

NUCLEAR REGULATORY COMMISSION

10 CFR Part 35

[Docket No. PRM-35-19]

William Stein III, M.D.;
Receipt of Petition for Rulemaking

AGENCY: Nuclear Regulatory Commission.

ACTION: Petition for rulemaking; Notice of receipt.

SUMMARY: The Nuclear Regulatory Commission (NRC) has received and requests public comment on a petition for rulemaking filed by William Stein III, M.D. (petitioner). The petition has been docketed by the NRC and has been assigned Docket No. PRM-35-19. The petitioner is requesting that the NRC amend the regulations that govern medical use of byproduct material concerning training for parenteral administration of certain radioactive drugs used to treat cancer. The petitioner believes that these regulations do not adequately consider the training necessary for a class of physicians, namely medical oncologists and hemotologists, to qualify as an Authorized User (AU) physician to administer these drugs. The petitioner requests that the regulations be amended to clearly codify an 80-hour training and experience requirement as appropriate and sufficient for physicians desiring to attain AU status for these unsealed byproduct materials.

DATE: Submit comments by (75 days following publication in the *Federal Register*).

Comments received after this date will be considered if it is practical to do so, but assurance of consideration cannot be given except as to comments received on or before this date.

ADDRESSES: You may submit comments by any one of the following methods. Please include the following number (PRM-35-19) in the subject line of your comments. Comments on petitions submitted in writing or in electronic form will be made available for public inspection. Because your comments will not be edited to remove any identifying or contact information, the

NRC cautions you against including personal information such as social security numbers and birth dates in your submission.

Mail comments to: Secretary, U.S. Nuclear Regulatory Commission, Washington, DC 20555. Attention: Rulemaking and Adjudications staff.

E-mail comments to: SECY@nrc.gov. If you do not receive a reply e-mail confirming that we have received your comments, contact us directly at (301) 415-1966. You may also submit comments via the NRC's rulemaking website at <http://ruleforum.llnl.gov>. Address comments about our rulemaking website to Carol Gallagher, (301) 415-5905; (e-mail cag@nrc.gov). Comments can also be submitted via the Federal eRulemaking Portal <http://www.regulations.gov>.

Hand deliver comments to 11555 Rockville Pike, Rockville, Maryland, between 7:30 am and 4:15 pm on Federal workdays.

Publicly available documents related to this petition may be viewed electronically on the public computers located at the NRC Public Document Room (PDR), O1 F21, One White Flint North, 11555 Rockville Pike, Rockville, Maryland. The PDR reproduction contractor will copy documents for a fee. Selected documents, including comments, may be viewed and downloaded electronically via the NRC rulemaking website at <http://ruleforum.llnl.gov>.

Publically available documents created or received at the NRC after November 1, 1999 are also available electronically at the NRC's Electronic Reading Room at <http://www.nrc.gov/reading-rm/adams.html>. From this site, the public can gain entry into the NRC's Agencywide Documents Access and Management System (ADAMS), which provides text and image files of NRC's public documents. If you do not have access to ADAMS or if there are problems in accessing the documents located in ADAMS, contact the NRC PDR Reference staff at 1-800-397-4209, 301-415-4737 or by e-mail to pdr@nrc.gov.

For a copy of the petition, write to Michael T. Lesar, Chief, Rules and Directives Branch,

Division of Administrative Services, Office of Administration, U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001.

FOR FURTHER INFORMATION CONTACT: Michael T. Lesar, Office of Administration, U.S. Nuclear Regulatory Commission, Washington, DC 20555. Telephone: 301-415-7163 or Toll-Free: 1-800-368-5642 or E-mail: MTL@NRC.Gov.

SUPPLEMENTARY INFORMATION:

Background

The NRC has received a petition for rulemaking dated March 20, 2006, submitted by William Stein III, M.D. (petitioner). The petitioner requests that the NRC amend 10 CFR Part 35, "Medical Use of Byproduct Material." Specifically, the petitioner requests that a requirement be added to 10 CFR Part 35 or that 10 CFR 35.396 be revised to define and specify the number of classroom and laboratory training hours appropriate and sufficient for physicians who seek AU status limited to parenteral administrations of Sm-153-lexidronam (Quadramet), I-131-tositumomab (Bexxar), and Y-90-ibritumomab tiuxetan (Zevalin).

The petitioner believes the current regulations are burdensome and deficient. The NRC has determined that the petition meets the threshold sufficiency requirements for a petition for rulemaking under 10 CFR 2.802. The petition has been docketed as PRM-35-19. The NRC is soliciting public comment on the petition for rulemaking.

Discussion of the Petition

The petitioner states that the training and experience requirements for physicians who seek AU status for parenteral administration of Quadramet, Bexxar, and Zevalin to treat certain cancers should reflect current requirements in 10 CFR 35.394, "Training for the oral administration of sodium iodide I-131 requiring a written directive in quantities greater than 1.22 Gigabecquerels (33 millicuries)," and not those currently in 10 CFR 35.396, "Training for the parenteral administration of unsealed byproduct material requiring a written directive." The

petitioner believes that the requirements in 10 CFR 35.396 are too restrictive and unnecessarily burdensome because they require 700 hours of training and board-certification in radiation oncology.

Quadramet is approved by the Food and Drug Administration (FDA) for pain relief in bone cancer patients and is administered intravenously. The petitioner states that the average dosage is 70 mCi and that the main route of elimination is urinary excretion which is usually complete within the first six hours of administration. Less than one percent of the administered dosage remains in the blood five hours after administration. Any remaining activity will be retained in the skeleton for the physical half-life of Sm-153 and results in minimal risk of radiation exposure to health care workers, family members, or other individuals who have contact with the patient. The petitioner believes that the patient can be released under the provisions specified in NUREG 1556, Vol. 9. The petitioner also states that patients can be released immediately if the administered activity of Sm-153 is less than 700 mCi and that no instructions are required if the administered activity is less than 140 mCi.

Bexxar has been approved by the FDA for intravenous treatment of non-Hodgkin's lymphoma. The petitioner indicates that the average dosage administered ranges from 33 to 161 mCi, averaging about 84 mCi, generally less than the dosage used for oral treatment of thyroid cancer with Na I-131. The petitioner states that a patient who receives an oral dosage of 30 mCi of I-131 for hyperthyroidism presents more of a radiation exposure hazard than a patient who is treated with an average dosage of Bexxar, for which the dose to other persons is usually less than the 500 mrem limit. The petitioner believes an oral dosage of I-131 remains in the body much longer than the typical Bexxar dosage. The petitioner also states that the I-131 present in Bexxar is firmly attached to the protein antibody and therefore, represents a much lower contamination hazard than from oral I-131 administration.

Zevalin has also been approved by the FDA for intravenous treatment of non-Hodgkin's

lymphoma and is administered according to the patients body weight up to a maximum dosage of 32 mCi. The petitioner states that the Y-90 radionuclide presents a minimal risk to individuals who may come in contact with the patient and that the patient can be released after treatment under the provisions specified in NUREG 1556, Vol. 9.

The petitioner notes that all administrations of Quadramet, Bexxar, and Zevalin require written directives and believes that these drugs are generally less hazardous than oral dosages of I-131. The petitioner therefore believes that the training and experience requirements should not exceed the 80 hours specified for an endocrinologist who treats thyroid disorders with oral dosages of I-131. (See, 10 CFR 35.392 and 35.394.) The petitioner has concluded that the training and experience requirement for parenteral administrations under 10 CFR 35.396 is unnecessarily burdensome because it requires board certification in radiation oncology.

The petitioner notes that 10 CFR 35.390 requires 200 hours of classroom training and laboratory experience for oral administration of I-131 and all parenteral administrations, §§ 35.392 and 35.394 require 80 hours of training for oral administration of I-131, and § 35.396 requires 80 hours for all parenteral administrations, but only applies to board-certified radiation oncologists. The petitioner also notes that in SECY-05-0020, "Final Rule: Medical Use of Byproduct Material—Recognition of Specialty Boards" (January 19, 2005), the NRC justified the 200-hour classroom training requirement in § 35.390 by stating that these physicians are authorized to prepare radioactive drugs and administer many types of radionuclides that require written directives and that pose a greater risk of exposure to radiation.

The petitioner states that § 35.396 was published in the Federal Register on March 30, 2005 (70 FR 16335), as part of the final rule that amended training and experience requirements for administration of radiopharmaceuticals. The petitioner believes that the NRC's rationale for the training and experience requirements in §35.396 is not known and that an opportunity for public comment period was not provided for this provision before it appeared in

the final rule. The petitioner also states that preparation of Quadramet, Bexxar, and Zevalin does not require use of generators and reagent kits. These radiopharmaceuticals are usually prepared at a commercial facility and then supplied to medical facilities as a unit dosage that the petitioner believes is much less than the dosage used for oral administration of I-131 for thyroid cancer treatment. The petitioner has concluded that because the parenteral administration of Quadramet, Bexxar, and Zevalin poses no greater potential risk than oral administration of I-131, use of these drugs should be considered a medical issue, not a radiation safety issue.

The petitioner believes that physicians who seek AU status for the limited authorization of parenteral administration of Quadramet, Bexxar, and Zevalin should only be subject to an 80-hour training and experience requirement, plus supervised work experience and written attestation, similar to the current requirement for oral I-131 administrations at 10 CFR 35.394. The petitioner states that, moreover, the NRC has not considered codification of new drugs that require written directives as they become available for medical use and that there is an unmet regulatory need to address the ability of physicians to qualify for medical use authorization for certain unsealed byproduct materials that are currently commercially available and for which written directives are required. The petitioner also states that under 10 CFR 35.390(b)(1)(ii)(G)(3) and (4) and § 35.396 (d)(2)(iv), only two generic types of parenteral administrations for which written directives have been considered: parenteral administration of any beta emitter, or photon-emitting radionuclide with a photon energy of less than 150 keV; and parenteral administrations of any other radionuclide.

The petitioner states that the current training and experience requirements governing all parenteral administrations do not adequately consider the training necessary to attain AU status for Quadramet, Bexxar, and Zevalin. The petitioner recognizes that other more hazardous parenterally-administered drugs may become commercially available that require the increased

training specified in §§ 35.390 and 35.396. However, the petitioner believes that radiopharmaceuticals should be subjected to training requirements according to potential radiation risk as is the case for oral administrations of I-131, rather than being lumped into a collective group, which the petitioner characterizes as being the NRC's current practice. The petitioner believes that the current requirements are burdensome and deficient in this regard and that, without regulatory relief, physicians would be discouraged from providing these FDA-approved and commercially available treatments resulting in an adverse impact on their ability to practice medicine. Under the current requirements, the petitioner believes that physicians would be required to become board-certified radiation oncologists under § 35.396 or complete 700 hours of training (including 200 hours of classroom and laboratory training) under § 35.390 to attain AU status to parenterally administer Quadramet, Bexxar, or Zevalin.

The petitioner also states that to be able to conclude that parenteral administration of Quadramet, Bexxar, and Zevalin requires more than 80 hours of training, the NRC would have to assert that each of these drugs presents more potential radiation hazard than oral administration of I-131. The petitioner believes this is more of a practice of medicine issue than a radiation safety issue. The petitioner also states that the NRC would be intruding into the practice of medicine if it did not conclude that medical oncologists/hematologists who have completed 80 hours of classroom and laboratory training, appropriate work experience, and obtained written attestation could be granted AU status for these drugs. The petitioner also believes that such a prohibition would prevent physicians from administering these radiopharmaceuticals and limit patients' access to treatments for life threatening diseases. The petitioner therefore requests that the NRC recognize as adequate and sufficient the 80-hour classroom and laboratory training requirement for physicians to attain AU status to administer Quadramet, Bexxar, and Zevalin as is required for oral Na I-131 administrations to treat thyroid cancer.

The petitioner states that the additional training required under §§ 35.390 and 35.396 is justified because these physicians prepare radioactive drugs and handle unsealed source material in quantities that can involve increased radiation exposure risks. However, the petitioner notes that physicians who administer parenteral doses of Quadramet, Bexxar, and Zevalin do not need to prepare radioactive drugs.

The Petitioner's Conclusion

The petitioner has concluded that the current 700-hour training and experience requirement (that includes a minimum of 200 hours of classroom and laboratory training) governing parenteral administrations of radiopharmaceuticals in 10 CFR Part 35 with regard to administration of Quadramet, Bexxar, and Zevalin is unnecessarily burdensome. The petitioner therefore requests that the NRC recognize that 80 hours of classroom and laboratory training, supervised work experience, and a written attestation for physicians is adequate and sufficient to attain AU status for parenteral administrations of Quadramet, Bexxar, and Zevalin, all requiring written directives. The petitioner offers the following options for addressing this issue:

(1) A specific requirement should be added to 10 CFR Part 35 essentially equivalent to the language in § 35.394 that governs oral administration of I-131 particularly with regard to the alternate pathway. An important language change should be made as specified in § 35.394(c)(2)(vi) to require administering dosages to patients or human research subjects that includes at least three cases involving each of these parenteral administrations.

(2) A separate requirement should be added for Quadramet, Bexxar, and Zevalin similar to the training and experience codification for administration of I-131 to allow the NRC to evaluate each substance individually so all radioactive drugs can be handled appropriately from a radiation safety perspective.

(3) 10 CFR 35.396 should be revised to specify an 80-hour classroom and laboratory training period, appropriate work experience, and a written attestation to apply to the alternate

pathway for any physician, not limited to board-certified radiation oncologists. Specifically, the petitioner recommends removing the current § 35.396(c) and redesignating §§ 35.396(d)(1), (d)(2), and (d)(3) as §§ 35.396(c)(1), (c)(2), and (c)(3). However, the petitioner recognizes that the Commission may not agree with this change if other more hazardous parenterally-administered radiopharmaceuticals become available, necessitating the increased training currently specified in this requirement.

Dated at Rockville, Maryland, this 8th day of June, 2006.

For the Nuclear Regulatory Commission.

/RA/

Annette L. Vietti-Cook,
Secretary of the Commission.