September 20, 1979

SECY-79-542

For: The Commissioners

From: Robert B. Minogue, Director
Office of Standards Development

Thru: Executive Director for Operations

Subject: THERAPEUTIC TREATMENT OF CARDIAC DYSFUNCTION BY IODINE-131

Purpose: To obtain Commission approval of a Federal Register Notice of NRC's intent to retain the therapeutic treatment of cardiac dysfunction in the regulations.

Category: This paper covers a minor policy question.

Issue: Should NRC continue to allow physicians to use iodine-131 for the therapeutic treatment of cardiac dysfunction since the Food and Drug Administration has reclassified this treatment as lacking substantial evidence of effectiveness?

Alternatives:

1. Delete the therapeutic treatment of cardiac dysfunction by iodine-131 from NRC regulations.

2. Publish for public comment in the Federal Register NRC's intent to retain the therapeutic treatment of cardiac dysfunction in NRC regulations (a minor exception to the Medical Policy Statement).

3. Change the Medical Policy Statement's handling of the therapeutic uses of radionuclides to allow for exceptions as regards FDA approv

Discussion:

Background

NRC's Medical Policy Statement specifies regulatory policy for restricting the uses of therapeutic radioactive drugs to the clinical procedures that have been approved by the Food and Drug Administration. In 1976, FDA reclassified the therapeutic treatment of cardiac dysfunction by iodine-131 as lacking substantial evidence of effectiveness.

Contact:
Deborah A. Bozik, SD
443-5860

Enclosure 1

The Problem

In order to be consistent with the Medical Policy Statement, NRC should delete the therapeutic treatment of cardiac dysfunction from §35.100(d)(1) of 10 CFR Part 35, since FDA has removed this treatment from its list of approved procedures. However, NRC's Advisory Committee on the Medical Use of Isotopes, the American College of Cardiology and several physicians have indicated that this treatment should not be removed from NRC regulations since this would be detrimental to the health of some patients.

Facts Bearing on the Problem

a. Iodine-131 for use in the treatment of patients with cardiac dysfunction was introduced approximately thirty years ago. The treatment employs iodine-131, in the form of sodium-iodide, as a therapeutic agent for management of euthyroid heart diseases such as angina pectoris and congestive heart failure.

b. FDA has on record clinical studies which document safety when iodine-131 is used to treat cardiac dysfunction. While the application of iodine-131 to the thyroid during the therapeutic treatment of cardiac dysfunction does damage the thyroid, the net effect on patients has been demonstrated through clinical tests to be beneficial and no major adverse side effects have been identified.

c. In 1971, the FDA classified the treatment of cardiac dysfunction with iodine-131 as possibly effective and invited persons to submit any data in support of this possibly effective indication.

d. Since no clinical data were submitted in support of the possibly effective indication, in 1976 the FDA reclassified the treatment of cardiac dysfunction as lacking substantial evidence of effectiveness. (However, lack of evidence of effectiveness does not constitute evidence of ineffectiveness.)

e. FDA's action, which removed cardiac dysfunction from the official labeling, by itself, does not prevent physicians from using iodine-131 for the therapeutic treatment of cardiac dysfunction. Indeed, we are aware of several physicians who still claim that there is adequate evidence for using the drug for this purpose, although it is neither on the package insert nor on the official labeling. (The physician can determine that the benefit-risk of using a particular drug in a particular patient is justified.)

f. Other alternatives to the use of iodine-131, principally nonradioactive drug therapy, are currently available and used much more often for treatment of cardiac dysfunction.

g. Iodine-131 has been and still is used for treatment of hyperthyroidism, and the reclassification by FDA did not significantly affect manufacturers which still have a market for iodine-131.

Therefore, there was little incentive to perform clinical trials to show FDA the effectiveness of iodine-131 for treatment of cardiac dysfunction.

h. Since 1951, the FDA has recorded three adverse reactions to the use of iodine-131 in the therapeutic treatment of cardiac dysfunction. Two of these reactions were classified as possibly drug related and the third was classified as remotely drug related.

i. For whatever reasons, including lack of monetary resources, individual physicians who wished to continue using iodine-131 to treat cardiac dysfunction did not conduct clinical experiments and thus prove effectiveness to FDA.

j. NRC currently authorizes the use of iodine-131 for treatment of hyperthyroidism and cardiac dysfunction in Group IV[1] of §35.100(d)(of 10 CFR Part 35. However, if NRC removes the authorization, then iodine-131 could not be used by any physician for the therapeutic treatment of cardiac dysfunction.

k. When the Medical Policy Statement was written, the staff looked to prospective FDA approval rather than retrospective denial, that is, it thought of NRC adding to its regulations new treatments already approved by FDA rather than deleting already allowed treatments. This is the first time NRC has had to consider deleting a therapeutic procedure that has been removed from an approved list by FDA.

l. We believe that this is a unique situation and do not anticipate any future administrative removal actions by FDA.

The proposed action will not require any additional Commission resources. The alternatives are evaluated as follows:

Alternative 1: Delete the therapeutic treatment of cardiac dysfunction by iodine-131 from NRC regulations.

Pro: a. Consistent with NRC Medical Policy Statement; and,

b. Nonradioactive drug treatment is now most often used for cardiac dysfunction.

Con: a. Deletion of this therapeutic procedure would remove this option from the physician's use in those cases where other treatments may not be effective; and,

[1]Group IV refers to the use of prepared radiopharmaceuticals for certain therapeutic uses that do not normally require hospitalization for purposes of radiation safety.

b. Deletion of this therapeutic use could possibly jeopardize some patients; and,

c. FDA's action was based on lack of evidence of effectiveness (not evidence of ineffectiveness or patient safety considerations).

Alternative 2: Publish for public comment in the Federal Register NRC's intent to retain the therapeutic treatment of cardiac dysfunction in the regulations (a minor exception to the Medical Policy Statement).

Pro: a. FDA's action was based on lack of evidence of effectiveness (not evidence of ineffectiveness or patient safety considerations); and

b. The possibility exists that individual physicians lacked the monetary resources to conduct clinical trials to show substantial evidence of effectiveness; and,

c. This would retain for physicians the option to use iodine-131 for cardiac dysfunction.

Con: a. Inconsistent with that part of the Medical Policy Statement which says that NRC will authorize only those therapeutic procedures approved by FDA; and,

b. NRC would be approving the use of a radioisotope for patient therapy which has no established finding of efficacy.

Alternative 3: Change the Medical Policy Statement's treatment of the therapeutic uses of radionuclides to allow for exceptions as regards FDA approval.

Pro: a. The Medical Policy Statement was intended to deal with the addition of drug uses approved by FDA and does not specifically cover the separate problem of deletion of procedures reclassified by FDA; and,

b. FDA's action in removing this use of iodine-131 was administrative. It was not based on any adverse evidence.

Con: a. NRC would be approving the use of a radioisotope for patient therapy which has no established finding of efficacy; and,

b. We believe that this is a unique situation; therefore, the effort to change the Medical Policy Statement may be unnecess

Recommendation: That the Commission: Approve Alternative 2 (Publish for public comment in the Federal Register NRC's intent to retain the therapeutic treatment of cardiac dysfunction in the regulations as a minor exception to the Medical Policy Statement). A Federal Register Notice detailing this is provided as an enclosure.

Since the Federal Register Notice is only stating that the therapeutic treatment of cardiac dysfunction by iodine-131 is being retained in §35.100(d)(1) of 10 CFR Part 35, the Congressional Committees are not being informed of this Commission action.

Coordination: This has been concurred in by the Office of Nuclear Material Safety and Safeguards and the Division of Rules and Records. The Office of the Executive Legal Director has no legal objection. OGC recommended deletion of treatment of cardiac dysfunction by Iodine-131 from NRC regulations; OPE's comments on safety have been incorporated in the paper (see Enclosure 2 for responses to OGC/OPE comments).

Robert B Minogue SEP 20 1979

Robert B. Minogue, Director
Office of Standards Development

Enclosures:
1. Federal Register Notice
2. Response to OGC/OPE Comments

NOTE: Commissioners' comments or consent should be provided directly to the Office of the Secretary by c.o.b. Thursday, October 4, 1979.

Commission Staff Office comments, if any, should be submitted to the Commissioners NLT September 28, 1979, with an information copy to the Office of the Secretary. If the paper is of such a nature that it requires additional time for analytical review and comment, the Commissioners and the Secretariat should be apprised of when comments may be expected.

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NUCLEAR REGULATORY COMMISSION

THERAPEUTIC TREATMENT OF CARDIAC DYSFUNCTION BY IODINE-131

AGENCY: U.S. Nuclear Regulatory Commission.

ACTION: NRC intent to retain the treatment of cardiac dysfunction by iodine-131 as an accepted therapeutic procedure.

SUMMARY: The Nuclear Regulatory Commission is issuing this notice of intent to retain in its regulations the treatment of cardiac dysfunction by iodine-131 as an accepted therapeutic procedure. In 1976, this procedure was reclassified by the Food and Drug Administration as lacking substantial evidence of effectiveness. NRC has generally restricted the uses of therapeutic radioactive drugs to procedures that FDA has approved. However, NRC's Advisory Committee on the Medical Use of Isotopes, the American College of Cardiology and several physicians have recommended that this treatment should not be removed from NRC regulations since this would be detrimental to the health of some patients.

DATES: Comment period expires _____.*

ADDRESSES: Interested persons are invited to submit written comments and suggestions on this notice to the Secretary of the Commission, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, Attention: Docketing and Service Branch. Copies of comments received by the Commission may be examined at the Commission's Public Document Room at 1717 H Street, NW., Washington, D.C.

*Insert date 60 days from publication in the FEDERAL REGISTER.

FOR FURTHER INFORMATION CONTACT: Deborah A. Bozik, Office of Standards Development, U.S. Nuclear Regulatory Commission, Washington, DC 20555 (phone 301-443-5860).

SUPPLEMENTARY INFORMATION: Iodine-131 in the form of sodium-iodide is used as a therapeutic agent in the treatment of euthyroid heart diseases such as angina pectoris and congestive heart failure. This treatment of cardiac dysfunction with iodine-131 was introduced approximately thirty years ago. FDA has on record clinical studies which document safety when iodine-131 is used to treat cardiac dysfunction. While the application of iodine-131 to the thyroid during the therapeutic treatment of cardiac dysfunction does damage the thyroid, the net effect on patients has been demonstrated through clinical tests to be beneficial and no major adverse side effects have been identified. In 1971, the Food and Drug Administration classified the therapeutic treatment of cardiac dysfunction with iodine-131 as possibly effective. Since no person submitted any clinical data to support the possibly effective indication, in 1976, the FDA reclassified the treatment of cardiac dysfunction as lacking substantial evidence of effectiveness (41 FR 38800). Other alternatives, principally non-radioactive drug therapy, have largely replaced iodine-131 for the treatment of cardiac dysfunction.

Although FDA's action is based on lack of evidence of effectiveness, this should not be taken as a definite conclusion that the treatment of cardiac dysfunction with iodine-131 is ineffective.

Since 1951, the FDA has recorded three adverse reactions to the use of iodine-131 in the therapeutic treatment of cardiac dysfunction. Two of these reactions were classified as possibly drug related and the third was classified as remotely drug related.

On February 9, 1979, NRC published a final Medical Policy Statement, 44 FR 8242, which included a policy of restricting therapeutic radioactive drugs to the procedures which have been approved by the FDA. However, NRC's Advisory Committee on the Medical Use of Isotopes, the American College of Cardiology and several physicians have indicated that the therapeutic treatment of cardiac dysfunction by iodine-131 should not be removed from NRC regulations since this would be detrimental to the health of some patients.

Group IV of §35.100 of 10 CFR Part 35 is a list of prepared radiopharmaceuticals for therapy which does not normally require hospitalization for radiation safety. Iodine-131 for the treatment of cardiac dysfunction is listed in Group IV of §35.100. Since deletion of this therapeutic procedure would remove an option for the physician in cases where other treatments may not be effective, NRC has decided to retain the therapeutic treatment of cardiac dysfunction by iodine-131 in Group IV of §35.100.

(Secs. 81, 161, Pub. Law 83-703, 68 Stat. 935, 948 (42 U.S.C. 2111, 2201); Sec. 201, Pub. Law 93-438, 88 Stat. 1242 (42 U.S.C. 5841)).

Dated at _____ this _____ day of _____ 198_.

For the Nuclear Regulatory Commission.

_____
Samuel J. Chilk
Secretary of the Commission

Office of General Counsel and Office of Policy Evaluation Comments

I. Office of the General Counsel

A. Comments: OGC stated the following:

(1) If the therapeutic treatment of cardiac dysfunction by iodine-131 is important to the few doctors who use it and threatened to sue NRC if it is removed, then these doctors should have expressed this to FDA when it was soliciting comments.

(2) Such comments from a small segment of the medical community do not seem to provide a strong basis for departing from NRC's general policy of deferring to FDA on matters within its sphere of influence.

(3) The question of whether NRC would conform to its own Medical Policy Statement and delete this procedure makes this issue additionally significant.

OGC recommended that the staff paper be redrafted to propose deletion of the therapeutic treatment of cardiac dysfunction by iodine-131 from NRC regulations.

B. Response: We have the following responses to OGC's comments:

(1) Iodine-131 has been and still is used for treatment of hyperthyroidism, and the reclassification by FDA did not significantly affect the drug manufacturers which still have a market for iodine-131. There was little incentive for the manufacturers to perform the clinical trials which are needed to show FDA the evidence of effectiveness of iodine-131 for treating cardiac dysfunction. In addition, NRC's Advisory Committee

on the Medical Use of Isotopes, the American College of Cardiology and several physicians have indicated that this treatment should not be removed from NRC regulations since this would be detrimental to the health of some patients.

(2) FDA's action of removing cardiac dysfunction from the official labeling, by itself, does not prevent physicians from using iodine-131 for the therapeutic treatment of cardiac dysfunction. Indeed, we are aware of several physicians who still claim that there is adequate evidence for using the drug for this purpose, although it is neither on the package insert nor on the official labeling. (The physician can determine that the benefit-risk of using a particular drug in a particular patient is justified.)

(3) When the Medical Policy Statement was written, the staff looked to prospective FDA approval rather than retrospective denial. That is, it thought of NRC adding to its regulations new treatments already approved by FDA rather than deleting already allowed treatments. This is the first time NRC has had to consider deleting a therapeutic procedure that has been removed from an approved list by FDA. We believe that this is a unique situation and do not anticipate any future administrative removal actions by FDA.

Therefore, NMSS and SD believe that the use of iodine-131 for the treatment of cardiac dysfunction should not be removed from NRC's regulations.

II. Office of Policy Evaluation

A. Comment: Discussions with OPE revealed their concern that the paper should indicate somewhere a position on safety to show that NRC would be approving the use of a radioisotope for patient therapy which has an established finding of safety even though there is lack of substantial evidence of effectiveness.

B. Response: OPE's suggestion is responded to by including an indication of safety both in the Commission paper (page 2, Part b.) and in the Federal Register Notice. While the application of iodine-131 to the thyroid during the therapeutic treatment of cardiac dysfunction does damage the thyroid, the net effect on patients has been demonstrated through clinical tests to be beneficial and no major adverse side effects have been identified.

ENCLOSURE 2

PP 129-136 - EXCERPT FROM MINUTES

OF ACMUI 8/18/80 MEETING

the board, you should still put down the number of cases. This would answer the problem about the intracavitary use of phosphates for instance. You might have the American Board of Nuclear Medicine having never seen a chromic phosphate patient done. I don't think you should just be able to go out and do one of these until you have at least been in on three of them as is required.

MR. CUNNINGHAM: Any other comments? If not, we will move to the next agenda item. I think the Staff has some guidance on this one.

I want to bring up again the issue of treatment of cardiac dysfunction. Very briefly, you may recall that the FDA request about the use of iodine for cardiac dysfunction has lacked substantial evidence of the effectiveness. This use has been in existence for years. The basis for the lack of evidence is that no manufacturer has come forward with the information normally required in an IND to establish effectiveness, and the reason, as nearly as we can ascertain, that the industry hasn't stepped forward to do this is that there is very little demand for iodine for the treatment of cardiac dysfunction.

This has been reviewed when the issue came up whether or not the NRC should continue to permit its use in light of the FDA position on this matter. It was reviewed at least twice by the Medical Advisory Committee with everybody agreeing that its use was very small, but there are some

occasions for its possible use, and that the physician managing the patient should at least have the option of using this, if he chooses.

This position was brought up to our Commission again in a Staff paper, and they have asked the Staff to obtain from the Advisory Committee a formal recommendation about the use of iodine-131 for the treatment of cardiac dysfunction, and to include in that recommendation our basis for the recommendation.

Now in order to accomplish this objective, I believe that there are possibly three positions that we might take. The first is to delete the treatment from the licensing.

The second is to retain the treatment as it now stands, or to retain the treatment, but limit its use to some statement about limiting its use to appropriate cases.

Bill, do you want to expand on this before we try to reach some consensus of whether it should be in or out? And if it's in, the conditions under which it is in, and the basis for it.

DR. WALKER: Not really.

(Laughter.)

MR. CUNNINGHAM: Okay, you have answered my question.

DR. WALKER: I think it is pretty straightforward, as most of the committee members have already discussed this, and I think most of them have pretty set opinions on it.

MR. CUNNINGHAM: All right, then, I will call for

members of the committee to give an opinion, and this is one that we do need some opinion put forward on with regard to this.

Dr. Holman?

DR. HOLMAN: I preface my statement by certainly realizing that iodine-131 is treatment for cardiac dysfunction disease is rarely used at the present time; but on the other hand, that the issue does raise certain questions of precedence. And in that regard I found Commissioner Kennedy's memorandum to be a highly succinct and to very effectively reflect my position on the matter, which is that in fact, as opposed to the FDA dropping a particular pharmaceutical from a specific application, in which case the pharmaceutical can still be applied by a physician at his discretion, if the benefit-risk ratio is sufficient to justify it, in the case where the NRC drops a particular radiopharmaceutical from a specific procedure, this is no longer the case. It is now illegal to use that radiopharmaceutical for an application unless the individual applies for an IND.

On that basis I feel quite strongly that the NRC should take a position of option No. 2, which would allow the physician the prerogative to use iodine-131 for cardiac dysfunction if the physician feels that this is the most effective treatment for that patient.

MR. CUNNINGHAM: Dr. Holman, you are basing your reason for keeping it up on the difference between the way NRC

and FDA laws would work?

DR. HOLMAN: Precisely.

MR. CUNNINGHAM: And that you feel that the physician should have the option of access to this treatment, if he chose it, without specifying the conditions under which he would use it?

DR. HOLMAN: Exactly.

MR. CUNNINGHAM: Do any other members of the committee want to make comments on this?

Dr. Webster?

DR. WEBSTER: Well, I'm not sure I'm really the person to speak to this, but I did read very carefully the three options which were placed before the committee, and Dr. Holman seems to have elected option 2.

On the other hand, option 3 would allow the same thing, but in a more cautious way, and my preference was option 3, which says to retain the use of iodine-131 for therapeutic treatment of cardiac dysfunction in group IV, but limit the treatment in cases in which it is the preferred method of therapy, and in which the potential benefits to the patient far exceed the risk.

That's a little bit more enclosed, restricted than option 2, which is sort ofwide open. It says retain the use of iodine for therapeutic treatment, period.

I'd like to hear some further discussion on this.

MR. CUNNINGHAM: Dr. DeNardo?

DR. DE NARDO: Well, there is nothing wrong with

that statement, except I hope that it is true of everything we do, and I don't think -- you know, it seems somewhat icing on the cake to make that comment, in that the therapy you are giving has less risk than what you are giving it for.

It seems like a comment that should be present on everything, if we need to put it on.

Also I might just comment on No. 3, as well, in cases where nonradioactive drug therapy is not effective, I don't believe a suitable claim to impose upon the practice of medicine. There are some people who believe that nonradioactive drug therapy may be indeed more dangerous to many patients than radioactive iodine-131 therapy.

MR. CUNNINGHAM: Any other discussion on this point? If not, I will try to summarize the position of the committee to see if we have a consensus on it.

The first point is that use of iodine-131 for treatment of cardiac dysfunction has been in existence for a number of years.

The second point is that its use is very limited today, but nevertheless some physicians will want to use this in certain circumstances.

Number three, the committee feels that physicians should have the option of using this if they feel it is in the interest of the patient, for patient care.

Number four, under the FDA rules, particularly those rules under which they withdrew the drug as an effective drug,

a physician still has the option of using this in patient manageme
without violation of FDA rules. If the NRC were to take a similar action, it would in fact remove the option of the physician to use this as he chose, because he would either have to have a special license amendment, which would be difficult to obtain for the patient he has to treat immediately; or he would have to file an IND for the FDA rules which, of course, we recognize again all this happens too late to treat the patient, when such a need is indicated.

I might add one point to this, that is that the committee in general believes that the use of iodine-131 for treatment of cardiac dysfunction is safe and that there may be instances where its use might indeed benefit the patient better than alternative uses.

That is where I'm coming out. Do we have some consensu
from the committee on a statement like that, to go back to the Commission? Any discussion on this?

Capt. Briner.

CAPT. BRINER: I think there is one other thing that has not been addressed and that is the overall feeling, I think, in nuclear medicine that wherever possible, so long as safety is not impaired, there should not be any dichotomy in the regulations, in the Food & Drug Administration and those of the Nuclear Regulatory Commission.

That is to say, they should not be in opposition to

each other. In this case, where safety is not really an issue, that the issue exists, it may be an issue of effectiveness.

I could certainly support Dr. Holman's opinion, that when a physician decides that in a specific patient it would be beneficial, I think that right ought to exist for the physician, without the filing of an IND or an exemption.

MR. CUNNINGHAM: Any other comments? I see nods of agreement.

Dr. Goodrich?

DR. GOODRICH: I would just ask under alternative 2, what is the intent or what is the need for publishing this for public comment in the Federal Register?

MR. CUNNINGHAM: I don't know the exact status of the rulemaking, but -- do you know the answer to that, Bill?

DR. WALKER: I think this probably is because this probably infringes a little bit on the medical policy statement and therefore we would have to say that we are making an exception in this case.

MR. CUNNINGHAM: I think if you go back to our medical policy statement, a number of those things we have included in that statement was the fact that we were not going to examine on safety and efficacy, provided there was an effective IND from FDA. They don't have an NDA for this, so we are really going in the face of our policy statement. So we need to publish something, and that's why the Commission needs this

statement.

Are there any other comments on it? If not, we will use a statement something along the lines that I summarized as representing the consensus of this committee, and I see nods as I look up and down the line here.

If that is satisfactory, we will move on to the next subject.

The next subject that I want to cover, very briefly, is the work we are doing to amend our regulations to provide some relief in disposal of waste generated in medical and biomedical research.

By way of background on this, when waste disposal groun started to close down, there was a squeeze affecting mainly biomedical research on storage capacity, and there was some question whether or not this was leading to curtailment of research work.

In examining the problem, we find that about 50 percent by volume of wastes generated in biomedical work that goes to burial grounds is either the scintillation fluids used in scintillation counting, mainly toluene, slightly contaminated with tritium, carbon-14, a few other things used to a lesser extent, and animal wastes, animal carcasses. Again, slightly contaminated with tritium or carbon-14, in the main.

We researched this some and have found that the radioactivity in scintillation fluids and in animals would amount

[7590-01]

NUCLEAR REGULATORY COMMISSION

10 CFR Part 35

Therapeutic Treatment of Cardiac
Dysfunction by Iodine-131

AGENCY: Nuclear Regulatory Commission.

ACTION: Notice of intention to retain existing regulation.

SUMMARY: The Nuclear Regulatory Commission is issuing this notice of intent to retain in its regulations the treatment of cardiac dysfunction by iodine-131 as an accepted therapeutic procedure. In 1976, this procedure was reclassified by the Food and Drug Administration (FDA) as lacking substantial evidence of effectiveness. However, NRC's Advisory Committee on the Medical Use of Isotopes, the American College of Cardiology and several physicians have recommended that this treatment should not be removed from NRC regulations since this would be detrimental to the health of some patients.

DATES: Comment period expires (60 days from date of publication).

ADDRESSES: Interested persons are invited to submit written comments and suggestions on this notice to the Secretary of the Commission, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, Attention: Docketing and Service Branch. Copies of comments received by the Commission may be examined at the Commission's Public Document Room at 1717 H Street, NW., Washington, D.C.

FOR FURTHER INFORMATION CONTACT: Deborah A. Bozik, Office of Standards Development, U.S. Nuclear Regulatory Commission, Washington, DC 20555 (Phone 301-443-5860).

SUPPLEMENTARY INFORMATION: Section 35.100(d)(1) of 10 CFR Part 35, "Human Uses of Byproduct Material," permits the use of iodine-131 as therapeutic treatment for cardiac dysfunction. This notice sets out the reasons for the Commission's decision to retain this regulation. Iodine-131 in the form of sodium-iodide is used as a therapeutic agent in the treatment of euthyroid heart diseases such as angina pectoris and congestive heart failure. This treatment of cardiac dysfunction with iodine-131 was introduced approximately thirty years ago. FDA has on record clinical studies which document safety when iodine-131 is used to treat cardiac dysfunction. While the application of iodine-131 to the thyroid during the therapeutic treatment of cardiac dysfunction does damage the thyroid, the net effect on patients has been demonstrated through clinical tests to be beneficial and no major adverse side effects have been identified. In 1971, the Food and Drug Administration classified the therapeutic treatment of cardiac dysfunction with iodine-131 as possibly effective. Since no person submitted any clinical data to support the possibly effective indication, the FDA reclassified the treatment of cardiac dysfunction as lacking substantial evidence of effectiveness in 1976 (41 FR 38800). Other alternatives, principally non-radioactive drug therapy, have largely replaced iodine-131 for the treatment of cardiac dysfunction.

Although FDA's action was based on lack of evidence of effectiveness, this should not be taken as a definite conclusion that the treatment of cardiac dysfunction with iodine-131 is ineffective.

Since 1951, the FDA has recorded three adverse reactions to the use of iodine-131 in the therapeutic treatment of cardiac dysfunction. Two of these reactions were classified as possibly drug related, and the third was classified as remotely drug related.

On February 9, 1979, NRC published a final Medical Policy Statement, 44 FR 8242, which stated in part that "NRC will continue to restrict the uses of therapeutic and certain diagnostic radioactive drugs to the indicated procedures that have been approved by FDA." However, FDA's basic regulatory policy does not infringe on the physician's medical treatment prerogatives. NRC's Medical Policy Statement establishes that, in the best interest of the patient, a proper balance and flexibility should exist between the exercise of governmental regulatory authority in the nuclear medicine area and the practice of medicine by physicians. The Policy Statement conveys this idea as follows:

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

- "The Commission recognizes that physicians have the primary responsibility for the protection of their patients. The Commission believes that basic decisions concerning the diagnosis and treatment of disease are a part of the physician-patient relationship and are traditionally considered to be a part of the practice of medicine. NRC regulations are predicated on the assumption that properly trained and adequately informed physicians will make decisions in the best interest of their patients."

Both the American College of Cardiology and several physicians have indicated that the therapeutic treatment of cardiac dysfunction by iodine-131 should not be removed from NRC regulations since this would be detrimental to the health of some patients. In accord with this indication, at its most recent meeting on August 18, 1980, NRC's Advisory Committee on the Medical Uses of Radioisotopes recommended that cardiac dysfunction therapy with iodine-131 should be unconditionally retained in the regulations.

The Commission has concluded that NRC should unconditionally retain in § 35.100(d)(1) of 10 CFR the use of iodine-131 for the therapeutic treatment of cardiac dysfunction. The Commission believes that this decision is in consonance with the expressed intent of the Medical Policy Statement which was formulated to encompass a proper balance and flexibility so that the best interests of patients would not be compromised. The Commission believes that this position exemplifies and accentuates the balance which was built into the Medical Policy Statement.

Comments, suggestions, or recommendations concerning this action by the Commission are invited from all interested persons.

(Secs. 81, 161, Pub. Law 83-703, 68 Stat. 935, 948 (42 U.S.C. 2111, 2201); Sec. 201, Pub. Law 93-438, 88 Stat. 1242 (42 U.S.C. 5841)).

Dated at _____ this _____day of _____1981.

For the Nuclear Regulatory Commission.

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Samuel J. Chilk
Secretary of the Commission