Docket File

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

February 19, 1992

Docket No. 50-20

Dr. Otto K. Harling, Director
Nuclear Reactor Laboratory
Massachusetts Institute of Technology
138 Albany Street
Cambridge, Massachusetts 02139

Dear Dr. Harling:

SUBJECT: MEDICAL BEAM THERAPY FACILITY

I am responding to your letters of April 3, and 16, and June 6, 1991, concerning the use of the Massachusetts Institute of Technology (MIT) Research Reactor (MITR-II) medical beam therapy facility to treat patients suffering from glioblastoma multiforme and metastasized melanoma. Your letters outlined the current MIT practice and procedures for using neutron beams in patient therapy, the history of the 1960-1962 patient trials, and historical information on the procedures for the medical beam therapy facility.

In your letter of April 3, 1991, you stated your opinion that MIT currently satisfies all U.S. Nuclear Regulatory Commission (NRC) regulations concerning the use of neutron beams for the treatment of human patients. The only regulations in this area are found in Section 50.21(a) of Title 10 of the Code of Federal Regulations (10 CFR 50.21(a)) and Section 50.41(a) which place no requirements or restrictions on the irradiation of humans. The facility operating license for the MITR-II licenses the facility under Sections 104a and 104c of the Atomic Energy Act. The MITR-II is the only research reactor licensed under Section 104a of the Atomic Energy Act, which refers to the use of special nuclear material for medical therapy.

Your facility license issued in 1958 and the patient trials conducted during 1960-1962 were completed before the NRC issued many of the regulatory requirements to which NRC medical licensees are subject today. During the past 29 years, the NRC has issued no new Section 104a licenses and MIT has conducted no other human trials. Thus, the NRC has not developed regulations for the use of special nuclear material for medical therapy at research reactors equivalent to those for the medical use of byproduct material as found in 10 CFR Part 35, "Medical Use of Byproduct Material."

The NRC staff is proposing to apply criteria equivalent to those of 10 CFR Part 35 to the use of neutron beams for the treatment of human patients. The staff discussed this approach with MIT and New England Medical Center (NEMC) staff at a meeting at MIT on September 12, 1991.

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NRC is considering the neutron beam capture therapy studies to be divided into two components: beam generation and beam use. Beam generation consists of the treatment room, the production of the neutron beam, the physical characteristics of the beam when it contacts the human subject, all health physics considerations associated with the beam, and radioactive contamination of the beam therapy room, its contents, and areas within MIT occupied by the patient. This component of the studies is the responsibility of MIT under its reactor license.

MIT should submit an amendment to NRC Facility Operating License R-37 to add requirements to the technical specifications that are equivalent to the regulations in Subpart I of 10 CFR Part 35. The NRC recognizes that use of a neutron beam from the MITR-II is similar but not identical to the use of a teletherapy unit. Therefore, you may propose alternative criteria for the technical specifications to replace the information required by Subpart I if the alternative criteria are based on scientific or instrumentation limitations or the design of the reactor. The submittal should provide the following information:

(1) A commitment to limit the delivery of neutrons only to human subjects pursuant to a written directive from NRC medical use licensee No. 20-03857-06.

(2) A commitment to record events equivalent to "recordable events" in 10 CFR 35.2, report events equivalent to "misadministrations" in 10 CFR 35.2, and establish a written quality management program using the criteria specified in 10 CFR Part 35 for teletherapy (the neutron beam). The NRC recognizes that use of the neutron beam in neutron beam capture therapy is similar to, but not identical to current teletherapy. Therefore, you may propose alternative criteria for determining action levels for recording and reporting events equivalent to "reportable events" and "misadministrations" if the alternative criteria are based on limitations of the scientific method or instrumentation. You must submit the alternative criteria proposal and written quality management program with your amendment request.

(3) The methodology to ensure that the neutron flux, fluence, and spectrum delivered to the patient are as requested by the medical use of byproduct material licensee.

(4) The design aspects of the neutron beam delivery system that are important to patient or user safety such that these aspects cannot be changed without license amendment.

(5) The reactor operator and physician communication system and the method for terminating the treatment exposures.

(6) A list of the anticipated activities that may alter beam characteristics and may require spot-checks before the beam use and the spot-checks that will be performed in these situations.

(7) The interlock systems and safety precautions used to prevent personnel

from being accidentally exposed to the beam in the treatment room and the safety precautions to be followed before, during, and after treatment exposures to limit occupational exposure to ionizing radiation. Include information on surveillances, if required.

(8) The applicable U.S. Food and Drug Administration (FDA) requirements for medical devices involved with the human use of the neutron beam used in your study of neutron beam capture therapy. Provide the status of the FDA appr val for those aspects of the study regulated by FDA. Describe internal reviews and commitments for those aspects of the studies for which you believe FDA requirements are not appropriate.

The second component, beam use, involves the interaction of the neutron beam with both the boronated and the non-boronated human tissues, blood vessels, body fluids, and tumor cells. Neutrons in the beam interact with different atomic nuclei to produce byproduct material. While the therapy focuses on producing unstable boron-11 and its fission products, lithium-7 and an alpha particle, other activation products are also formed. This byproduct material will be the responsibility of NEMC in accordance with its medical use of byproduct material license.

NEMC should submit an amendment to NRC License 20-03857-06 to authorize use of the neutron beam at the MIT Medical Beam Therapy Facility for neutron beam capture therapy on human subjects, and to authorize possession of neutron activation products resulting from neutron beam capture therapy procedures. The submittal should provide the following information:

(1) The applicable U.S. Food and Drug Administration (FDA) drug requirements involved with the human use of the boronated drugs used in your study of neutron beam capture therapy. Provide the status of the FDA approval for those aspects of the study regulated by FDA. Describe internal reviews and commitments for those aspects of the studies for which you believe FDA requirements are not appropriate. (For licensing, you may either identify each boron product and provide a characterization of your research protocol for that product or request generic approval to study boron products for which FDA has accepted an "Investigational New Drug" (IND) application for use in human neutron beam capture therapy procedures. If you choose the generic approval, you should also commit to following the IND protocol).

(2) A commitment to release patients, record events equivalent to "recordable events" in 10 CFR 35.2, report events equivalent to "misadministrations" in 10 CFR 35.2, and establish a written quality management program using the criteria specified in 10 CFR Part 35 for therapeutic radiopharmaceuticals (the boron-11 fission products and other neutron activation products). The NRC recognizes that elements of neutron beam capture therapy are similar to but not identical to current radiopharmaceutical therapy. Therefore, you may propose alternative criteria for determining action levels for recording and reporting events equivalent to "reportable events" and "misadministrations" if the alternative criteria are based on limitations of the scientific method or

instrumentation. You must submit the alternative criteria proposal and written quality management program with your amendment request.

(3) NEMC's method to determine the combined radiation dose to the patient from boron-11 fission and from other neutron activation products and to ensure this radiation dose is delivered. Provide the protocol to be used in determining the neutron dose and total dose. The protocol should include identification and description of the dosimetry system that will be used to determine the dose.

(4) The training and experience requirements set by your radiation safety committee to authorize the "teletherapy physicist" to perform the neutron dosimetry measurements and your neutron dosimetry training program for an inexperienced "teletherapy physicist."

(5) Your method to calibrate the neutron dosimetry system, the dosimetry comparisons you will use, and the criteria for determining the conditions under which the comparisons are acceptable.

The NRC staff shares the common desire with MIT to provide a cure for those suffering from glioblastoma multiforme and metastasized melanoma, and we will work with you to resolve the regulatory issues in a satisfactory manner. If you have any questions concerning this issue, please contact Alexander Adams of my staff at (301) 504-1127.

Sincerely,
- original signed by -
Seymour H. Weiss, Director
Non-Power Reactors, Decommissioning and
Environmental Project Directorate
Division of Advanced Reactors
and Special Projects
Office of Nuclear Reactor Regulation

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