Nuclear Regulatory Commission
Region I
475 Allendale Road
King of Prussia, PA 19406-1415

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223 North Van Dien Avenue
Ridgewood NJ 07450-2736

May 27, 2005

Dear Sir/Madame,

We would like to amend our license, **#29-03845-01** as per the following;

To Add the Proxima Therapeutics GliaSite® Brachytherapy Systems

Specifically, we wish to add the following line item to our license:

Material in 10CFR35.1000:

- **Radionuclide:** **I-125**
- **Physical Form:** **an aqueous solution containing Na-3-[I-125] iodo-4-hydroxybenzenesulfonate (Iotrex®)**
- **Inventory Limit:** **as needed (or 8 Ci)**
- **Purpose:** **Brachytherapy with the GliaSite catheter.**

Liquid Brachytherapy Sources and Devices

Licensing Guidance - I-125 Iotrex Liquid Brachytherapy Source in Proxima GliaSite® Radiation Therapy System:

1. I-125 Iotrex liquid brachytherapy sources are manual brachytherapy sources used for temporary brachytherapy implantation therapy in the Proxima Therapeutics' GliaSite Radiotherapy system.

2. The Proxima Therapeutics' GliaSite Radiotherapy system (RTS) consists of the Proxima Therapeutics' GliaSite Radiotherapy system balloon catheter and Iotrex liquid brachytherapy source.

We are requesting a line item amendment to use the Proxima Therapeutics GliaSite catheters and Iotrex. Iotrex is a liquid brachytherapy radioactive source and the GliaSite catheters are used to temporarily contain the Iotrex during brachytherapy. The GliaSite catheters are listed on the U.S. NRC Sealed Source and Device Registry (GA-1148-D-101-S).

3. Required training and experience for authorized users is specified in 10 CFR 35.490 or, until October 25, 2004, 10 CFR 35.940 for use with materials governed by 10 CFR 35.400, as well as vendor training in use of the Proxima Therapeutics' GliaSite RTS.

   Authorized users for this procedure will be Michael Forbes Wesson, M.D. and David R. Greenblatt, M.D.

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Proxima Therapeutics will provide training for the authorized user(s) prior to the licensee performing the first brachytherapy procedure using the GliaSite inpatients.

4. An authorized user with experience in radiopharmaceutical therapy procedures should be on call to provide guidance in case of leakage of the implanted device.

Our authorized physician will be on call to provide guidance and assistance in case of actual or suspected leakage of the implanted device.

We shall follow all of the requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use, except where the following license conditions provide regulatory relief:

5. For brachytherapy using Proxima Therapeutics' GliaSite RTS, "prescribed dose" means the total dose documented in the written directive.

Per our Written Directive for brachytherapy with the GliaSite, the "prescribed dose" is the prescribed radiation dose, in units of Gy delivered.

6. The written directive should include: (1) prior to implantation: the treatment site, the radionuclide (including the chemical/physical form (Iotrex)), and dose; and (2) after implantation but prior to completion of the procedure: the radionuclide (including the chemical /physical form (Iotrex)), treatment site, and the total dose.

Our Written Directive for brachytherapy with the GliaSite catheters includes the nuclide (I-125), the chemical/physical form (Iotrex), prescribed radiation dose (Gy), administered dosage of Iotrex (mCi) and dwell time (hours).

7. Procedures should specify how to confirm that the balloon does not leak prior to injection of the Iotrex or while Iotrex is implanted in the patient or human research subject.

Prior to afterloading the Iotrex, the integrity of the GliaSite catheter will be determined using one of a variety of imaging modalities such as MRI, CT or radiographs. The images will be obtained with the GliaSite catheter inflated, demonstrating the continued capability of the catheter to maintain its inflated fluid volume. The images used in this assessment will be kept in the patient's medical records as required by state regulations.

One method of assessing GliaSite integrity during brachytherapy that we may use (not exclusively though) is via radiation survey measurements. Upon completing the Iotrex afterloading periodic radiation exposure rate measurements will be used to monitor unexpected leakage of radioactive material from the GliaSite catheter. Radiation measurements will be performed over the injection site surface (at 20 to 30 centimeters from the injection site), at 1 meter from the injection site, and over the patient's bladder. These measurements will be repeated periodically until the radioactive material is retrieved. Any significant changes from the initial readings (e.g., large decrease in cranial exposure rates concomitant with large increases in bladder exposure rates) will be documented and evaluated for further action as appropriate.

If patients are treated during brachytherapy on an outpatient basis, we will follow the model guidance provided in US NRC NUREG –1556, vol. 9, Appendix U in releasing these patients for the duration of their brachytherapy treatment, making only the minor changes made necessary to satisfy 10 CFR 35.1000. Documentation demonstrating

compliance with Section 35.75 requirements that the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 5 mSv is provided. Documentation includes forms describing the evaluation process for determining which patients are suitable for outpatient treatment, patient release forms and appropriate patient instructions.

8. "Source leakage" for the Iotrex implanted in the GliaSite RTS means leakage of I-125 that results in a dose that exceeds 0.5 Sv (50 rem) dose equivalent to any individual organ other than the treatment site (based on definition of a medical event).

We will evaluate all events which occur involving the unexpected loss of retained radioactivity in the catheter and assess the dose to the critical organ (bladder wall, per Iotrex Package Insert). If the dose to the critical organ exceeds 50 rem, the event will be handled and reported as a misadministration.

Per the manufacturer's product information, a small quantity of radioactivity diffuses from the catheter during normal operation.

In addition, there may be cases where in the medical opinion of the physician(s), the patient would best benefit from leaving the drained GliaSite in place (this is an "off-label" use of the GliaSite). Having said this, the federal food, drug and cosmetic act allows a practitioner to use a cleared device for an "off-label" use if the physician(s) believes that using the GliaSite is in the best interest of this patient (Practice of Medicine Clause).

Thus, GliaSite patients are expected to have some residual radioactivity present in their bodies after therapy is completed.

We will evaluate each patient treatment to determine if the prescribed dose was successfully delivered to the treatment site. Specifically, a delivered radiation dose that differs by more than 20% from the prescribed radiation dose will be evaluated as a medical event.

9. We shall retain a record of the leak test for 3 years (the period that 10 CFR 35.2067 requires for brachytherapy sources).

Diagnostic quality images will be obtained with the GliaSite catheter inflated, demonstrating the continued capability of the catheter to maintain its inflated fluid volume. The images used in this assessment will be kept in the patient's medical records as required by state regulations. The leak tests typically required of brachytherapy sources (e.g., removable contamination) are not possible as the GliaSite catheter is completely subcutaneous while the radioactive material resides within it. Also, the SSDR document states leak tests are not applicable to the GliaSite system.

10. We shall report a leaking source to the NRC within 5 days of the leakage test to the locations specified and provide the information identified in 10 CFR 35.3067.

The GliaSite catheter is a single use device that will not be inflated with Iotrex if the integrity of the device is not demonstrated prior to afterloading Iotrex. In addition, leak tests are not required for the GliaSite as stated on Page 1 of the Sealed Source and Device Registry No. GA-1148-D-101-S.

11. We shall provide instructions on how to safely handle contamination of unsealed materials, in addition to the instructions required by 10 CFR 35.410, "Safety instructions."

    We will follow our policies and procedures for safe use of radioactive materials and provide instructions to the appropriate staff as necessary.

The following additional guidance applies when Iotrex™ is placed in vials, syringes, or radiation shields that are not labeled by the manufacturer:

12. Label syringes and syringe radiation shields with the radioisotope, form, and therapeutic procedure (i.e., I-125 Iotrex for brain brachytherapy).

13. Label vials and vial radiation shields with the radioisotope and form (i.e., I-125 Iotrex).

    We will label syringes, syringe shields, vials and vial shields with the form of the byproduct material (e.g., I-125 Iotrex). Syringes and syringe shields will also include the procedure (e.g. GliaSite or brain brachytherapy).

    We would like to be authorized for the procedure both at the Valley Hospital (in-patients) and at Luckow Pavilion (out-patients)

    If there are any questions, please call Ki-chuen Chak, Physicist at (201) 634-5403

Sincerely,

Fran Cartwright
Director of Oncology