February 7, 1997 SECY-97-031

TO: The Commissioners

FROM: Hugh L. Thompson, Jr. /s/
Acting Executive Director for Operations

SUBJECT: FINAL RULEMAKING PLAN: EXEMPT DISTRIBUTION AND USE OF A RADIOACTIVE DRUG CONTAINING ONE MICROCURIE OF CARBON 14 UREA (PARTS 30 AND 32)

PURPOSE:

To inform the Commission of the staff's rulemaking plan for amending Parts 30 and 32 to allow the distribution of a radioactive drug containing one microcurie of ^{14}C-urea as an exempt material for "in vivo" diagnostic testing.

BACKGROUND:

On October 6, 1994, the Commission docketed a petition for rulemaking (Docket No. PRM-35-12) from Tri-Med Specialties, Inc. (Tri-Med). In a letter dated August 23, 1994, Tri-Med petitioned the NRC to amend its regulations "to allow for the general licensing and/or exemption for the commercial distribution by licensed pharmaceutical manufacturers of a capsule containing one micro-Curie (µCi) of ^{14}C-urea for in vivo diagnostic testing." The purpose of this diagnostic test is to detect the presence of the bacterium Helicobacter pylori (H.pylori), a cause of peptic ulcers.

The petition for rulemaking was noticed for comment in the Federal Register on Decemeber 2, 1994. A total of 315 comment letters were received. There were 313 letters supporting the petition (mostly form letters) and 2 letters opposing the petition.

DISCUSSION:

CONTACT:
Sam Jones, RES
415-6198

In accordance with the SRM-COMSECY-96-035 dated June 11, 1996, a copy of the draft rulemaking plan, recommending a general license approach, was provided to the Agreement States for review and comment. The comment period closed on October 31, 1996. Ten comment letters were received from Agreement States. Six States agreed with the staff's initial position to grant the petition by making the ^{14}C-urea capsules available to any physician under a general license. However, three States - Georgia, Illinois, and New York - while agreeing that the petition should be granted, opposed the staff's recommendation and argued that the capsules should be made available as exempt material. One State, Oregon, stated that it would continue to require that any person who administers a radioactive drug be specifically licensed.

In addition, there were some comments related to the process of Agreement State involvement in NRC rulemaking that the staff believes were addressed in SECY-96-035, and, therefore, are not addressed in the memorandum to the Commission or in the final rulemaking plan.

After considering Agreement States' comments, the staff has changed its recommendation. We now recommend that manufacturers and distributors be permitted to distribute this radioactive drug as exempt material to "any person" who is permitted to receive and use the drug under the appropriate Federal or State law governing the distribution and use of the drug.

AGREEMENT STATE COMMENTS ON DRAFT RULEMAKING PLAN:

In accordance with Management Directive 6.3, "The Rulemaking Process," the staff drafted a rulemaking plan in response to a petition for rulemaking submitted by Tri-Med Specialties, Inc. Under the draft plan, the staff would have developed a direct final rule amending 10 CFR Part 35 to permit, under a general license, any physician to administer to patients

capsules containing one microcurie of C-14 as a diagnostic tool for detecting peptic ulcers caused by the Helicobacter pylori bacterium.

In accordance with COMSECY-96-035 dated June 11, 1996, a copy of the draft rulemaking plan was provided to the Agreement States on October 1, 1996, for a 30-day period of review and comment. Comments were received from ten Agreement States.

Six States (Kentucky, Nebraska, Colorado, Washington, Utah, and Louisiana) supported the staff's initial position to grant the petition via a general license to permit physicians who are not authorized users to receive and use capsules containing 1 µCi of ^{14}C-urea. Kentucky indicated they already have provisions for a general license for "in vivo" use in their regulations.

One State, Oregon indicated that it would not permit administration of the capsules under a general license, but would continue to require that all physicians who administer radioactive drugs, including the C-14 capsules, be specifically licensed.

Three States, New York, Georgia and Illinois, opposed the general license approach recommended by the staff. Georgia and Illinois recommended that physicians who are not "authorized users" be permitted to receive and use capsules containing 1 µCi of ^{14}C - urea as exempt material. Georgia argued that their burden would be increased by distribution and use under a general license because of reports required from distributors, invoicing of physicians for general license fees, and possible amendment of all of their distribution licenses. Illinois stated that distribution of the capsules as exempt material is consistent with the NRC's technical evaluation and would ensure that physicians could have access to the capsules without a specific or general license. Illinois further stated that if the NRC were to require distribution and administration under a general license, Agreement States would need to incur the expense of modifying their regulations. Illinois seems to imply that they could avoid rulemaking if the NRC were to adopt the exemption approach. However, as Georgia correctly observed, the exemption approach would require States to make conforming changes in their regulations as well. New York stated that they agreed that the widespread medical use of the capsules would involve no risk to the public health and safety or the environment, and would provide significant medical benefits to the population. New York also stated that using a risk-based regulatory approach, there is no need to regulate the capsules for their radioactive content. Further, New York argued that a general license is an ineffective means of regulatory control in any case. New York also noted that the Food and Drug Administration will regulate the capsules as a drug.

There were further comments from the States addressing the process of Agreement State involvement in NRC rulemaking that the staff believes were addressed in SECY 96-035, and therefore are not addressed here. Copies of the comment letters are enclosed.

STAFF RESPONSE:

The staff initially recommended distribution of the capsules under a general license because if the capsules were to be distributed as an exempt material, manufacturers and distributors located in Agreement States would be required to obtain and maintain both an NRC and Agreement State license. Since the staff had concluded that there was no significant radiological safety or environmental risk, it did not intend that the general license would be used as a means of exercising regulatory control beyond limiting distribution to physicians. However, in light of the

comments received from New York, Illinois, and Georgia, the staff changed its position from permitting distribution to any physician under a general license to permitting exempt distribution to any physician. After further consideration, the staff decided that manufacturers and distributors should be permitted to distribute this radioactive drug as exempt material to any person who is permitted to receive and use the drug under the appropriate Federal or State law governing the distribution and use of the drug. Permitting exempt distribution to "any person," rather than "any physician," would avoid the need for NRC to amend its regulations if other Federal or State authorities permit the distribution and use of the radioactive drug to persons who are not physicians. Moreover, the drug will be manufactured under a specific Part 32 license to ensure that capsules contain only one microcurie of carbon 14 and do not contain any other radioactive contaminants.

POLICY ISSUES:

NRC regulations specify that persons administering radioactive drugs containing byproduct material to patients or human research subjects must have specific authorization. Also, there are no provisions in NRC regulations for the "in vivo" use of byproduct material as an exempt material. However, in light of the above, the staff is recommending the distribution of the capsules as exempt material to any person.

In addition, the Commission should note that current regulations (§ 35.6) addressing the use of byproduct material in research require licensees to meet specific provisions for the protection of human subjects. Under the staff's recommendation, the exempt distribution of the capsules for use in research involving humans subjects would not be authorized.

The Commission also should note that all of the options in the draft rulemaking plan given to the Agreement States for review in June, 1996, explicitly limited the use of the drug to physicians. Hence, the position of the Agreement States on the staff's recommendation in this final rule plan to not limit the use to physicians only, but rely on FDA and State Boards of Pharmacy regulations for determining use, is not known.

AGREEMENT STATE COMPATIBILITY:

Under the Atomic Energy Act, certain regulatory functions are reserved to the NRC. Among these are the distribution of exempt materials and quantities, as discussed in 10 CFR Part 150. Hence, the staff's recommended approach is a Division 4 matter of compatibility, with regard to the manufacture and distribution of the capsules (Part 32), and a Division 1 matter of compatibility with regard to possession and use (Part 30). All Agreement States will need to adopt regulations to allow any person to receive capsules containing 1 µCi of ^{14}C-urea as an exempt material.

The Commission should note that under the staff's initial recommendation, Oregon (and possibly other States, since not all States commented) could have continued its current practice of requiring physicians administering radioactive drugs to humans to be specifically licensed, because the general license amendments would have been a Division 3 matter of compatibility.

COORDINATION:

The Office of the General Counsel has reviewed this paper and has no legal objection. The Office of the Chief Financial Officer concurs that there will be no resource impacts beyond those currently budgeted. The Office of the Chief Information Officer concurs that there will be no information technology or management impacts beyond those needed for rulemaking.

RECOMMENDATION:

Unless the Commission directs otherwise within 10 days from the date of this paper, I will implement the rulemaking plan and direct the staff to begin development of a proposed rule to permit the distribution of the radioactive drug as an exempt material for distribution to any person.

Hugh L. Thompson, Jr.
Acting Executive Director
for Operations

Enclosures:
1. Final Rulemaking Plan
2. Agreement State Comment Letters

RULEMAKING PLAN FOR

EXEMPT DISTRIBUTION AND USE OF A RADIOACTIVE DRUG CONTAINING ONE MICROCURIE OF CARBON 14 UREA (PARTS 30 AND 32)

Lead Office: Office of Nuclear Regulatory Research

Staff Contact: S. Jones, RES/RPHEB

Concurrences:

SIGNED 8/13/96
D. Morrison, RES Date

SIGNED 9/19/96
C. Paperiello, NMSS Date

SIGNED 9/20/96
R. Bangart, OSP Date

(memo from Stuart Treby) 9/20/96
W. Olmstead, OCG Date

(memo from David Meyer) 8/20/96
D. Meyer, ADM Date

Approval: _____
H. L. Thompson, AEDO Date

Rulemaking Plan

[Title of Rulemaking]

Regulatory Issue

[Define the regulatory problem or issue to be resolved.]

Existing Regulatory Framework

[List any existing regulatory requirements and describe how they would be affected.]

How the Regulatory Problem Will be Addressed By Rulemaking

[Describe a preliminary concept of actions that are needed to resolve the problem.]

- Discuss Consistency of Proposed Approach with Other NRC Regulations

Assessment of Likely Impacts on Licensees

[Describe any burdens that may be placed on licensees.]

Assessment of Cost Effectiveness

[Provide the basis for believing that the rulemaking will be cost-effective.]

OGC Legal Analysis

[Provide OGC's analysis of legal sufficiency, demonstrating no known basis exists for a legal objective.]

Agreement State Implementation Problems

[Indicate whether any known Agreement State problems exist.]

Supporting Documents

[Identify any supporting documents.]

Resources Needed

- __ FTEs
- Contractor support dollars

[Identify resources required to complete and implement the rulemaking.]

Lead Office Staff and Staff From Supporting Offices

- Project Manager:
- User office cognizant staff:
- OGC cognizant staff:

[Identify the lead office staff and staff participating offices, including the office representatives and an alternate who will be included in the rulemaking process.]

Steering Group/Working Group

[Identify members of a steering group or working group, if appropriate.]

Enhanced Public Participation

[Consider whether enhanced public participation should be employed in the rulemaking process and describe measures to be employed.]

EDO or Commission Issuance

[Indicate whether the office recommends EDO issuance or Commission action.]

Schedule

- Proposed rule published:
- Final rule published:

[Include schedules for preparing supporting information and completing the proposal and comment process.]

FINAL RULEMAKING PLAN
10 CFR PARTS 30 AND 32

EXEMPT DISTRIBUTION OF A RADIOACTIVE DRUG
CONTAINING ONE MICROCURIE OF CARBON 14 UREA
(PRM-35-12)

BACKGROUND

On October 6, 1994, the Commission docketed a petition for rulemaking (Docket No. PRM-35-12) from Tri-Med Specialties, Inc (Tri-Med). In a letter dated August 23, 1994, Tri-Med petitioned the NRC to amend its regulations "to allow for the general licensing and/or exemption for the commercial distribution by licensed pharmaceutical manufacturers of a capsule containing one micro-Curie (µCi) of ^{14}C-urea for in vivo diagnostic testing." The purpose of this diagnostic test is to detect the presence of the bacterium Helicobacter pylori (H. pylori), a cause of peptic ulcers.

"Peptic ulcer disease is a chronic inflammatory condition of the stomach and duodenum that affects as many as 10% of people in the United States at some time in their lives. The disease has relatively low mortality, but it results in substantial human suffering and high economic costs." (Source: Article included as an appendix to the petition, from JAMA, July 6, 1994-Vol 272, No. 1, "H. pylori in Peptic Ulcer Disease-NIH Consensus Conference").

In the petition dated August 23, 1994, the petitioner stated the following:

> Recent medical research has found that peptic ulcers are commonly caused by a bacterium called H. pylori. This bacterium lives in the stomach of most ulcer sufferers. By treating ulcer patients with antibiotics, doctors can now cure most ulcer problems.
>
> It is therefore necessary to detect the presence of H. pylori bacteria in ulcer patients so that the new treatment can be given appropriately. In the past, this was done by a gastroenterologist who took biopsy samples of the stomach lining at endoscopy, a procedure which was uncomfortable and expensive ($1000).
>
> With the new test, H. pylori can be detected non-invasively using a ^{14}C-urea tracer. ^{14}C-urea is broken down by H. pylori to form labeled CO_2 which is expired in the breath. To do the test, a doctor asks the patient to swallow the capsule with 30 mls of water. After 15 minutes the patient blows 2 liters of breath into a collection bag (a Mylar balloon) which is mailed to a testing laboratory. If ^{14}C-CO_2 more than twice background is present in the breath sample, then the patient must be infected with H. pylori.

CURRENT REGULATIONS

10 CFR Part 32, "Specific Domestic Licenses To Manufacture or Transfer Certain Items Containing Byproduct Materials," § 32.72, "Manufacture, preparation, or transfer for commercial distribution of radioactive drugs containing byproduct material for medical use under Part 35," provides for commercial distribution of radioactive drugs containing byproduct material for use by persons authorized pursuant to Part 35. Thus, the regulations currently would permit Part 32

licensees to commercially distribute capsules containing 1 µCi of ^{14}C-urea to persons authorized pursuant to Part 35.

10 CFR Part 35, "Medical Use of Byproduct Material," sets forth radiation safety requirements, including requirements for the training and experience of authorized user physicians to assure the safe possession and use of radioactive drugs containing byproduct material.

Existing exemptions for use of byproduct material in § 30.14, "Exempt concentrations" and § 32.18, "Manufacture, distribution and transfer of exempt quantities of byproduct material: Requirements for license," do not permit the exempt transfer of byproduct material contained in any food, beverage, cosmetic, drug, or any product designed for ingestion or inhalation by, or application to, a human being.

REGULATORY ISSUE

The regulatory issue is whether the ^{14}C-urea capsules present a sufficiently small radiation risk that they can be safely distributed to and used by physicians who are not “authorized users” under 10 CFR Part 35.

SAFETY ANALYSIS

Based on a safety analysis conducted by an NRC contractor, the staff has concluded that the human use of these capsules results in insignificant exposures as depicted below:

Scenario	**Maximum Exposed Individual**	**Routine Exposure**
Worker administering ^{14}C-urea breath tests	Full-time worker, 8,000 patients/yr	Less than 0.7 mrem/yr
Routine exposure of patients from ^{14}C-urea breath tests	Patient tests negative	0.38 mrem/capsule
	Patient tests positive	0.18 mrem/capsule
Release of 150 µCi of $^{14}C0_2$ into administration area	Member of public in the administration area	Less than 0.0002 mrem
Rupture of a capsule causing skin contamination of worker or patient	Skin (100 cm^2) exposed for one hour prior to washing	5.8 mrad skin dose 0.075 µCi skin absorption 0.029 mrem CEDE

Pathways to the Environment

Based on an environmental report prepared by an NRC contractor, the staff concluded that the impacts associated with any releases of ^{14}C to the surrounding environment are expected to be very small and the expected risks are minimal.

The earth's atmosphere contains an inventory of naturally occurring ^{14}C of about 3.8 million curies (equivalent to the activity in 3.8 trillion breath tests), which is in addition to the huge inventory of about 240 million curies in the world's oceans. The ^{14}C released into the atmosphere from the use of this test would mix with the global inventory and expose the public and other biotic components of the environment to ^{14}C intakes from inhalation, drinking water, and all possible food pathways in the same manner as naturally occurring ^{14}C. The current world inventory of naturally occurring ^{14}C results in an average dose to the public of about 1.25 mrem/year, and the release of 0.6 curies of ^{14}C from the total of 600,000 tests assumed to be administered annually (see the REGULATORY ANALYSIS section below) would result in an additional average annual dose of 2×10^{-7} mrem. This is far below the EPA reporting level of 1 mrem/year required under the Clean Air Act for routine exposures to a member of the public, or the 4 mrem/year EPA limit for public drinking water. In a total population of about 260 million people in the U.S., the collective annual dose from the breath tests would be about 0.051 person-rem. In addition, the doses from normal use of breath tests, or from any accidental release of ^{14}C to the environment also are expected to be very small because the concentration of CO_2 released is very low and it would mix immediately with the atmosphere.

Collective Exposures to Members of the Public

The small doses from naturally occurring ^{14}C are of little significance to human health and the environment. Potential long-term impacts from widespread releases of the long-lived ^{14}C (5,730-year radiological half-life) from breath tests were concluded to be insignificant. Assuming that the testing in the U.S. would increase over a period of time to an average of a million tests per year for 50 years, the collective annual dose to the U.S. population would be about 5 person-rem over the next 50 years. This dose is very small when compared to the annual collective dose to the U.S. population from naturally occurring ^{14}C of over 300,000 person-rem, and about 78,000,000 person-rem from all naturally occurring radiation. Clearly, an increase of a few person-rem will not significantly change these exposures, and thus there is no expected impact from the widespread use of the breath test on the entire U.S. population.

COMMENTS FROM THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES (ACMUI)

This petition was discussed with the ACMUI at the October 1995 meeting. The ACMUI indicated that it endorsed the wide availability of this diagnostic test and that the radioactive drug could be used under a general license or an exemption, whichever the NRC thought to be procedurally easier.

COMMENTS FROM THE PUBLIC

The "Notice of receipt of petition for rulemaking" was published for public comment in the Federal Register on December 2, 1994 (59 FR 61831). A total of 315 public comment letters, 313 supporting (mostly form letters) and 2 opposing letters, were received.

The two letters opposing the petition made the following two comments:

(1) The product should not receive an exempt status because the uncontrolled distribution and application of this product could lead to significant risk to the public, and

(2) Medical uses should be restricted to short-lived isotopes because of disposal problems presented by long-lived isotopes.

The staff disagrees with both comments.

(1) As shown in the "SAFETY ANALYSIS" section of this plan, the radiation dose to workers, patients, and the public is very low.

(2) As discussed in the "Pathways to the Environment" section of this plan, the impacts associated with any releases of ^{14}C to the surrounding environment are expected to be very small and the expected risks are minimal. Also, as discussed in the "Collective Exposures to Members of the Public" section of this plan, the small doses from naturally occurring ^{14}C are of little significance to human health and the environment. Potential long-term impacts from widespread releases of the long-lived ^{14}C (5,730-year radiological half-life) from breath tests were concluded to be insignificant.

DRAFT RULEMAKING PLAN

In accordance with Management Directive 6.3, “The Rulemaking Process,” the staff drafted a rulemaking plan in response to a petition for rulemaking submitted by Tri-Med Specialties, Inc. Three alternatives were considered in the draft rulemaking plan:

Alternative 1 - Deny the petition.

Alternative 2 - Grant the petition via an exemption to permit physicians who are not "authorized users" to receive and use capsules containing 1 µCi of ^{14}C-urea.

Alternative 3 - Grant the petition via a general license to permit physicians who are not "authorized users" to receive and use capsules containing 1 µCi of ^{14}C-urea

Under the draft plan, the staff would have developed a direct final rule amending 10 CFR Part 35 to permit, under a general license, any physician to administer to patients capsules containing one microcurie of C-14 as a diagnostic tool for detecting peptic ulcers caused by the Helicobacter pylori bacterium (Alternative 3).

Distribution of byproduct material as exempt material requires an NRC license, even in an Agreement State. Hence, manufacturers and distributors licensed by Agreement States would

need to obtain and maintain both NRC and Agreement State licenses to distribute the ^{14}C capsules as exempt material. This is not the case for byproduct material to be possessed and used under a general license. The staff viewed this potential dual licensing as an unnecessary burden with no safety benefit. Therefore, the staff did not recommend distribution to and use as exempt material in the draft rulemaking plan. In terms of public health and safety, either Alternative 2 or 3 could be adopted because the radiological risk is negligible.

In accordance with COMSECY-96-035 dated June 11, 1996, a copy of the draft rulemaking plan was provided to the Agreement States on October 1, 1996, for a 30-day period of review and comment. Comments were received from ten Agreement States.

AGREEMENT STATE COMMENTS ON DRAFT RULEMAKING PLAN

Six States (Kentucky, Nebraska, Colorado, Washington, Utah, and Louisiana) supported the staff's recommended approach (i.e., grant the petition, and permit physicians who are not authorized users to receive and use capsules containing 1 µCi of ^{14}C-urea via a general license). Kentucky indicated they already have provisions for a general license for "in vivo" use in their regulations.

One State, Oregon indicated that it would not permit administration of the capsules under a general license, but would continue to require that all physicians who administer radioactive drugs, including the ^{14}C-urea capsules, be specifically licensed.

Three States, New York, Georgia and Illinois, opposed the general license approach recommended by the staff. Georgia and Illinois recommended that physicians who are not "authorized users" be permitted to receive and use capsules containing 1 µCi of ^{14}C - urea as exempt material. Georgia argued that their burden would be increased by distribution and use under a general license because of reports required from distributors, invoicing of physicians for general license fees, and possible amendment of all of their distribution licenses. Illinois stated that distribution of the capsules as exempt material is consistent with the NRC's technical evaluation and would ensure that physicians could have access to the capsules without a specific or general license. Illinois further stated that if the NRC were to require distribution and administration under a general license, Agreement States would need to incur the expense of modifying their regulations. Illinois seems to imply that they could avoid rulemaking if the NRC were to adopt the exemption approach. However, as Georgia correctly observed, the exemption approach would require States to make conforming changes in their regulations as well. New York stated that they agreed that the widespread medical use of the capsules would involve no risk to the public health and safety or the environment, and would provide significant medical benefits to the population. New York also stated that using a risk-based regulatory approach, there is no need to regulate the capsules for their radioactive content. Further, New York argued that a general license is an ineffective means of regulatory control in any case. New York also noted that the Food and Drug Administration will regulate the capsules as a drug.

RECOMMENDED APPROACH

The staff has determined that the radiological risk of this drug presents such a small radiation hazard that the capsules can be treated without regard to their radioactivity. Hence, no control of the capsules is necessary for radiation safety after they are manufactured and distributed. In light of this, and in light of the comments from Illinois, and Georgia, the staff has decided not to recommend distribution and use of the ^{14}C-urea capsules under a general license. Rather, the staff is now recommending that Part 30 be amended to permit the ^{14}C-urea capsules to be distributed to and used by any person, without need of an NRC (or Agreement State) license, who is permitted to receive and use the drug under an appropriate Federal or State law governing the distribution and use of the drug. Thus regulation of receipt and use of the drug will be left to other Federal and State agencies with the responsibility and authority to regulate drugs (as is the case for other drugs that do not contain byproduct materials). The staff believes that permitting exempt receipt of the capsules by "any person who is permitted to receive and use the drug under an appropriate Federal or State law," rather than limiting receipt and use to physicians only will provide any controls needed for regulation of the capsules as a drug, and avoid the need for NRC to amend its regulations if other Federal or State agencies permit under their authority the distribution and use the radioactive drug to persons who are not physicians.

The staff believes that NRC should require the drug to be manufactured under a specific Part 32 license to ensure that capsules contain only one microcurie of carbon-14 and do not contain any other radioactive contaminants. Hence, conforming amendments would be made to Part 32 to provide requirements for a specific license to manufacture, process, produce, package, repackage, or transfer capsules containing one microcurie of ^{14}C-urea, as a radioactive drug, to be distributed as an exempt material to any person for "in vivo" diagnostic testing. Licensees distributing the radioactive drug as an exempt material would not be relieved from other applicable Federal (e.g., FDA) or State drug manufacturing and distribution requirements.

PRELIMINARY REGULATORY ANALYSIS

In the letter dated August 23, 1994, the petitioner stated,

> If exempted, the C-14 breath test could be done by most doctors for less than $100 cost to the patient. This is a considerable savings over endoscopy and biopsy ($1000).

In a letter on November 30, 1994, the petitioner stated:

> ... The test is 95% accurate and quite inexpensive because of its simplicity. The test would permit doctors to determine easily whether or not ulcer patients have been cured of their infection. By providing the public with an inexpensive, easily accessible diagnostic test, more individuals would be accurately diagnosed and treated for their H. pylori infection. This would save the United States an estimated $500 million per annum over conventional therapy.

Tri-Med estimates annual benefits to be on the order of $500 million/year. This assumes approximately 600,000 ^{14}C-urea breath tests/year, at an average cost of $100, in lieu of performing endoscopy at an average cost of $1000/test. It assumes that the lower cost and greater availability of an unregulated breath test would result in a complete substitution for endoscopy. Tri-Med's benefit analysis provides a measure of the total benefits associated with the test and does not focus on the incremental benefits of administering the test pursuant to 10 CFR 35.100 regulation (status quo) versus releasing the test to all physicians (NRC licensed and non licensed alike). Implicit in Tri-Med's estimated annual benefits is the presumption that none of these ^{14}C tests and corresponding savings would accrue if the petition were denied. In reality, under the status quo, the test would be available and administered by physicians or clinics holding a license under NRC's Part 35. Further, Tri-Med's estimate did not allow for the substitution of other non-invasive tests (e.g., serological test for IgG antibodies to H. pylori antigens) for both endoscopy and ^{14}C-urea tests. In addition, wire service articles dated September 19, 1996, stated that the FDA has approved a non-radiological diagnostic breath test using ^{13}C for detecting the presence of H. pylori infections.

The staff's benefit analysis focuses on the incremental benefits of granting relief based on the petition. The analysis looks solely at changes relative to the base case or status quo. In this analysis, the comparison is between regulated and unregulated ^{14}C-urea breath tests, not unregulated ^{14}C-urea breath tests and endoscopies or other non-invasive tests. For the purposes of this regulatory analysis, the staff assumes that the same number of breath tests (i.e., 600,000 tests) will be administered regardless of the level of NRC regulatory control. This view is predicated on the belief that each physician's primary motivation is to provide the best possible care to his or her patients. If the breath test is judged preferable to endoscopy, or other procedure, any physician not authorized to use the test will refer his or her patient to authorized users who could perform the test under existing NRC regulations. This appears fully consistent with standard medical practice, whereby patients are referred routinely to laboratories and specialists for a wide array of tests and procedures.

In the NRC's analysis, the benefits of adopting the petition accrue as a result of reduced patient cost and reduced health care cost resulting from the elimination of the need for referrals from a physician who is not an authorized user (e.g., gastrointestinal specialist). There would also be

some regulatory savings because the NRC would not have to expend resources reviewing new applications for specific medical use licenses. However, the NRC savings would be small because the staff expects that few physicians who are not authorized users would apply for a specific NRC license for use of this one product.

The staff's benefit calculation is based on the assumption that a significant portion of the 600,000 patients would receive the ^{14}C breath test from physicians who are not authorized users (e.g., gastrointestinal specialists) instead of authorized users (e.g., nuclear medicine specialists). The actual savings would be dependent on the number of tests ultimately administered by physicians who are not authorized users, thereby eliminating the need for a referral.

The annual savings could be as high as approximately $20 million if there was a complete shift of the administration of the tests from physicians who are authorized users (i.e., base case) to physicians who are not authorized users.
The basis for this estimate is as follows.

Assuming adoption of the petition eliminates the need for 600,000 referrals, patient savings in averted travel expenses (transportation and personal time incurred with medical referral) would be:

> Assuming round trip of 20 miles @ $0.25/mile, and personal time of 0.5/hours/trip valued at $25.00/hour
>
> 600,000 trips/year x (20 miles/trip x $0.25/mile + 0.5 hours/trip x $25.00/hour) = $10.5 million/year

Health Care Savings in averted administrative expenses (administrative costs incurred with medical referral) would be:

> 600,000 patients/year x $19.00/patient = $11.4 million/year
>
> Assuming $19.00 (administrative cost/patient) as the differential between the cost of an office visit to a general family practice physician by an established patient ($45.90), and the cost to a new patient ($64.90 per visit) for completion of new patient paperwork, reviewing health history, maintaining medical records, etc. The patient who is referred to an authorized user (e.g., nuclear medicine specialist) for the ^{14}C-urea breath test would most likely be a new patient for the authorized user.

Total Savings:

> $10.5 million/year + $11.4 million/year = $ 21.9 million/year

Alternatively, if only 200,000 or 400,000 of the 600,000 tests were performed by a physician who is not an authorized user, the annual cost savings would be approximately $7 million/year and $15 million/year, respectively.

COMPARISON OF ALTERNATIVES

Alternative 1 - Deny the Petition

This alternative would maintain the status quo. Only physicians who are authorized users under Part 35 would be allowed to possess and administer the ^{14}C-urea test. Any physician could apply to become an authorized user. However, the NRC expects few physicians would apply for a Part 35 license for the sole purpose of using such capsules because of the requirement for training and experience and the associated costs of obtaining and maintaining a Part 35 license. Alternatively, physicians who are not authorized users could refer their patients to physicians who are authorized users to undergo the diagnostic test, but this would add expense, inconvenience, and delay to an otherwise straight-forward procedure.

Alternative 2 - Grant the petition to permit the ^{14}C-urea capsules to be distributed to and used by any person, without need of an NRC (or Agreement State) license, who is permitted to receive and use the drug under an appropriate Federal or State law governing the distribution and use of the drug.

Parts 30 and 32 would be amended to permit the manufacture and distribution of capsules containing one microcurie of ^{14}C-urea as an exempt material to any person. The staff has determined that the radioactive component of this drug presents a minimal radiation risk and, therefore, regulatory control of the human use of capsules for radiation safety is not necessary.

Alternative 3 - Grant the petition via a general license to permit physicians who are not "authorized users" to receive and use capsules containing 1 µCi of ^{14}C-urea for in vivo diagnostic testing.

This alternative would permit any physician to receive and use capsules containing 1 µCi ^{14}C-urea for human use under a general license. The health and safety concerns for this alternative are the same as Alternative 2. However, if this alternative were adopted, there could be a burden to those Agreement States and Agreement State licensees in States that assess licensing or registration fees for general license holders.

RECOMMENDED COURSE OF ACTION

The staff recommends proceeding with a rulemaking amending Parts 30 and 32 in conformance with Alternative 2 for the following reasons:

- Health and Safety

  Based upon the analysis of the radiological impacts discussed above, there do not appear to be any safety or technical reasons why the capsules, breath test materials, counting fluids and vials, and urine from patients cannot be treated without regard to their radioactivity.

- Avoided Costs

Under Alternative 1, physicians who are not authorized users would have to refer patients to authorized users to undergo the diagnostic test. These referrals and attendant expense could be avoided under either Alternatives 2 or Alternative 3. However, compared with Alternative 3, Alternative 2 appears to be less burden for Agreement States and their licensees.

AGREEMENT STATE IMPLEMENTATION

Rules pertaining to the distribution of products to persons exempt from NRC requirements fall into the class of regulatory functions reserved to the NRC pursuant to the AEA and delineated in 10 CFR Part 150. Therefore, the staff's recommended amendment to Part 32 pertaining to the manufacture and distribution of capsules containing 1 µCi of ^{14}C - urea for "in vivo" diagnostic testing by persons exempt from licensing would be a Division 4 matter of compatibility. The amendment to Part 30 would be a Division 1 matter of compatibility since Agreement States would need to conform their regulations to recognize that possession and use of ^{14}C-urea capsules is exempt from licensing. States (e.g., Oregon, and possibly others) would not be able to require that physicians administering radioactive drugs to humans be specifically or generally licensed.

OGC LEGAL SUFFICIENCY ANALYSIS DEMONSTRATING THAT NO KNOWN BASIS EXISTS FOR LEGAL OBJECTION

OGC has reviewed the rulemaking plan and has not identified any environmental issues that would present significant difficulties in pursuing the proposed rule.

Since this rulemaking would address the resolution of PRM-35-12, the staff will need to ensure that appropriate procedural actions are taken to close the actions associated with that petition. These actions include specifically granting or denying the petition for rulemaking, either in the Federal Register notice associated with the rulemaking or in a separate Federal Register notice, and informing the petitioner of the Commission's decision. The detailed procedures for responding to the rulemaking petition are contained in Part 11 of the Regulations Handbook (NUREG/BR-0053, Rev. 3).

ASSESSMENT OF LIKELY IMPACTS ON NRC AND AGREEMENT STATE LICENSEES

This rulemaking would not result in any additional regulatory burden to NRC medical use licensees. Authorized users would continue to be authorized to receive and use this product for medical use.

SUPPORTING DOCUMENTS

A regulatory analysis, an environmental assessment, and an OMB information collection approval package will be provided for this rulemaking.

RESOURCES

Resources to complete and implement this rule are included in the current budget.

LEAD OFFICE STAFF AND STAFF FROM SUPPORTING OFFICES

Staff-Level Working Group	Concurring Official
RES - Sam Jones	Bill M. Morris
NMSS - Donna-Beth Howe	Donald A. Cool
OGC - Marjorie Rothschild	Stuart A. Treby
OSP - Lloyd Bolling	Richard L. Bangart
ADM - Mike Lesar	David L. Meyer

STEERING GROUPS/WORKING GROUP

There is no need for a steering group for this rulemaking. The Working Group is identified above.

ENHANCED PUBLIC PARTICIPATION

This rulemaking will be placed on the electronic bulletin board at FedWorld and will also be published in the Federal Register.

EDO OR COMMISSION ISSUANCE

Because the amendment involves a policy issue (i.e., the capsules would be distributed to any person who would be exempt from NRC regulations), it is recommended that the Commission issue the rule.

SCHEDULE

Proposed Rule:	Weeks from the date EDO/Comm approves the Rulemaking plan
Send proposed rule to office for concurrence	2 weeks

Send proposed rule to EDO	6 weeks
Send proposed rule to Commission	8 weeks
Receive Commission approval	10 weeks
Publish in the Federal Register for a 75-day public comment period; and submit information collection approval package to OMB	13 weeks