Medical Products Divi..on/3M

3M Center
St. Paul, Minnesota 55101
612/733 1110

2301

August 3, 1979

3M

Joseph DelMedico
U. S. Nuclear Regulatory Commission
License Management Branch
Division of Fuel Cycle and Material Safety
Washington, DC 20555

Re: Byproduct Material License 22-00057-59MD, Amendment 02
Control 99111

Dear Mr. DelMedico:

This letter is to advise you that we have received today from your office two copies of Byproduct Material License 22-00057-59MD, which has been amended to provide for distribution of I-125 Seeds from the New Brighton manufacturing facility. We appreciate your efforts in expediting the review and approval of this amendment.

In our original application of March 15, 1979, the model 6702 I-125 Seed was described as a source containing 0.10 to 40 mCi/comp. Similarly, it was noted that a seed of the model 6701 configuration, although typically containing 0.10 to 1.0 mCi/comp, was available upon special request with a contained activity up to 40 mCi/comp. You will recall that the calibrated value "mCi/comp" is related to the actual number of millicuries per source, "mCi", by the equation, mCi = 1.25 X mCi/comp. Therefore, an I-125 Seed of either model 6701 or 6702, calibrated at 40 mCi/comp, would contain a maximum quantity of 50 millicuries I-125.

In reviewing the license, we note that 50 millicuries has been specified as the maximum quantity to be contained in a model 6702 I-125 Seed (Condition 1, item G). However, a significantly lower maximum, 1.25 millicuries, has been specified (in item F) for a seed of the 6701 configuration. This corresponds to a calibrated value of only 1.0 mCi/comp, and does not provide for distribution of sources up to 40 mCi/comp, as originally described in submissions to NRC and in promotional labeling (package insert) for the product.

It is our intention to make available model 6701 I-125 Seeds calibrated to 40 mCi/comp, as planned, and we realize that a change in the license

amendment 02 is necessary. In this regard, we would appreciate your assistance in verifying the license condition for the model 6701 seed and advising us as to the maximum quantity of I-125 to be contained therein. I am enclosing, for convenience in your review, a copy of page 03 of our March 15 submission and the package insert for the 6701 I-125 Seed, which contain quantitative descriptions of the source.

If you have any questions regarding this, please feel free to contact me (612/733-6421).

Sincerely yours,

Jacquelyn D. Bush

Jacquelyn D. Bush
Sr. Regulatory Affairs Coordinator
Diagnostic Products Department/3M
3M Center, 230-3
St. Paul, Minnesota 55101

JDB/
Enclosures:2

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Telecon: Licensees who want the 6701 source @ 40 mCi comp for calibration purposes will need to be specifically authorized to receive it. Calibration sources cannot be distributed under Group III.

(2) THE APPLICANT SUBMITS SUFFICIENT INFORMATION REGARDING EACH TYPE OF SOURCE OF DEVICE PERTINENT TO AN EVALUATION OF ITS RADIATION SAFETY, INCLUDING:

(i) The byproduct material contained, its chemical and physical form and amount.

Byproduct material: Iodine-125

Chemical form: Iodide, as a part of a quaternary ammonium compound, namely Dowex^{R} 21K (AG 21K) anion exchange resin.

Radioactive iodine-125 is affixed to the resin by simple ion exchange in an aqueous solution of pH > 10 (ϕ-$CH_2N^+(CH_3)_3Cl^- + {}^{125}I^- \longrightarrow \phi$-$CH_2N^+(CH_3)_3{}^{125}I^- + Cl^-$.) This is followed by two washes with distilled water and drying prior to placement within the titanium can.

Physical form: Solid spheres of ϕ-$CH_2N^+(CH_3)_3{}^{125}I^-$

Amount: Model No. 6701 (formerly LSR 101) for permanent interstitial implants contains 0.10 to 1.0 mCi/comp. (nominal 0.55 mCi/comp.). I-125 Seeds containing up to 40 mCi/comp. are available upon special request for use as check sources for assay calibration.

Model No. 6702 (formerly LSR 102) for temporary interstitial implants contains 0.1 to 40 mCi/comp.

NOTE: The term "mCi/comp." is the unit used to calibrate I-125 Seeds, as described on page 14 of this submission. The relationship between this term and actual number of mCi per source is described by the following equation:

$$mCi = 1.25 \times mCi/comp.$$

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St. Paul, Minnesota 55101
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I-125 SEEDS ®

No. 6701

DESCRIPTION

I-125 Seeds 6701 consist of a welded titanium capsule containing Iodine-125 adsorbed on two anion exchange resin spheres. A spherical gold x-ray marker is included, which serves as a means of visualization on radiographs.

Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic x-rays and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal radiation emissions are x-rays of 27.4 keV and 35.5 keV.

To correct for the physical decay of Iodine-125, the decay factor at selected days after the assay date are shown in table below.

TABLE

Decay Chart Iodine-125, Half-Life 60.2 Days

Days	Decay Factor	Days	Decay Factor	Days	Decay Factor
0	1.000	24	0.759	48	0.575
2	0.977	26	0.741	50	0.562
4	0.955	28	0.724	52	0.550
6	0.933	30	0.708	54	0.537
8	0.912	32	0.692	56	0.525
10	0.891	34	0.676	58	0.513
12	0.871	36	0.661	60	0.501
14	0.851	38	0.646	62	0.490
16	0.832	40	0.631	64	0.479
18	0.813	42	0.617	66	0.468
80	0.794	44	0.603	68	0.457
22	0.776	46	0.589	70	0.447

Radiation Protection

The first half value thickness of lead for iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide a 99.9% reduction in exposure.

ACTIONS

I-125 Seeds emit x-rays of 27.4 and 35.5 keV. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility and results in a total self-absorption to approximately 25%.

INDICATIONS

I-125 Seeds are indicated for interstitial treatment of cancerous tumors which have the following characteristics: unresectable, localized, size less than 7-8 cm, slow growth rate, and low to moderate radiosensitivity.

I-125 Seeds may be used to treat superficial, intraabdominal, or intrathoracic tumors. Tumors of the head, neck, lung, pancreas and prostate (stage B and early stage C) are commonly treated.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

CONTRAINDICATIONS

As with other brachytherapy sources, treatment of tumors in generally poor condition (eg. ulcerated) is not recommended with I-125 Seeds.[1]

WARNINGS

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

PRECAUTIONS

Preparation for Use/Sterilization

I-125 Seeds are radioactive and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel consistent with published exposure limits.

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate detection.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121°C at 30 PSI to 138°C at 50 PSI. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138°C and 50 PSI).

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immedicate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of Iodine-125.

Application to Patient

I-125 Seeds should be used only by individuals who are qualified by training and experience in the safe use and handling of radionulides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Radiation detection equipment, capable of detecting 30 keV x-rays, should be available whenever I-125 Seeds are being handled. The seeds are quite small and it may be difficult to locate a dropped seed visually.

All practical physical protection should be provided during the implantation procedure. Frequently, however, protective barriers are not practical in the surgery. In this circumstance, operators must rely upon distance and speed to minimize radiation exposure.[2]

Treatment of Patient

All patients should be informed of the nature of I-125 Seed implants and the expected period of time during which radiation precautions will be necessary. Patients, their close associates,and associated medical personnel should be instructed in the necessary radiation safety procedures required for someone who has received an I-125 Seed implant. Guidelines for necessary precautions have been established by National Council on Radiation Protection and Measurements and are detailed in NCRP Reports.[2,3,4,5,6]

All patients should be advised of the possibility that, during a course of treatment, one or more I-125 Seeds might slough off and become detached as a tumor regresses and becomes smaller. Under these circumstances, any bandages or linens which come into contact with the site of the implant should be scrutinized for small metallic seeds (1/4 of an inch long). Patients should be advised that whenever seeds are found, they should be picked up with a spoon and placed in a jar or other container, and placedin an inaccessible area in the home. The radiation center should be notified of such an event as soon as possible after its occurrence.

Accountability/Disposal

Iodine-125 is an accountable radioactive material. I-125 Seeds should, therefore, be strictly controlled and stored in a locked safe. If any significant material cannot be accounted for, the loss must be reported to the appropriate federal or state licensing agency.

When disposal is indicated, I-125 Seeds should be transferred to an authorized radioactive waste disposal agency. I-125 Seeds should never be disposed of in normal waste.

An I-125 Seed disposal service is provided by 3M Radiation Therapy Products. Customers wishing to dispose of I-125 Seeds in this manner must contact the 3M Company for approval and specific shipping container and forms.

Material approved for return must comply with Department of Transportation regulations (49 CFR, Parts 171-177) regarding packaging and labeling. Shipments are to be directed to: 3M/Radiation Therapy Products, TCAAP Building 590, New Brighton, Minnesota, 55112.

Leak Testing

NRC regulations (10 CFR 35.14) describe requirements for leak testing radioactive sources.

I-125 Seeds that retain clinical utility for periods of more than six months must be leak tested at intervals of six months or less as defined in NRC regulations.

I-125 Seeds are leak tested prior to shipment and the results are shown on the shipment identification papers that accompany each shipment. I-125 Seeds having a nominal activity of 0.55 mCi/comp. will decay to 0.07 mCi/comp. in 180 days and will not require leak testing by the user.

ADVERSE REACTIONS

No adverse reactions involving I-125 Seeds have been reported.

DOSAGE AND ADMINISTRATION

The total activity of I-125 Seeds required for any given treatment depends upon the tumor volume and the previous radiation history of the tumor site. Established practice [9] should be followed for the calculation of the total activity to be implanted, the proper placement of the sources within the tissue, and the evaluation of the radiation dose distribution achieved.

Dose distribution around each individual seed is not isotropic.[8] This anisotropy should be included in dose distribution calculations.

Iodine-125 has a 60.2 day half-life. Decay corrections must be made in order to properly calculate the activity of the seeds on the day they are implanted.

Directions for Use

I-125 Seeds will pass through a No. 17 gauge needle. Most implants have been performed with after-loading techniques using an inserter attached to hollow needles. Several devices are manufactured for this purpose. Individual seeds may be implanted using the familiar radon seed implanters, and Scott, Mick, and Henschke applicators designed for this purpose. The Royal Marsden Gold Grain gun will not accept I-125 Seeds.

HOW SUPPLIED

I-125 Seeds are available with an activity per seed of 0.10 to 1.00 mCi/comp. (nominal 0.55 mCi/comp.). The product is supplied as a group of seeds with an assay within a stated range on the assay date. For example, seeds may be supplied in the grouping 0.50 - 0.54 mCi/comp. per seed. Individual seeds within this group are assayed to ± 5%. I-125 Seeds with an activity to 40 mCi/comp. are available upon special request.

I-125 Seeds are packaged in a screw-cap, 1 dram glass vial, which is labeled to indicate the isotope amount of activity, activity range and the assay date. The vial is contained in a lead pig which is labeled to contain the same information, as well as the number of seeds and precautionary regulatory statements pertaining to licensing of the product.

I-125 Seeds are NOT sterile when shipped.

LICENSING

I-125 Seeds are licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to §§ 35.14 and 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.

Federal law restricts this device to sale by or on the order of a physician.

REFERENCES

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