case-by-case basis, from one medical use licensee to another medical use licensee. These case-specific transfers would not be considered commercial transfers by the NRC and, therefore, would not require a Part 32 license.

Section 35.300 Use of unsealed byproduct material for therapeutic administration.

Paragraph (a) of the current § 35.300 restricts medical use licensees to use byproduct material in a radiopharmaceutical for which the FDA has accepted an IND or approved an NDA. Also, this paragraph requires licensees to comply with the package insert instructions regarding indications and

method of administration unless a departure is directed by an physician authorized user.

While recognizing that therapeutic dosages result in greater radiation exposure, the Commission believes that these restrictions can be eased without compromising the level of protection of public health and safety against radiological hazards because of certain conditions which must be met (discussed below). In addition, the Commission recognizes that physicians have the primary responsibility for the diagnosis and treatment of their patients. Commission regulations are predicated on the assumption that properly trained and adequately informed physicians will make decisions that are in the best interest of their patients. Furthermore, the pharmacological aspects of radioactive drugs, including drug safety and efficacy, are regulated by the FDA.

Detailed discussions of proposed changes are presented below.

(1) The Commission is proposing to use the term "unsealed byproduct material" instead of the term "radiopharmaceutical" in this proposed section to avoid the connotation that the Commission is regulating drug safety and efficacy. Also, this phrase includes "IND" and "NDA," as specified in the existing § 35.300, and other radioactive drugs containing byproduct material that are not specified in the existing § 35.300.

(2) This proposed modification would provide medical use licensees with the maximum flexibility to use any byproduct material for medical use provided that the material is: (a) obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or (b) prepared by an authorized nuclear pharmacist, a physician authorized user who meets the training requirements specified in

§ 35.920, or an individual under supervision of either, as specified in proposed § 35.25.

(3) The supplier or preparer of unsealed byproduct material for medical use would be specified under this section. A licensee may obtain byproduct material from a manufacturer or a commercial nuclear pharmacy.

(4) This proposed section would allow licensees to use unsealed byproduct material to prepare (including compound) radioactive drugs by physician authorized users who meet § 35.920, authorized nuclear pharmacists, or individuals under their supervision.

(5) This proposed section would also allow an individual under the supervision of a physician authorized user or an authorized nuclear pharmacist to use byproduct material to prepare (including compound) radioactive drugs. The proposed rule language in § 35.25 would require the supervising physician authorized user or authorized nuclear pharmacist to instruct the individual on radiation safety principles and procedures and would require the individual to follow the procedures.

(6) The Commission recognizes that, in the course of patient care, it is sometimes necessary to transfer a dosage of a radioactive drug, on a case-by-case basis, from one medical use licensee to another medical use licensee. These case-specific transfers would not be considered commercial transfers by the NRC and, therefore, would not require a Part 32 license.

Section 35.900 Radiation Safety Officer.

The Commission is proposing to modify this section to recognize the certification in nuclear medicine by the Royal College of Physicians and Surgeons of Canada and in radiation oncology physics by the American Board of Medical Physics.

Section 35.910 Training for uptake, dilution, and excretion studies.

The Commission is proposing, as recommended by the ACMUI, to modify this section to recognize the certification in nuclear medicine by the Royal College of Physicians and Surgeons of Canada.

Section 35.920 Training for imaging and localization studies.

The Commission is proposing, as recommended by the ACMUI, to modify this section to recognize the certification in nuclear medicine by the Royal College of Physicians and Surgeons of Canada.

Section 35.930 Training for therapeutic use of unsealed byproduct material.

The Commission is proposing to amend § 35.930(a)(2) to recognize the certification in radiation oncology by the American Board of Radiology (ABR). In 1987, the ABR renamed "therapeutic radiology" as "radiation oncology" but the criteria for certification remain the same. Therefore, it is necessary to recognize both certifications.

Section 35.940 Training for use of brachytherapy sources.

The Commission is proposing to amend § 35.940(a)(1) to recognize the certification in radiation oncology by the American Board of Radiology (ABR).

Section 35.950 Training for use of sealed sources for diagnosis.

The Commission is proposing to amend § 35.950(a)(1) to recognize the certification in radiation oncology by the American Board of Radiology (ABR) and the certification in nuclear medicine by the Royal College of Physicians and Surgeons of Canada.

Section 35.960 Training for teletherapy.

The Commission is proposing to amend § 35.960(a)(1) to recognize the certification in radiation oncology by the American Board of Radiology (ABR).

Section 35.961 Training for teletherapy physicist.

The Commission is proposing to modify this section to recognize the certification in radiation oncology physics by the American Board of Medical Physics.

Section 35.972 Recentness of training.

Existing § 35.972 required that an individual's training must have been acquired within the last 5 years. The Board of Pharmaceutical Specialties (BPS) recertifies board certified nuclear pharmacists (BCNP) every 7 years. Based on BPS's 11 years experience with recertification, the Commission is proposing to replace 5 years with 7 years. This action is necessary to achieve consistency for recentness of training requirements among authorized users, Radiation Safety Officers, teletherapy physicists, and authorized nuclear pharmacists. The Commission is requesting public comment on which period (either 5 or 7 years) is more appropriate and the basis for any recommendation.

Section 35.980 Training for authorized nuclear pharmacist.

The Commission is proposing to add a new section that would contain specific training requirements for an authorized nuclear pharmacist. This action is necessary because an authorized nuclear pharmacist may be responsible for handling, preparing, and distributing radioactive drugs to multiple medical institutions. Thus, authorized nuclear pharmacists potentially impact the radiological safety of patients at many medical institutions. The effect of these training requirements will provide sufficient assurance that individuals satisfying these training criteria will safely prepare and distribute radioactive drugs.

In this section, the Commission is proposing two methods for an individual to qualify as an authorized nuclear pharmacist:

(1) In paragraph (a), the Commission is proposing to recognize certification by the Board of Pharmaceutical Specialties as a nuclear pharmacist as satisfying the training requirements.

(2) In paragraph (b), in lieu of board certification, an alternative method to qualify for authorized nuclear pharmacist is proposed. A candidate would be required to: (i) complete 700 hours in a structured educational program consisting of both didactic training and supervised experience in a nuclear pharmacy, and (ii) obtain a written certification from a preceptor that the candidate has achieved a level of competency sufficient to independently operate a nuclear pharmacy.

Implementation Plan and Agreement State Compatibility

The effective date of this amendment would be 6 months after the publication of the final amendment in the Federal Register.

On July 15 and 16, 1992, the NRC held a workshop with representatives of 23 Agreement States to discuss the draft rule language for the proposed rulemaking. The Agreement State participants expressed a clear consensus that this proposed rulemaking be either not an item of compatibility or the lowest level of compatibility possible.

However, because this amendment has safety significance for Agreement State licensees as well as NRC licensees, this proposed amendment would be an item of compatibility for the Agreement States. All definitions contained in §§ 30.4 and 35.2 would be Division 1 items of compatibility. The definitions contained in this rulemaking must be the same for all NRC and Agreement State licensees so that consistency will be maintained.

Additionally, the Commission believes that §§ 32.72, 35.6, 35.22(b)(2), 35.25, 35.50, 35.52, 35.53, 35.920, 35.972 and 35.980 should be Division 2 items of compatibility, because these requirements are necessary to ensure adequate protection of the public health and safety. For example, §§ 35.920 and 35.980 provide the radiation safety training and experience criteria for authorized users and authorized nuclear pharmacists that are important prerequisites for ensuring that byproduct material is handled safely. It should be noted that changing § 35.920 to a Division 2 item of compatibility would impact those authorized users who want to compound radioactive drugs as well as those authorized users who only want to perform imaging procedures currently allowed under § 35.200. The Agreement States would be allowed to establish requirements that are more stringent than NRC's requirements, but not less stringent.

It would be appropriate for Agreement States to adopt the remaining sections of Part 35 in this proposed rulemaking, but it is not necessary to require any degree of uniformity between NRC and the States. Therefore, a Division 3 item of compatibility would be appropriate for such sections.

The Commission is currently reevaluating its practices concerning the implementation of the provision in the Atomic Energy Act which provides that the Agreement States' regulatory programs are to be compatible with NRC's. This reevaluation will include early and significant involvement of the Agreement States. At the conclusion of this effort, the Commission will implement generic guidance on the application of compatibility.

For comparison, the existing compatibility levels are as follows: definitions in § 30.4 are Division 1 items of compatibility; § 32.72 is a Division 2 item of compatibility; the definitions associated with the quality

management rule and misadministrations in § 35.2 are Division 1 items of compatibility; §§ 35.32 and 35.33 are Division 2 items of compatibility; § 35.8 is a Division 4 item of compatibility; and all other sections of Part 35 are Division 3 items of compatibility.

Finding of No Significant Environmental Impact: Availability

The Commission has determined under the National Environmental Policy Act of 1969, as amended, and the Commission's regulations in Subpart A of 10 CFR Part 51, that the proposed amendments, if adopted, would not be a major Federal action significantly affecting the quality of the human environment, and therefore an environmental impact statement is not required. The proposed amendments would provide greater flexibility for physician authorized users to use byproduct material in the practice of medicine. The proposed amendments would also incorporate into the regulations the concept of authorized nuclear pharmacists to permit properly qualified pharmacists to prepare radioactive drugs containing byproduct material in the practice of pharmacy.

The proposed amendments would allow physician authorized users greater discretion to prepare and use radioactive drugs containing byproduct material. The proposed amendments would also allow authorized nuclear pharmacists greater discretion to prepare radioactive drugs containing byproduct material. It is expected that there will be no increase in radiation exposure to the public or to the environment beyond the exposures currently resulting from delivering the byproduct material or radiation from byproduct material to the patient. The draft environmental assessment and finding of no significant impact on which this determination is based is available for inspection at the

NRC Public Document Room, 2120 L Street NW. (Lower Level), Washington, DC. Single copies of the draft environmental assessment and the finding of no significant impact are available from Samuel Z. Jones or Anthony N. Tse (see FOR FURTHER INFORMATION CONTACT heading).

Paperwork Reduction Act

This proposed rule amends information collection requirements that are subject to the Paperwork Reduction Act of 1980 (44 U.S.C. 3501 et seq.). This rule has been submitted to the Office of Management and Budget for review and approval of the paperwork requirements.

The reduction in public burden for this collection of information is estimated to be a savings of 1,300 hours per year for 900 licensees, or an average 1.5 hours per year per licensee, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions on this burden reduction, to the Information and Records Management Branch (MNBB-7714), U.S. Nuclear Regulatory Commission, Washington, DC 20555, and to the Desk Officer, Office of Information and Regulatory Affairs, NEOB-3019, (3150-0001, -0010, and -0017), Office of Management and Budget, Washington, DC 20503.

Regulatory Analysis

The Commission has prepared a draft regulatory analysis on this proposed regulation. The analysis examines the benefits and impacts considered by the Commission. The draft regulatory analysis is available for inspection at the NRC Public Document Room at 2120 L Street NW. (Lower Level), Washington, DC. Single copies of the draft analysis are available from Samuel Z. Jones or Anthony N. Tse (see FOR FURTHER INFORMATION CONTACT heading).

The Commission requests public comments on the draft regulatory analysis. Comments on the draft regulatory analysis may be submitted to the NRC as indicated under the ADDRESSES heading.

Regulatory Flexibility Certification

As required by the Regulatory Flexibility Act of 1980, 5 U.S.C. 605(b), the Commission certifies that, if adopted, this proposed rule would not have a significant economic impact on a substantial number of small entities. This proposed rule would affect medical use licensees including some private practice physicians. Some of these licensees would be considered small entities under the NRC's size standards (56 FR 56672; November 6, 1991). The proposed amendments would provide greater discretion for physician authorized users to use byproduct material in the practice of medicine. The proposed amendments would also incorporate into the regulations the concept of authorized nuclear pharmacists to allow properly qualified pharmacists greater discretion to prepare (including compound) radioactive drugs containing

byproduct material for medical use. This rulemaking, if adopted, would reduce regulatory burdens on medical use licensees, including small entities.

Any small entity subject to this regulation who determines that, because of its size, it is likely to bear a disproportionate adverse economic impact should notify the Commission by a letter that indicates the following:

(a) The licensee's size and how the proposed regulation would result in a significant economic burden or whether the resources necessary to implement this amendment could be more effectively used in other ways to optimize patient safety, as compared to the economic burden on a larger licensee;

(b) How the proposed regulation could be modified to take into account the licensee's differing needs or capabilities;

(c) The benefits that would accrue, or the detriments that would be avoided, if the proposed regulation were modified as suggested by the licensee;

(d) How the proposed regulation, as modified, could more closely equalize the impact of NRC regulations or create more equal access to the benefits of Federal programs as opposed to providing special advantages to any individual or group;

(e) How the proposed regulation, as modified, would still adequately protect the public health and safety.

Backfit Analysis

The Commission has determined that the backfit rule, 10 CFR 50.109, does not apply to this proposed amendment because this amendment does not involve

any provisions which would impose backfits as defined in 10 CFR 50.109(a)(1). Therefore, a backfit analysis is not required for this proposed amendment.

List of Subjects

10 CFR Part 30

Byproduct material, Criminal penalty, Government contracts, Intergovernmental relations, Isotopes, Nuclear materials, Radiation protection, Reporting and recordkeeping requirements.

10 CFR Part 32

Byproduct material, Labeling, Nuclear materials, Criminal Penalty, Radiation protection, Reporting and recordkeeping requirements.

10 CFR Part 35

Byproduct material, Criminal penalty, Drugs, Health facilities, Health professions, Incorporation by reference, Medical devices, Nuclear materials, Occupational safety and health, Radiation protection, Reporting and recordkeeping requirements.

For the reasons set out in the preamble and under the authority of the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974,

as amended, and 5 U.S.C. 553, the Commission is proposing to adopt the following amendments to 10 CFR Parts 30, 32, and 35.

PART 30 - RULES OF GENERAL APPLICABILITY TO DOMESTIC LICENSING OF BYPRODUCT MATERIAL

1. The authority citation for Part 30 continues to read as follows:

AUTHORITY: Secs. 81, 82, 161, 182, 183, 186, 68 Stat. 935, 948, 953, 954, 955, as amended, sec. 234, 83 Stat. 444, as amended (42 U.S.C. 2111, 2112, 2201, 2232, 2233, 2236, 2282); secs. 201, as amended, 202, 206, 88 Stat. 1242, as amended, 1244, 1246 (42 U.S.C. 5841, 5842, 5846).

Section 30.7 also issued under Pub. L. 95-601, sec. 10, 92 Stat. 2951 (42 U.S.C. 5851). Section 30.34(b) also issued under sec. 184, 68 Stat. 954, as amended (42 U.S.C. 2234). Section 30.61 also issued under sec. 187, 68 Stat. 955 (42 U.S.C. 2237).

2. In § 30.4, the definition of medical use is revised to read as follows:

§ 30.4 Definitions.

* * * * *

Medical use means the intentional internal or external administration of byproduct material or the radiation therefrom to patients under the supervision of an authorized user.

* * * * *

§ 30.34 [Amended]

3. Section 30.34 is amended by removing paragraph (i) in its entirety.

PART 32 - SPECIFIC DOMESTIC LICENSES TO MANUFACTURE OR TRANSFER CERTAIN ITEMS CONTAINING BYPRODUCT MATERIAL

4. The authority citation for Part 32 continues to read as follows:

AUTHORITY: Secs. 81, 161, 182, 183, 68 Stat. 935, 948, 953, 954, as amended (42 U.S.C. 2111, 2201, 2232, 2233); sec. 201, 88 Stat. 1242, as amended (42 U.S.C. 5841).

5. Section 32.72 is revised to read as follows:

§ 32.72 Manufacture, preparation, or transfer for commercial distribution of radioactive drugs containing byproduct material for medical use under Part 35.

(a) An application for a specific license to manufacture, prepare, or transfer for commercial distribution radioactive drugs containing byproduct material for use by persons authorized pursuant to Part 35 of this chapter will be approved if:

(1) The applicant satisfies the general requirements specified in 10 CFR 30.33;

(2) The applicant submits evidence that the applicant is at least one of the following:

(i) Registered or licensed with the U.S. Food and Drug Administration (FDA) as a drug manufacturer;

(ii) Registered or licensed with a state agency as a drug manufacturer;

(iii) Licensed as a pharmacy by a State Board of Pharmacy; or

(iv) Operating as a nuclear pharmacy within a Federal medical institution.

(3) The applicant submits information on the radionuclide; the chemical and physical form; the maximum activity per vial, syringe, generator, or other container of the radioactive drug; and the shielding provided by the packaging to show it is appropriate for the safe handling and storage of the radioactive drugs by medical use licensees; and

(4) 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. 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. 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 10 CFR 35.100, 35.200, or 35.300, as appropriate, and to persons who hold an equivalent license issued by an Agreement State. The label, or the leaflet or brochure must also note that other regulatory approvals may be required. NRC's labeling requirements are independent of requirements of the U.S. Food and Drug Administration (FDA).

(b) A licensee described by paragraph (a)(2)(iii) or (iv) of this section may prepare radioactive drugs for medical use, as defined in 10 CFR 35.2, provided that the radioactive drug is prepared by either an

authorized nuclear pharmacist, as defined in 10 CFR 35.2, or an individual under the supervision of an authorized nuclear pharmacist as specified in 10 CFR 35.25.

In addition, for purposes of this section, an authorized nuclear pharmacist is a pharmacist who is currently licensed or registered by a state to practice pharmacy and designated, as of the effective date of the final rule, as an "authorized user" on a nuclear pharmacy license issued by the Commission under this part.

A licensee shall provide to the Commission a copy of the individual's board certification, the license, or the permit, and the state pharmacy licensure or registration, respectively, for each individual within 30 days of the date that the licensee permits, pursuant to this section, the individual to work as an authorized nuclear pharmacist.

(c) A 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 determine, 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:

(1) Perform tests before initial use, periodically, and following repair, on each instrument for accuracy, linearity, and geometry dependence, as appropriate for the use of the instrument; and make adjustments when necessary; and

(2) Check each instrument for constancy and proper operation at the beginning of each day of use.

(d) Nothing in this section relieves the licensee from complying with applicable FDA, other Federal, and State requirements governing radioactive drugs.

§ 32.73 [Removed]

6. Section 32.73 is removed.

PART 35 - MEDICAL USE OF BYPRODUCT MATERIAL

7. The authority citation for Part 35 continues to read as follows:

AUTHORITY: Secs. 81, 161, 182, 183, 68 Stat. 935, 948, 953, 954, as amended (42 U.S.C. 2111, 2201, 2232, 2233); sec. 201, 88 Stat. 1242, as amended (42 U.S.C. 5841).

8. In § 35.2, the definitions of authorized nuclear pharmacist, patient, and pharmacist are added and the definitions of authorized user and medical use are revised to read as follows:

§ 35.2 Definitions.

* * * * *

Authorized nuclear pharmacist means a pharmacist who is:

(1) Currently board certified as a nuclear pharmacist by the Board of Pharmaceutical Specialties;

(2) Identified as an authorized nuclear pharmacist on a Commission or Agreement State license that authorizes the use of byproduct material in the practice of nuclear pharmacy; or

(3) Identified as an authorized nuclear pharmacist on a permit issued by a Commission or Agreement State specific licensee of broad scope that is authorized to permit the use of byproduct material in the practice of nuclear pharmacy.

Authorized user means a physician, dentist, or podiatrist who is:

(1) Board certified by at least one of the boards listed in Paragraph (a) of §§ 35.910, 35.920, 35.930, 35.940, 35.950, or 35.960;

(2) Identified as an authorized user on a Commission or Agreement State license that authorizes the medical use of byproduct material; or

(3) Identified as an authorized user on a permit issued by a Commission or Agreement State specific licensee of broad scope that is authorized to permit the medical use of byproduct material.

* * * * *

Medical use means the intentional internal or external administration of byproduct material or the radiation therefrom to patients under the supervision of an authorized user.

* * * * *

Patient means, for the purposes of this part, an individual who is undergoing a diagnostic or therapeutic procedure or participating as a human subject in a research procedure for the purpose of obtaining scientific information.

* * * * *

Pharmacist means an individual licensed by a State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico to practice pharmacy.

* * * * *

9. Section 35.6 is added to read as follows:

§ 35.6 Provisions for research involving human subjects.

A licensee may conduct research involving human subjects using byproduct material provided that the research is conducted, funded, supported, or regulated by another Federal Agency which has implemented the Federal Policy for the Protection of Human Subjects. Otherwise, a licensee shall apply for and receive approval of a specific amendment to its NRC license before conducting such research. Both types of licensees shall, at a minimum, obtain informed consent from the human subjects and obtain prior review and approval of the research activities by an "Institutional Review Board."

10. Section 35.7 is added to read as follows:

§ 35.7 FDA, other Federal, and State requirements.

Nothing in this part relieves the licensee from complying with applicable FDA, other Federal, and State requirements governing radioactive drugs or devices.

11. Section 35.8 is revised to read as follows:

§ 35.8 Information collection requirements: OMB approval.

* * * * *

(b) The approved information collection requirements contained in this part appear in §§ 35.6, 35.12, 35.13, 35.14, 35.21, 35.22, 35.23, 35.29, 35.31, 35.50, 35.51, 35.52, 35.53, 35.59, 35.60, 35.61, 35.70, 35.80, 35.92, 35.204, 35.205, 35.310, 35.315, 35.404, 35.406, 35.410, 35.415, 35.606, 35.615, 35.630, 35.632, 35.634, 35.636, 35.641, 35.643, 35.645, 35.647, and 35.980.

12. In § 35.11, paragraph (a) is revised and paragraph (c) is added to read as follows:

§ 35.11 License required.

(a) A person shall not manufacture, produce, acquire, receive, possess, use, or transfer byproduct material for medical use except in accordance with a specific license issued by the Commission or an Agreement State, or as allowed in paragraphs (b) or (c) of this section.

* * * * *

(c) An individual may prepare unsealed byproduct material for medical use in accordance with the regulations in this chapter under the supervision of an authorized nuclear pharmacist or authorized user as provided in § 35.25, unless prohibited by license condition.

13. In § 35.12, paragraph (e) is added to read as follows:

§ 35.12 Application for license, amendment, or renewal.

* * * * *

(e) An applicant that satisfies the requirements specified in 10 CFR 33.13 may apply for a Type A specific license of broad scope.

14. In § 35.13, paragraph (b) is revised to read as follows:

§ 35.13 License amendments

* * * * *

(b) Before it permits anyone to work as an authorized user or authorized nuclear pharmacist under the license, except an individual who is:

(1) An authorized user certified by the organizations specified in paragraph (a) of §§ 35.910, 35.920, 35.930, 35.940, 35.950, or 35.960;

(2) An authorized nuclear pharmacist certified by the organization specified in paragraph (a) of § 35.980;

(3) Identified as an authorized user or an authorized nuclear pharmacist on a Commission or Agreement State license that authorizes the use of byproduct material in medical use or in the practice of nuclear pharmacy, respectively; or

(4) Identified as an authorized user or an authorized nuclear pharmacist on a permit issued by a Commission or Agreement State specific licensee of broad scope that is authorized to permit the use of byproduct material in medical use or in the practice of nuclear pharmacy, respectively.

* * * * *

15. Section 35.14 is revised to read as follows:

§ 35.14 Notifications.

(a) A licensee shall provide to the Commission a copy of the board certification, the license, or the permit for each individual within 30 days of the date that the licensee permits, pursuant to § 35.13(b)(1) through (b)(4), the individual to work as an authorized user or an authorized nuclear pharmacist.

(b) A licensee shall notify the Commission by letter within 30 days when:

(1) An authorized user, an authorized nuclear pharmacist, Radiation Safety Officer, or teletherapy physicist permanently discontinues performance of duties under the license or has a name change; or

(2) The licensee's mailing address changes.

(c) The licensee shall mail the documents required in this section to the appropriate address identified in § 30.6 of this chapter.

16. Section 35.15 is added to read as follows:

§ 35.15 Exemptions regarding Type A specific licenses of broad scope.

A licensee possessing a Type A specific license of broad scope for medical use is exempt from the following:

(a) The provisions of § 35.13(b);

(b) The provisions of § 35.13(e) regarding additions to or changes in the areas of use only at the addresses specified in the license;

(c) The provisions of § 35.14(a); and

(d) The provisions of § 35.14(b)(1) for an authorized user or an authorized nuclear pharmacist.

17. In § 35.22, paragraph (b)(2) is revised to read as follows:

§ 35.22 Radiation Safety Committee.

* * * * *

(b) * * * * *

(2)(i) Review, on the basis of safety and with regard to the training and experience standards in Subpart J of this part, and approve or disapprove any individual who is to be listed as an authorized user, an authorized nuclear pharmacist, the Radiation Safety Officer, or a teletherapy physicist before submitting a license application or request for amendment or renewal; or

(ii) Review, pursuant to § 35.13(b)(1) through (b)(4), on the basis of the board certification, the license, or the permit identifying an individual, and approve or disapprove any individual prior to allowing that individual to work as an authorized user or authorized nuclear pharmacist;

* * * * *

18. In § 35.25, paragraph (b) is redesignated as paragraph (c) and a new paragraph (b) is added to read as follows.

§ 35.25 Supervision.

* * * * *

(b) A licensee that permits the preparation of byproduct material for medical use by an individual under the supervision of an authorized nuclear pharmacist or physician who is an authorized user, as allowed by § 35.11(c), shall require the supervising authorized nuclear pharmacist or physician who is an authorized user to:

(1) Instruct the supervised individual in the preparation of byproduct material for medical use and the principles of and procedures for radiation safety and in the licensee's written quality management program, as appropriate to that individual's use of byproduct material;

(2) Require the supervised individual to follow the instructions given pursuant to paragraph (b)(1) of this section and to comply with the regulations of this chapter and license conditions; and

(3) Periodically review the work of the supervised individual as it pertains to preparing byproduct material for medical use and the records kept to reflect that work.

* * * * *

§ 35.27 [Removed]

19. Section 35.27 is removed.

20. Section 35.49 is revised to read as follows:

§ 35.49 Suppliers for sealed sources or devices for medical use.

A licensee may use for medical use only:

(a) Sealed sources or devices manufactured, labeled, packaged, and distributed in accordance with a license issued pursuant to 10 CFR Part 30 and 32.74 or the equivalent regulations of an Agreement State; or

(b) Teletherapy sources manufactured or distributed in accordance with a license issued pursuant to 10 CFR Part 30 or the equivalent regulations of an Agreement State.

21. In § 35.50, paragraphs (a), (b)(3), and (e)(2) through (e)(4) are revised to read as follows:

§ 35.50 Possession, use, calibration, and check of dose calibrators.

(a) A licensee shall possess and use a dose calibrator to measure the activity of dosages of photon-emitting radionuclides prior to administration to each patient or human subject.

(b) * * * * *

(3) Test each dose calibrator for linearity upon installation and at least quarterly thereafter over the range of its use between the highest dosage that will be administered to a patient and 1.1 megabecquerels (30 microcuries); and

* * * * *

(e) * * * * *

(2) For paragraph (b)(2) of this section, the model and serial number of the dose calibrator, the model and serial number of each source used, the identity of the radionuclide contained in the source and its activity, the date of the test, the results of the test, and the identity of the individual performing the test.

(3) For paragraph (b)(3) of this section, the model and serial number of the dose calibrator, the calculated activities, the measured activities, the date of the test, and the identity of the individual performing the test.

(4) For paragraph (b)(4) of this section, the model and serial number of the dose calibrator, the configuration of the source measured, the activity measured for each volume measured, the date of the test, and the identity of the individual performing the test.

22. Section 35.52 is added to read as follows:

§ 35.52 Possession, use, calibration, and check of instruments to measure dosages of alpha- or beta-emitting radionuclides.

(a) This section does not apply to unit dosages of alpha- or beta-emitting radionuclides that are obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or equivalent Agreement State requirements.

(b) For other than unit dosages obtained pursuant to paragraph (a) of this section, a licensee shall possess and use instrumentation to measure the radioactivity of alpha- or beta-emitting radionuclides. The licensee shall have procedures for use of the instrumentation. The licensee shall determine, by direct measurement or by combination of measurements and calculations, the

amount of radioactivity in dosages of alpha- or beta-emitting radionuclides prior to administration to each patient or human subject. In addition, the licensee shall:

(1) Perform tests before initial use, periodically, and following repair, on each instrument for accuracy, linearity, and geometry dependence, as appropriate for the use of the instrument; and make adjustments when necessary; and

(2) Check each instrument for constancy and proper operation at the beginning of each day of use.

23. In § 35.53, the section heading and paragraphs (a), (b), and (c)(3) are revised as follows:

§ 35.53 Measurement of dosages of unsealed byproduct material for medical use.

* * * * *

(a) Measure the activity of each dosage of a photon-emitting radionuclide prior to medical use.

(b) Measure, by direct measurement or by combination of measurements and calculations, the activity of each dosage of an alpha- or beta-emitting radionuclide prior to medical use, except for unit dosages obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or equivalent Agreement State requirements;

(c) * * * * *

(3) Prescribed dosage and activity of the dosage at the time of measurement, or a notation that the total activity is less than 1.1 megabecquerels (30 microcuries);

* * * * *

24. Section 35.100 is revised to read as follows:

§ 35.100 Use of unsealed byproduct material for uptake, dilution, and excretion studies.

A licensee may use for uptake, dilution, or excretion studies any unsealed byproduct material prepared for medical use that is either:

(a) Obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or equivalent Agreement State requirements; or

(b) Prepared by an authorized nuclear pharmacist, a physician who is an authorized user and who meets the requirements specified in § 35.920, or an individual under the supervision of either as specified in § 35.25.

25. Section 35.200 is revised to read as follows:

§ 35.200 Use of unsealed byproduct material for imaging and localization studies.

A licensee may use for imaging and localization studies any unsealed byproduct material prepared for medical use that is either:

(a) Obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or equivalent Agreement State requirements; or

(b) Prepared by an authorized nuclear pharmacist, a physician who is an authorized user and who meets the requirements specified in § 35.920, or an individual under the supervision of either as specified in § 35.25.

26. Section 35.300 is revised to read as follows:

§ 35.300 Use of unsealed byproduct material for therapeutic administration.

A licensee may use for therapeutic administration any unsealed byproduct material prepared for medical use that is either:

(a) Obtained from a manufacturer or preparer licensed pursuant to 10 CFR 32.72 or equivalent Agreement State requirements; or

(b) Prepared by an authorized nuclear pharmacist, a physician who is an authorized user and who meets the requirements specified in § 35.920, or an individual under the supervision of either as specified in § 35.25.

27. In § 35.900, paragraphs (a)(6) and (a)(7) are added to read as follows:

* * * * *

(a) * * * * *

* * * * *

(6) American Board of Medical Physics in radiation oncology physics; or

(7) Royal College of Physicians and Surgeons of Canada in Nuclear medicine; or

* * * * *

28. In § 35.910, paragraph (a)(4) is added to read as follows:

§ 35.910 Training for uptake, dilution, and excretion studies.

* * * * *

(a) * * * * *

(4) Nuclear medicine by the Royal College of Physicians and Surgeons of Canada; or

* * * * *

29. In § 35.920, paragraph (a)(4) is added to read as follows:

§ 35.920 Training for imaging and localization studies.

* * * * *

(a) * * * * *

(4) Nuclear medicine by the Royal College of Physicians and Surgeons of Canada; or

* * * * *

30. In § 35.930, paragraph (a)(2) is revised to read as follows:

§ 35.930 Training for therapeutic use of unsealed byproduct material.

* * * * *

(a) * * * * *

(2) The American Board of Radiology in radiology, therapeutic radiology, or radiation oncology; or

* * * * *

31. In § 35.940, paragraph (a)(1) is revised to read as follows:

§ 35.940 Training for use of brachytherapy sources.

* * * * *

(a) * * * * *

(1) Radiology, therapeutic radiology, or radiation oncology by the American Board of Radiology;

* * * * *

32. In § 35.950, paragraph (a)(1) is revised to read as follows:

§ 35.950 Training for use of sealed sources for diagnosis.

* * * * *

(a) * * * * *

(1) Radiology, diagnostic radiology, therapeutic radiology, or radiation oncology by the American Board of Radiology;

* * * * *

(4) Nuclear medicine by the Royal College of Physicians and Surgeons of Canada; or

* * * * *

33. In § 35.960, paragraph (a)(1) is revised to read as follows:

§ 35.960 Training for teletherapy.

* * * * *

(a) * * * * *

(1) Radiology, therapeutic radiology, or radiation oncology by the American Board of Radiology;

* * * * *

34. In § 35.961, paragraph (b) is redesignated as paragraph (c) and a new paragraph (b) is added to read as follows:

§ 35.961 Training for teletherapy physicist.

* * * * *

(b) Is certified by the American Board of Medical Physics in radiation oncology physics; or

* * * * *

35. Section 35.972 is revised to read as follows:

§ 35.972 Recentness of training.

The training and experience specified in this subpart must have been obtained within the seven years preceding the date of application or the individual must have had related continuing education and experience since the required training and experience was completed.

36. Section 35.980 is added to read as follows:

§ 35.980 *Training for an authorized nuclear pharmacist.*

The licensee shall require the authorized nuclear pharmacist to be a pharmacist who:

(a) Has current board certification as a nuclear pharmacist by the Board of Pharmaceutical Specialties, or

(b)(1) Has completed 700 hours in a structured educational program consisting of both:

(i) Didactic training in the following areas:

(A) Radiation physics and instrumentation;

(B) Radiation protection;

(C) Mathematics pertaining to the use and measurement of radioactivity;

(D) Chemistry of byproduct material for medical use; and

(E) Radiation biology; and

(ii) Supervised experience in a nuclear pharmacy involving the following:

(A) Shipping, receiving, and performing related radiation surveys;

(B) Using and performing checks for proper operation of dose calibrators, survey meters, and, if appropriate, instruments used to measure alpha- or beta-emitting radionuclides;

(C) Calculating, assessing, and safely preparing patient dosages;

(D) Using administrative controls to avoid mistakes in the administration of byproduct material;

(E) Using procedures to prevent or minimize contamination and using proper decontamination procedures; and

(2) Has obtained written certification, signed by a preceptor authorized nuclear pharmacist, that the above training has been satisfactorily completed and that the individual has achieved a level of competency sufficient to independently operate a nuclear pharmacy.

Dated at Rockville, Maryland, this _____ day of _____, 1993.

For the Nuclear Regulatory Commission.

_____
Samuel J. Chilk,
Secretary of the Commission.

Enclosure 2

Draft Regulatory Analysis

Draft Regulatory Analysis
For Proposed Rulemaking Entitled
"Preparation, Transfer for Commercial Distribution,
and Use of Byproduct Material for Medical Use"
10 CFR Parts 30, 32, and 35

1. Background

1.1 Statement of the Problem

A petition for rulemaking (PRM-35-9) concerning the medical use of byproduct material was submitted jointly by the American College of Nuclear Physicians (ACNP) and the Society of Nuclear Medicine (SNM). The petition requested that the NRC amend its regulations to fully recognize the role of licensed nuclear pharmacists and physicians. The petition addressed issues related to the preparation and use of radioactive drugs containing byproduct material for diagnostic, therapeutic, or research purposes. In addition, certain portions of the existing regulations in Parts 32 and 35 need to be updated, clarified, or simplified. This proposed rulemaking has been prepared in response to the petition and to provide miscellaneous amendments to update or clarify the existing regulations.

1.2 NRC's Policy Statement on the Medical Use of Radioisotopes

In a policy statement published on February 9, 1979 (44 FR 8242), entitled "Regulation of the Medical Uses of Radioisotopes; Statement of General Policy," the NRC stated:

1. The NRC will continue to regulate the medical uses of radioisotopes as necessary to provide for the radiation safety of workers and the general public.

2. The NRC will regulate the radiation safety of patients where justified by the risk to patients and where voluntary standards, or compliance with these standards, are inadequate.

3. The NRC will minimize intrusion into medical judgments affecting patients and into other areas traditionally considered to be a part of the practice of medicine.

In conformance with this policy, the Commission proposes to eliminate certain restrictions in the NRC regulations regarding the preparation and use of byproduct material for medical use. In addition, the Commission proposes to provide the authority to licensees to conduct research involving human subjects and to use radiolabeled biologics. The Commission believes that these restrictions can be eliminated without compromising the level of protection of public health and safety against radiological hazards. The Commission recognizes that physicians have the primary responsibility for the diagnosis and treatment of their patients and recognizes that the nuclear pharmacists have the primary responsibility for the preparation of radioactive drugs. NRC regulations are predicated on the assumption that properly trained and adequately informed physicians and pharmacists will make decisions that are in the best interest of patients. Furthermore, the pharmacological aspects of radioactive drugs, including drug safety and efficacy, are regulated by the U.S. Food and Drug Administration (FDA).

1.3 Earlier NRC Actions

Following receipt of the petition, the NRC, in consultation with the FDA, determined that some issues of the petition should be addressed promptly. On August 23, 1990 (55 FR 34513), the Commission published an Interim Final Rule to allow, for a period of 3 years, the use of therapeutic radiopharmaceuticals for indications not listed in the package insert and to allow departures from the manufacturer's instructions for preparing diagnostic radiopharmaceuticals using radionuclide generators and reagent kits, provided that certain recordkeeping requirements were met. Based on the records collected from the affected licensees, both the NRC and FDA staff agreed that the major trends in departures that may be identified by the recordkeeping are already discernible and collecting additional data is unnecessary. On October 2, 1992 (57 FR 45566), the NRC published a rule eliminating the recordkeeping requirements.

In a parallel effort, the NRC continued to work on the remaining issues in the petition. On August 7, 1991, the NRC conducted a workshop in Rosemont, Illinois, presenting strawman language on the training and experience criteria for authorized nuclear pharmacists to representatives of the following organizations: Board of Pharmaceutical Specialties, American Board of Science in Nuclear Medicine, National Association of Boards of Pharmacy, Committee on Radionuclides and Radiopharmaceuticals of the U.S. Council for Energy Awareness, American Pharmaceutical Association, American Society of Hospital Pharmacists, and three graduate schools of pharmacy. Subsequently, the NRC also discussed the proposed resolution of these issues in meetings with the FDA, the NRC's Advisory Committee on the Medical Uses of Isotopes (ACMUI), and the Agreement States. This proposed rulemaking is the evolutionary result of numerous meetings with the aforementioned groups.

2. Objectives

The objective of this proposed rulemaking is to grant the petition and to eliminate certain restrictions in NRC's regulations regarding the medical use of byproduct material without compromising the level of protection of public health and safety against radiological hazards.

Specifically, among other things, the proposed rule would incorporate into NRC's regulations the concept of authorized nuclear pharmacists to allow properly qualified pharmacists greater discretion to prepare (including compound) radioactive drugs containing byproduct material. Also, the proposed rule would allow physician authorized users greater discretion to prepare and use radioactive drugs containing byproduct material, the use of byproduct material in research involving human subjects, and the use of radiolabeled biologics containing byproduct material.

In addition, the proposed rule also contains other miscellaneous and conforming amendments necessary to update or clarify the current regulations.

3. ALTERNATIVES

Two alternatives have been considered for the petition: maintain the status quo or grant the petition.

The first alternative would continue to restrict physicians and pharmacists in the medical use of byproduct material. This alternative would continue to require NRC medical use licensees to meet the current prescriptive regulations which restrict the activities of nuclear physicians in the preparation and use of radioactive drugs. In addition, this alternative would continue to restrict the activities of nuclear pharmacists in the preparation of radioactive drugs. Therefore, this alternative was not further considered.

The second alternative, promulgation of a proposed rule to grant the petition, would provide greater flexibility for physician authorized users to use byproduct material in the practice of medicine. The proposed amendments would also incorporate into the regulations the concept of authorized nuclear pharmacists to allow properly qualified pharmacists to prepare (including compound) radioactive drugs containing byproduct material. The Commission believes that granting this petition would eliminate certain restrictions regarding the medical use of byproduct material without compromising the level of protection of public health and safety against radiological hazards.

4. Brief Descriptions of the Proposed Amendments

In response to the petition for rulemaking, the Commission is proposing to:

1. Allow physician authorized users to use therapeutic radioactive drugs containing byproduct material for indications or methods of administration not listed in the FDA-approved package insert;

2. Allow physician authorized users to use radioactive drugs containing byproduct material for research involving human subjects;

3. Allow physician authorized users to use radiolabeled biologics containing byproduct material;

4. Allow medical use licensees and commercial nuclear pharmacies to depart from the manufacturer's instructions for preparing radioactive drugs using radionuclide generators and reagent kits;

5. Allow medical use licensees and commercial nuclear pharmacies to compound radioactive drugs using byproduct material;

6. Delete the existing regulations related to the nonradioactive reagent kits; and

7. Clarify regulatory requirements for specific licenses of broad scope.

Table 1 summarizes the requests made in the petition and the Commission's responses.

In addition to the proposed amendments in response to the issues raised in the petition, the Commission is proposing related or miscellaneous amendments to Parts 32 and 35. In general, the objective of these proposed amendments is to clarify, update, and simplify the current regulations. Specifically, these proposed amendments include:

1. In Part 32, the Commission is proposing to replace the word "radiopharmaceutical" with the term "radioactive drug" in proposed § 32.72. This change is necessary to include both radiopharmaceuticals and radiolabeled biologics in Part 32.

2. In Part 35, whenever applicable, the Commission is proposing to use the term "unsealed byproduct material for medical use" instead of "radiopharmaceutical" or "radioactive drug." This proposed change is intended to indicate that the Commission's regulations regarding the medical use of byproduct material are focused on radiation safety and are separate from FDA's regulations regarding radioactive drugs. However, to prevent massive changes in Part 35, the word "radiopharmaceutical" will continue to be used in the sections for which modifications are not proposed. Thus, the word "radiopharmaceutical" would be equivalent to "unsealed byproduct material for medical use" in the sections that are not modified by this proposed rule.

3. The Commission is proposing to modify the definition of "medical use" in Parts 30 and 35 by using the term "patient," which by its definition would include the administration of byproduct material to human subjects for the purpose of obtaining scientific information (i.e., research). In addition, the Commission proposes to delete the language in the definition of "medical use" that the administration of byproduct material be in the practice of medicine in accordance with a license to practice medicine. The definition of other terms in Part 35 (e.g., physician) include this licensing concept.

Also, the Commission is proposing to add a definition for "patient" in Part 35 to include an individual who is participating in a research procedure as a human subject. With this proposed new definition, applicable

Table 1

Summary of Requests in the Petition and the Commission's Responses

Request	Response
Permit authorized users to use radiopharmaceuticals for therapeutic uses not covered in the package insert.	Permit physician authorized users who are qualified for therapeutic administration greater discretion to use radioactive drugs for therapeutic uses.
Permit authorized users to use radioactive drugs for research involving human subjects.	Permit physician authorized users to use radioactive drugs for research provided that human subjects are protected.
Permit authorized users to use radiolabeled biologics.	Permit physician authorized users greater discretion to use radiolabeled biologics.
Permit medical use licensees and pharmacies to depart from package inserts when using generators and kits.	Permit physician authorized users and authorized nuclear pharmacists who meet certain training and experience criteria greater discretion to use generators and kits.
Permit medical use licensees and pharmacies to use byproduct material to compound radioactive drugs.	Permit physician authorized users and authorized nuclear pharmacists who meet certain training and experience criteria to prepare (including compound) radioactive drugs.
Permit nuclear pharmacists to prepare reagent kits.	Delete NRC regulations on reagent kits which do not contain byproduct material. Thus, nuclear pharmacists would be able to prepare reagent kits under applicable law.
Clarify requirements on licenses of broad scope.	Clarify the requirements by adding two exemptions in Part 35.

requirements in Part 35, such as misadministration reporting and quality management program, would also apply to human subjects; thus, an equivalent level of protection would be provided for both patients and human subjects.

4. In Part 32, the Commission is proposing to clarify the existing regulations regarding the labeling of syringes, vials, generators, or other containers of radioactive drugs. This proposed change is necessary to avoid confusion over the types of information to be submitted.

5. In Part 32, the Commission is proposing to delete the text in 32.72(b) because it is out of date.

6. In discussing the proposed regulations concerning transfer of radioactive drugs, the Commission has noted later in this preamble that it is sometimes necessary to transfer a dosage of a radioactive drug on a case-by-case basis from one medical use licensee to another medical use licensee. These case-specific transfers would not be considered commercial transfers by the NRC and, therefore, would not require a Part 32 license.

7. In Part 35, the Commission is proposing to change the lower limit for testing dose calibrators for linearity from 0.37 Megabecquerel (10 microcuries) to 1.1 Megabecquerels (30 microcuries) for consistency with 10 CFR 35.32, "Quality Management Program."

8. In regard to the accuracy, linearity, and geometry tests of dose calibrators, the Commission is proposing to replace the requirement for the Radiation Safety Officer's (RSO) signature with the requirement for the identity of the individual actually performing these tests. This proposed change is necessary to identify the individual who actually performed these tests. Furthermore, this change would provide additional time for the RSO to devote to other radiation safety issues. However, this change would not affect the responsibilities of the RSO that are defined in existing 10 CFR 35.21.

9. The Commission is proposing to update the regulations by recognizing several certification boards in the training and experience requirements.

10. The Commission is proposing that licensees may allow authorized users and authorized nuclear pharmacists who meet certain requirements to use byproduct material without the licensee first obtaining a license amendment from the NRC. Therefore, the Commission is proposing to delete the provisions in Part 35 addressing visiting authorized users.

11. The Commission is proposing to modify the requirements for recentness of training of certain authorized users.

12. The Commission is proposing to add requirements regarding the preparation of byproduct material for medical use under the supervision of a physician authorized user and to provide comparable requirements regarding the supervisory responsibilities of authorized nuclear pharmacists.

13. The responsibilities of the Radiation Safety Committee would be modified under the proposed rule to reflect the activities which the proposed changes to Part 35 would authorize.

5. ESTIMATION OF COST IMPACT

5.1 GENERAL DISCUSSION

The NRC has about 2,000 medical use licensees (licensed under Part 35) and about 50 licensees who manufacture or prepare radioactive drugs (licensed under Part 32). Agreement States have approximately twice the NRC's licensees mentioned above. It is expected that the requirements proposed in this rulemaking would be a matter of compatibility for the Agreement States: all proposed definitions contained in §§ 30.4 and 35.2 would be Division 1 items of compatibility; proposed sections 32.72, 35.6, 35.22(b)(2), 35.25, 35.50, 35.52, 35.53, 35.920, 35.972 and 35.980 would be Division 2 items of compatibility; and the remaining proposed sections in Part 35 would be Division 3 items of compatibility.

The cost estimates shown below are for affected NRC licensees only. Therefore, the total cost impacts (i.e., for NRC and Agreement State licensees) associated with this proposed rule would be approximately 3 times the cost to the affected NRC licensees.

The cost estimates are based on the following:

o	Fee per license amendment	$460
o	Unit labor costs (unloaded)	
	For licensee staff - Physician*	$85/hour
	- Scientific staff* (e.g. nuclear pharmacists)	$50/hour
	- Technical staff* (e.g. medical technologists)	$30/hour

- Clerical staff	$15/hour
For NRC (and Agreement State) staff*	$50/hour

* Includes prorated amounts for clerical staff.

5.2 IMPACTS TO AFFECTED NRC LICENSEES

Each section of the proposed rule has been evaluated in terms of the cost impact (i.e., increase, decrease, or no change as compared to the cost under existing situations) to affected licensees. In calculating the cost impacts, the cost savings are expressed as positive (+) values and the cost increases as negative (-) values. The cost impact of each proposed section is discussed below except for those sections that obviously have no cost impacts. Table 2 is a summary of the impact to affected licensees for each proposed section.

5.2.1 PART 30 - RULES OF GENERAL APPLICABILITY TO DOMESTIC LICENSING OF BYPRODUCT MATERIAL

§ 30.34 Terms and conditions of licenses.

The proposed amendment would delete paragraph § 30.34(i) in its entirety. Under the existing paragraph, licensees are permitted to depart from FDA-approved package inserts. Under the proposed rule, this permission would be moved to Part 32 for commercial nuclear pharmacies and to Part 35 for medical use licensees. Therefore, there would be no cost impact associated with this proposed amendment.

Table 2

Summary of Impacts to NRC Licensees

Proposed Section No.	No. of Amend, permission, or Record, etc./yr	Hours	$/hr	Fee	Impact/yr Savings: + Costs: -
Part 30					
30.4	No cost (See footnote 1)				
30.34(i)	No cost (See 5.2.1 of this analysis)				
Part 32					
32.72(a)	No cost (See footnote 2)				
32.72(b)	20 license amendments eliminated	4 hours	$50	$460	+ $13,200
	50 license amendments eliminated	2 hours	$50	$460	+ $28,000
	50 notifications required	1/2 hour	$30	----	- $750
32.72(c)	No cost (See 5.2.1 of this analysis)				
32.72(d)	No cost (See footnote 3)				
[32.73]	1 license application eliminated	32 hours	$50	$3,600	+ $5,200
32.74	No cost (See footnote 3)				

Table 2 (Continued)

Summary of Impacts to NRC Licensees

Proposed Section No.	No. of Amend, permission, or Record, etc./yr	Hours	$/hr	Fee	Impact/yr Savings: + Costs: -
Part 35					
35.2	No cost (See footnote 1)				
35.6	2 license amendments required	8 hours	$85	$460	- $2,280
35.7	No cost (See footnote 3)				
35.8	No cost (See footnote 2)				
35.11	No cost (See footnote 3)				
35.12	No cost (See footnote 3)				
35.13	200 license amendments eliminated	2 hours	$50	$460	+ $112,000
	10 license amendments required	2 hours	$50	$460	- $5,600
35.14	220 notifications required	1/2 hour	$30	----	- $3,300
35.15	No cost (See footnote 2)				
35.22(b)(2)	No cost (See footnote 2)				
35.25	No cost (See footnote 2)				
[35.27]	100 records eliminated	1/6 hour	$15	----	+ $250
35.49	No cost (See footnote 4)				

Table 2 (Continued)

Summary of Impacts to NRC Licensees

Proposed Section No.	No. of Amend, permission, or Record, etc./yr	Hours	$/hr	Fee	Impact/yr Savings: + Costs: -
35.50	No cost (See footnote 3)				
35.52	No cost (See 5.2.3 of this analysis)				
35.53	No cost (See footnote 2)				
35.100 to 35.300	20 license amendments eliminated	2 hours	$50	$460	+ $11,200
35.610 to 35.972	No cost (See footnote 2)				
35.980	20 certifications required	1 hour	$50	----	- $1,000
Subtotal				Savings	+ $169,850
				Costs	- $ 12,930
Savings (for NRC licensees)					+ $156,920
Total Savings (for NRC and Agreement State licensees)					+ $470,760

Footnotes:

1. This is a definition, thus no cost impact.

2. This is a clarification or update which would not substantively change the current practice.

3. This is to provide a reminder to licensees, to grandfather an existing situation, or to conform with changes made in other sections or chapters.

4. These requirements or a portion of the existing requirements are moved to other sections.

5.2.2 PART 32 - SPECIFIC DOMESTIC LICENSES TO MANUFACTURE OR TRANSFER CERTAIN ITEMS CONTAINING BYPRODUCT MATERIAL

§ 32.72 Manufacture, preparation, or transfer for commercial distribution of radioactive drugs containing byproduct material for medical use under Part 35.

§ 32.72(b)

(1) Proposed § 32.72(b) would allow commercial nuclear pharmacies to depart from FDA-approved package inserts and to compound radioactive drugs, without obtaining a license amendment from the NRC. Therefore, a cost saving is expected due to the elimination of these license amendments.

Assuming 20 amendments requesting departures or compounding would be eliminated per year and 4 hours of scientific staff's time would be avoided for preparing an application for a license amendment, the cost saving is estimated to be:

20 amend/yr x (4 hrs/amend x $50/hr + $460 fee/amend) = + $13,200/yr.

(2) This proposed paragraph would allow commercial nuclear pharmacies to permit an individual to work as an authorized nuclear pharmacist, without obtaining a license amendment from the NRC, if the individual is: (1) certified by the Board of Pharmaceutical Specialties; (2) listed on a Commission or an Agreement State license; or (3) listed on a permit issued by a specific licensee of broad scope as an authorized nuclear pharmacist. This proposed provision would eliminate a current licensing requirement that requires a licensee to obtain a license amendment from the NRC before permitting an "authorized user" to work.

Assuming 50 amendments requesting to add the names of the "authorized users" would be eliminated per year and 2 hours of scientific staff's time would be avoided for preparing an application for amendment, the cost saving is estimated to be:

50 amend/yr x (2 hr/amend x $50/hr + $460 fee/amend) = + $28,000/yr.

(3) This proposed paragraph would require licensees to provide to the NRC a copy of the individual's board certification, the license, or the permit, and the state pharmacy licensure or registration, respectively, for

each individual within 30 days of the date that the licensee permits, pursuant to this section, the individual to work as an authorized nuclear pharmacist. Therefore, a cost increase is expected due to this proposed notification requirement.

Assuming 50 notifications would be required per year and 1/2 hour of technical staff's time would be needed for preparing a notification, the cost increase is estimated to be:
50 notifications/yr x 1/2 hr/notification x $30/hr = - $750/yr.

§ 32.72(c)

This paragraph is proposed to clarify that Part 32 licensees measure and record dosages of radioactive drugs, including those containing alpha- or beta-emitting radionuclides, before transferring these drugs to a medical use licensee. Currently, these licensees already possess measurement instrumentation, perform the measurements, and record the dosages to provide information required under existing § 32.72(a)(4)(i). Therefore, there would be no cost impact associated with this proposed amendment.

§ 32.73 Manufacture and distribution of generators or reagent kits for preparation of radiopharmaceuticals containing byproduct material.

The section would be deleted in its entirety. This section requires that a licensee shall obtain a specific license from the NRC before the licensee may manufacture or distribute radionuclide generators containing byproduct material or reagent kits. Under the proposed rule, the existing requirements related to radionuclide generators would be moved to the proposed § 32.72. However, the existing requirements related to these reagent kits would be deleted because they do not contain byproduct material. Therefore, a cost saving is expected because the proposed elimination of the application for a license to manufacture or distribute these reagent kits.

The fee for NRC's review of an application to manufacture and distribute a new type of reagent kit is $3,600 per application. Assuming 1 application would be eliminated per year and 32 hours scientific staff's time would be

avoided by the licensee to prepare the application, the cost saving would be:
1 application/yr x (32 hrs/appl x $50/hr + $3,600 fee/appl) = + $5,200/yr.

5.2.3 PART 35 - MEDICAL USE OF BYPRODUCT MATERIAL

§ 35.6 Provisions for research involving human subjects.

This proposed section would allow licensees to conduct research involving human subjects using byproduct material provided that the research is conducted, funded, supported, or regulated by another Federal Agency which has implemented the Federal Policy for the Protection of Human Subjects. Otherwise, a licensee shall apply for and receive approval of a specific amendment to its NRC license before conducting such research. Thus, a cost increase is expected. However, the NRC believes that most human research involving byproduct material is currently conducted, funded, supported, or regulated by another Federal agency.

Assuming 2 license amendments would be needed per year and 8 hours of physician's time would be needed to prepare an application for amendment, the cost increase would be:
2 amend/yr x (8 hr/amend x $85/hr + $460 fee/amend) = - $2,280/yr.

§ 35.13 License amendments

(1) Proposed paragraph (b) of this section would allow medical use licenses to allow an individual to work as an authorized user, without submitting a license amendment to the NRC, if the physician authorized user is: (a) certified by the appropriate certification boards; (b) listed on a Commission or Agreement State license; or (c) listed on a permit of a Commission or Agreement State specific licensee of broad scope. Under current regulations, a license amendment must be obtained before the individual may work as an authorized user (except for a visiting authorized user). Thus, a cost saving is expected due to the elimination of these license amendments.

Assuming 200 license amendments would be eliminated per year and 2 hours of scientific staff's time would be avoided for preparing an application for amendment, the cost saving would be:
200 amend/yr x (2 hr/amend x $50/hr + $460 fee/amend) = + $112,000/yr.

(2) This proposed paragraph would permit medical use licenses to allow an individual to work as an authorized nuclear pharmacist, without submitting a license amendment to the NRC, if the authorized nuclear pharmacist is: (a) certified by the certification board; (b) listed on a Commission or Agreement State license; or (c) listed on a permit of a Commission or Agreement State specific licensee of broad scope.

However, if the individual does not meet the criteria stated above, a license amendment must be obtained by the licensee before the individual can work as an authorized nuclear pharmacist. Thus, a cost increase is expected due to the proposed requirement for these license amendments.

Assuming 10 license amendments would be required per year and 2 hours of scientific staff's time would be needed for preparing an application for amendment, the cost increase would be:
10 amend/yr x (2 hr/amend x $50/hr + $460 fee/amend) = - $5,600/yr

§ 35.14 Notifications.

In addition to the existing notification requirement, the NRC proposes to amend this section to require specific licensees of limited scope to submit a copy of an individual's board certification, the license, or the permit as discussed in § 35.13. Thus, a cost increase is expected.

Assuming 220 notifications would be needed (200 notifications for authorized users and 20 notifications for authorized nuclear pharmacists) and 1/2 hour of technical staff's time would be needed for preparing each notification, the cost increase would be:
220 notification/yr x 1/2 hr/notification x $30/hr = - $3,300/yr.

§ 35.27 Visiting authorized user.

The NRC is proposing to delete this section because, under the proposed rule, the concept of a visiting authorized user would no longer be necessary. Since a recordkeeping requirement in the existing section would also be eliminated, a cost saving is expected.

Assuming 100 records per year would be eliminated and 10 minutes of clerical staff's time would be avoided for each record, the cost saving would be:

100 records/yr x 1/6 hr x $15/hr = + $250/yr.

§ 35.52 Possession, use, calibration, and check of instruments to measure dosages of alpha- or beta-emitting radioactive drugs.

This paragraph is new and would require Part 35 licensees to possess instrumentation to measure the radioactivity of alpha- or beta-emitting radioactive drugs, except for unit doses obtained from manufacturers or commercial nuclear pharmacies. Most alpha- or beta-emitting radionuclides are used in radiolabeled biologics which are still under new drug investigation.

Under current practice, licensees preparing radiolabeled biologics containing alpha- or beta-emitters in their own facilities or purchase qualities of these radiolabeled biologics from manufacturers or commercial nuclear pharmacies other than unit doses already have instrumentations to measure the doses. In addition, licensees who purchase only unit doses would be exempt from this section. Therefore, no cost impact is expected.

§ 35.100 Use of unsealed byproduct material for uptake, dilution, and excretion studies.

§ 35.200 Use of unsealed byproduct material for imaging and localization studies.

§ 35.300 Use of unsealed byproduct material for therapeutic administration.

The proposed amendments in these three sections would allow medical use licensees to compound radioactive drugs using byproduct material without obtaining specific license amendments. Therefore, a cost saving is expected.

Departures from FDA-approved package inserts and manufacturers' instructions are already permitted under the Interim Final Rule.

Assuming 20 amendments per year would be eliminated and 2 hours of scientific staff's time would be avoided to prepare each application, the cost savings would be:

20 amend/yr x (2 hr/amend x $50/hr + $460 fee/amend) = + $11,200/yr.

§ 35.980 Training for an authorized nuclear pharmacist.

This proposed section would require authorized nuclear pharmacists to meet the training and experience criteria. Because the criteria proposed in this section are nearly identical to those in the current licensing guidance, there would be no cost impact to implement this section, with an exception of requiring a written certification from preceptors. Thus, a cost increase is expected.

Assuming 20 certifications would be written per year and 1 hour of scientific staff's time would be needed to complete each certification, the cost increase would be:

20 certification/yr x 1 hr/certification x $50/hr = - $1,000/yr.

Total impacts to affected NRC licensees

The cost impact to affected NRC licensees is estimated to be a saving of $156,920 per year (See Table 2).

5.3 IMPACTS TO AFFECTED AGREEMENT STATES LICENSEES

Since Agreement States have approximately twice the NRC's licensees, the impacts for Agreement State licensees associated with this proposed rule would be approximately twice the impact to the affected NRC licensees. Therefore, the savings for Agreement State licensees would be:

2 x $156,920/yr = + $313,840/yr.

5.4 TOTAL IMPACT TO AFFECTED LICENSEES

The impact to both the NRC licensees and Agreement State licensees would be a savings of
$156,920/yr + $313,840/yr = $470,760/yr.

5.4 COST IMPACT TO NRC

The predominant factor affecting the NRC's operating costs as a result of this proposed action is the decreased number of license amendments which will no longer need to be processed by the NRC. However, this impact is already addressed in the cost impact to the licensees and is included as the change in fees charged to the licensees.

5.5 IMPACT TO AGREEMENT STATES

Since the requirements proposed in this rulemaking would be expected to be a matter of compatibility for the Agreement States, each Agreement State would be required to adopt certain sections of the proposed rule. The impact to the Agreement States would be associated with the adoption of certain sections of the proposed rule into their State regulations.

The impact for each Agreement State may be estimated as follows:

o	Draft a proposed rule	40 hours
o	Review by an Advisory Committee	8 hours
o	Send the proposed rule to NRC for review	4 hours
o	Prepare a final rule	20 hours
	Impact for an Agreement State	72 hours

Since there are 29 Agreement States, the total impact to the Agreement States to incorporate certain sections of the proposed rule is estimated to be:
29 Agreement State x 72 hrs/Agreement State x $50/hr = - $104,400.

6. BENEFITS

This proposed rule would benefit the public by permitting medical use licensees to increase the scope of the applications of radioactive drugs and to increase efficiencies in the preparation and use of radioactive drugs. Specifically, this proposed rule would provide physician authorized users greater flexibility in the medical use of byproduct material. Similarly, the proposed rule would permit qualified nuclear pharmacists to use byproduct material to prepare radioactive drugs. Even though the proposed rule would eliminate certain restrictions related to the medical use of by byproduct material, the NRC believes that additional safeguards against radiological hazards are included in the proposed rule that will continue to ensure adequate protection of public health and safety.

7. DECISION RATIONALE

Based on the above analysis, NRC believes that the proposed rule, if adopted, would provide physician authorized users with greater flexibility to use and would allow authorized nuclear pharmacists to prepare radioactive drugs containing byproduct material. The NRC believes that additional safeguards against radiological hazards are included in the proposed amendments that will continue to ensure adequate protection of public health and safety. Therefore, the NRC is publishing the proposed rule for public comments.

Enclosure 3

Draft Environmental Assessment

DRAFT ENVIRONMENTAL ASSESSMENT FOR PROPOSED AMENDMENTS TO 10 CFR PARTS 30, 32, AND 35, "PREPARATION, TRANSFER FOR COMMERCIAL DISTRIBUTION, AND USE OF BYPRODUCT MATERIAL FOR MEDICAL USE"; FINDING OF NO SIGNIFICANT IMPACT

1. Introduction

The Nuclear Regulatory Commission (NRC) is proposing to amend its regulations for the medical use of byproduct material. This action is necessary to respond to a petition for rulemaking and to fully recognize the role of licensed nuclear pharmacists and physicians. The petition for rulemaking (PRM-35-9) was submitted by the American College of Nuclear Physicians and the Society of Nuclear Medicine. The proposed rule is intended to provide greater flexibility for authorized user physicians to prepare and use radioactive drugs containing byproduct material. The proposed rule would also incorporate into the regulation the concept of authorized nuclear pharmacists to allow properly qualified pharmacists greater discretion to prepare radioactive drugs containing byproduct material.

The major features of the proposed amendments include: (1) allowing medical use licensees to depart from the U.S. Food and Drug Administration (FDA) approved package insert instructions regarding the preparation and use of radioactive drugs; (2) creating the concept of an "authorized nuclear pharmacist" and specifying training and experience requirements; (3) allowing authorized nuclear pharmacists and physician authorized users to use byproduct material to prepare radioactive drugs; (4) allowing the use of byproduct material in research involving human subjects; and (5) allowing the use of radiolabeled biologics.

2. Need for the Amendment: Rejection of the No Action Alternative

The proposed amendments have been developed to grant the petition for rulemaking. The Commission recognizes that physicians have the primary responsibility for the diagnosis and treatment of their patients, and recognizes that the nuclear pharmacists have the primary responsibility for the preparation of radioactive drugs. The Commission's regulations are

predicated on the assumption that properly trained and adequately informed physicians and pharmacists will make decisions that are in the best interest of patients. Furthermore, the pharmacological aspects of radioactive drugs, including drug safety and efficacy, are regulated by the FDA. Therefore, the proposed amendments would allow physician authorized users greater discretion in the medical use of byproduct material, and allow authorized user physicians and authorized nuclear pharmacists greater discretion to prepare radioactive drugs containing byproduct material.

This no-action alternative is not favored because the Commission's regulations are more restrictive than FDA and State pharmacy regulations. Moreover, the current regulatory philosophy of linking NRC regulations (e.g., 10 CFR 35.200) to FDA approval of package inserts to ensure the radiation safety of radioactive drugs does not allow NRC licensees sufficient flexibility to use or prepare radioactive drugs. The Commission believes that greater flexibility can be provided while continuing adequate protection of public health and safety.

3. Impact on the Public and the Environment

The proposed amendments would have no significant impact on the public and the environment. The additional research activities allowed by the proposed amendments are expected to be small in comparison to the current total activities involving radioactive drugs containing byproduct material. Therefore, the proposed amendments would not cause a significant increase in the total activity. Furthermore, allowing compounding could reduce radiation exposures to workers. For example, allowing the use of specific additives could decrease the volatility of certain radioactive drugs, thus, reducing the concentration of radionuclides in air. In other cases, exposures may increase if a licensee markedly increases the amount of compounding, however, such a scenario is extremely unlikely and the workers are protected under the provisions contained in 10 CFR Part 20. Therefore, it is expected that there would be no increase in radiation exposure to the public, health care workers, or the environment, beyond the exposures currently resulting from the preparation and administration of radioactive drugs containing byproduct

material. Thus, there would be no discernible impact on the public or the environment resulting from the proposed amendments.

4. List of Agencies and Persons Consulted and Identification of Sources Used

The NRC held public meetings concerning the preparation and use of radioactive drugs containing byproduct material. Appropriate suggestions from the meetings have been incorporated in the proposed amendments. The following table lists the date, location, and the groups represented at each meeting.

Public Meetings Held

Date	Location	Groups Represented
08/07/91	Rosemont, IL	Board of Pharmaceutical Specialties American Board of Science in Nuclear Medicine National Association of Boards of Pharmacy Committee on Radionuclides and Radiopharmaceuticals of the U.S. Council for Energy Awareness American Pharmaceutical Association American Society of Hospital Pharmacists Purdue University-School of Pharmacy and Pharmacal Sciences University of New Mexico-College of Pharmacy University of Pittsburgh-School of Pharmacy
07/15/92 07/16/92	Atlanta, GA	Agreement States: AL, AR, AZ, CA, CO, FL, GA, IL, KS, KY, LA, MD, NC, ND, NE, NH, NV, NY (including NY city), OR, SC, TX, UT, WA.
11/07/91 05/08/92 10/23/92	Reston, VA Reston, VA Rockville, MD	Advisory Committee on the Medical Uses of Isotopes

5. Finding of No Significant Impact

The Commission has determined under the National Environmental Policy Act of 1969, as amended, and the Commission's regulations in Subpart A of 10 CFR Part 51, that the proposed amendments, if adopted, would not be a major Federal action significantly affecting the quality of the human environment, and therefore an environmental impact statement is not required. The proposed amendments would relax certain requirements and eliminate specific restrictions associated with the medical use of byproduct material. The Commission believes these proposed amendments would provide greater flexibility in the medical use of byproduct material while continuing to adequately protect public health and safety. It is expected that this proposed rule, if adopted, would not cause any significant increase in radiation exposure to the public or radiation release to the environment beyond the exposures or releases currently resulting from the medical use of byproduct material.

Enclosure 4

Congressional Letters

Identical letters to:
Philip R. Sharp
cc: Michael Bilirakis
Bob Graham
cc: Alan K. Simpson

The Honorable Richard H. Lehman, Chairman
Subcommittee on Energy and Mineral Resources
Committee on Natural Resources
United States House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

In the near future the Nuclear Regulatory Commission (NRC) intends to publish in the Federal Register the enclosed proposed rule. This proposed rule would amend the NRC's regulations in 10 CFR Parts 30, 32, and 35 to eliminate certain restrictions regarding the medical use of byproduct material without compromising the level of protection of public health and safety against radiological hazards.

Specifically, among other things, the proposed rule would incorporate into NRC's regulations the concept of authorized nuclear pharmacists to allow properly qualified pharmacists greater discretion to prepare radioactive drugs containing byproduct material. Also, the proposed rule would allow physician authorized users greater discretion to prepare and use radioactive drugs containing byproduct material, the use of byproduct material in research involving human subjects, and the use of radiolabeled biologics containing byproduct material.

The Commission believes that the proposed rule, if adopted, would result in a small cost reduction for medical use licensees.

Sincerely,

Dennis K. Rathbun, Director
Office of Congressional Affairs

Enclosure:
Federal Register Notice

cc: Representative Barbara Vucanovich

Enclosure 5

Public Announcement

NRC PROPOSES CHANGES TO INCREASE FLEXIBILITY IN MEDICAL USES OF NUCLEAR MATERIAL

The Nuclear Regulatory Commission is considering changing its regulations for the medical use of nuclear material to provide greater flexibility for authorized user physicians and qualified pharmacists.

The proposed changes are responsive to a petition for rulemaking submitted to the NRC by the American College of Nuclear Physicians and the Society of Nuclear Medicine. Notice of receipt of the petition and opportunity for public comment was published in the Federal Register on September 15, 1989.

The Commission has already addressed some issues raised in the ACNP-SNM petition by publishing, on August 23, 1990, an interim rule that allows, for a period of three years, specific departures from the package inserts under the direction of a physician authorized user.

Previously, NRC regulations restricted medical use licensees to using or preparing certain radioactive drugs in accordance with the Food and Drug Administration (FDA) approved package inserts, although FDA generally does not require physicians or pharmacists to follow these inserts.

In addition, current NRC regulations do not specifically allow medical use licensees to use byproduct material in research involving human subjects, in radiolabeled biologics (blood and other body materials to which radioactive material has been added) and in preparing radioactive drugs.

In response to the petition, the Commission is proposing to amend its regulations to

(1) Allow departures from FDA-approved package inserts regarding the preparation and use of radioactive drugs by deleting the remaining restrictions of the interim rule published on August 23, 1990;

(2) Include the concept of an "authorized nuclear pharmacist" and specify training and experience requirements;

(3) Allow physician authorized users and authorized nuclear pharmacists to use byproduct material to prepare radioactive drugs;

(4) Allow the use of byproduct material in research involving human subjects; and

(5) Allow the use of radiolabeled biologics containing byproduct material.

The proposed changes also include miscellaneous changes to clarify, update and simplify the current regulations, such as accepting certification in nuclear medicine by the Royal College of Physicians and Surgeons of Canada.

The Commission does not believe that these proposed changes will result in any significant increase in radiation exposure to the public or the environment beyond the exposures currently resulting from medical uses of nuclear material.

Interested persons are invited to submit written comments on the proposed regulations by _____(120 day following publication in the Federal Register on (date). The

comments should be addressed to the Secretary of the Commission, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Attention: Docketing and Service Branch.

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