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

MAR 7 1980

Minnesota Mining & Manufacturing
ATTN: Jacquelyn D. Bush
Sr. Regulatory Affairs Coordinator
Diagnostic Products Department
3M Center
Saint Paul, Minnesota 55101

REFUND OF APPLICATION FEE

1. BACKGROUND:

Check Received	February 25, 1980
Application Dated	February 8, 1980
Check Number	330384
Check Amount	$340

2. REFUND:

Amount	$190

This refund is now being processed by our Controller's office, and will be sent as soon as possible.

3. REASON FOR REFUND

Overpayment of amendment fee for License 22-00057-59MD as specified in fee Category 3B ($40) and application fee as specified in fee Category 9B ($110) of Section 170.31, 10 CFR 170. Total fee required $150.

/s/

Glenda Jackson
License Fee Management Branch
Silver Spring Office
Office of Administration

APPLICATION FOR SPECIFIC LICENSE TO DISTRIBUTE

I-125 SEEDS^{R}

Model 6711

The following is submitted as an amendment application for license 22-00057-59MD to distribute I-125 Seeds^{R}, model 6711, containing by-product material to persons licensed pursuant to part 35.14 of 10 CFR for use as listed in Group VI, Schedule A of part 35.100 of 10 CFR. The source to be distributed under this license is described in the following information, as specified in 10 CFR 32.74

Table of Contents

(1) THE APPLICANT SATISFIES THE GENERAL REQUIREMENTS IN §30.33 IN THIS CHAPTER.

Reference is made to previous submissions pursuant to our issued NRC Byproduct Material License 22-00057-06. All the requirements of paragraph 30.33 have been satisfied under this license.

(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: Silver iodide on a silver rod

Radioactive iodine-125 is affixed to the silver rod coated with silver chloride by simple ion exchange in aqueous solution of pH $\geq$ 10, according to the equation,

silver rod/AgCl + $Na^{125}I$ $\longrightarrow$

silver rod/$Ag^{125}I$ + NaCl

followed by three washes with acetone and drying prior to placement within titanium can.

Physical form: Solid silver rod with adsorbed I-125 and hermetically sealed within a titanium can.

Amount: I-125 Seeds, model 6711, contain a maximum of 62 mCi iodine-125 per source. Allowing for attenuation by the silver rod and titanium capsule of 35%, the maximum effective output of the model 6711 is 40 millicuries of iodine-125 (which is identified as 40 millicuries compensated or 40 mCi comp.).

(ii) Details of design and construction of the source or device.

A model 6711 I-125 Seed consists of a cylindrical titanium capsule containing a silver rod with adsorbed Iodine-125 and welded at both ends. The silver rod serves to enhance the visibility of the sources in a radiograph. A schematic diagram of the model 6711 seed is presented as Figure 1 below.

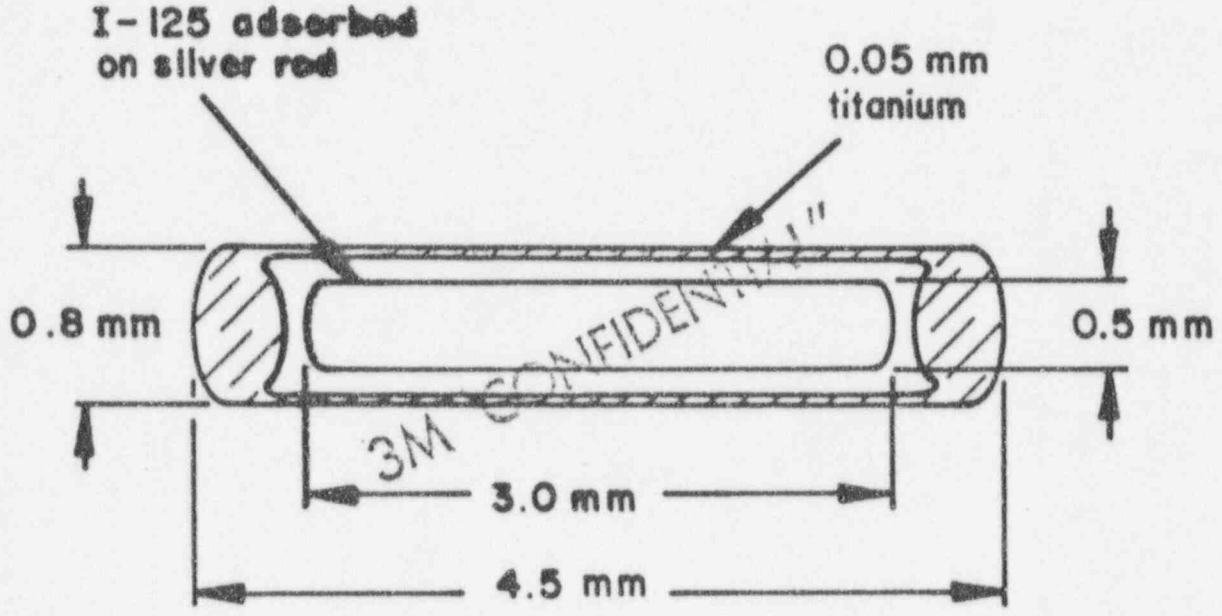


FIGURE 1. Schematic diagram of I-125 Seed, Model No. 6711

(iii) Procedures for, and results of, prototype tests to demonstrate that the source or device will maintain its integrity under stresses likely to be encountered in normal use and accidents.

I-125 Seeds have been subjected to four prototype tests to demonstrate that the sources maintain their integrity under stresses of use and accidents. These procedures are provided for source evaluation under the following stress conditions, along the lines of those suggested in NBS Handbook 126, ANSI N 542-1977, Appendix C, and ANSI N44.1-1973: 1) autoclave, 2) impact, 3) percussion, and 4) bend.

Following each prototype test procedure, I-125 Seeds were subjected to a soak test, according to the following procedure. Each seed was placed into a 1 (one) dram vial (3.7 ml) containing 3.0 ml of a wash solution (0.01M NaI, 0.01M NaOH, and liquid detergent, preparation of which is described in Appendix A).

The vial was closed using a screw cap and allowed to stand at ambient temperature for at least 20 hours. At this time, the vial supernatant was withdrawn from the seed and assayed for radioactivity using a Searle model 1195 automatic gamma counter with a sodium iodide well crystal. Each I-125 Seed was considered to have passed the prototype test described if removable activity was less than 0.005μCi.

The four prototype tests and resulting experimental data are are described below. Seeds evaluated were of the model 6711 configuration, with separate seeds evaluated in each test procedure.

A. Autoclave Test

The autoclave test duplicated the normal method used by physicians to sterilize commercial I-125 Seeds (models 6701 and 6702) prior to implantation. Each model 6711 I-125 Seed was placed into a 1 dram vial with a screw cap positioned loosely on top. The vial was autoclaved under normal conditions of 121° C and 15 psi for 30 minutes, then allowed to cool to ambient temperature. A soak test was performed on each seed, results of which (tabulated below) indicate that I-125 Seeds maintain their integrity under normal autoclave conditions. This is the most severe temperature to which the seeds will normally be exposed.

TABLE 1. Results of Autoclave Testing of I-125 Seeds, Model 6711

Sample No.	Lot No.	Activity (mCi comp.)	Removable activity
1	53250-13	0.55 - 0.59	$<2.0 \times 10^{-6}$ µCi*
2	53250-13	0.55 - 0.59	$<2.0 \times 10^{-6}$ µCi
3	53250-13	0.55 - 0.59	$<2.0 \times 10^{-6}$ µCi

*Lower limit of detectability

B. Impact Test

Each I-125 Seed was positioned above a 30-foot (9.1 meter) length of hollow, 5/8" (inside diameter) conduit, constructed from 3-10 foot lengths coupled with metal connectors. This was necessary to avoid loss of the small (≈1/4") sources. Each seed was then dropped vertically, through the tubing, onto a 13 x 10 x 1.3 cm thick steel plate. Following the test, each seed was visually inspected for damage and then dropped into a 1 dram vial containing 3 ml of wash solution and then assayed for removable radioactivity.

No damage to the seeds, such as bending or denting, was observed. Data tabulated below indicate that the I-125 Seeds maintain their integrity under the conditions of the impact test.

TABLE 2. Results of Impact Testing of I-125 Seeds, Model 6711

Sample No.	Lot No.	Activity (mCi comp.)	Removable activity
1	53250-13	0.30 - 0.34	7.7×10^{-6} µCi
2	53250-13	0.45 - 0.49	4.1×10^{-6} µCi
3	53250-13	0.65 - 0.69	5.4×10^{-6} µCi

C. Percussion Test

Each I-125 Seed was positioned horizontally on a 1.5 cm thick lead plate, which was supported by an aluminum plate resting on a steel table top. A 2.5 cm (diameter) steel rod weighing 1.42 kg was dropped vertically on the seed,

positioned in the center of the impact circle, from a height of 1 meter. Following each test, each seed was inspected for damage, then dropped into a 1 dram vial containing 3 ml of wash solution, and assayed for removable radioactivity.

Visual inspection indicated that the seed configuration was altered significantly by the test. The source was flattened evenly throughout the middle portion of its lengths, bulging somewhat at the end welds. The end welds did not appear to lose their integrity (i.e. separate from the titanium can). The crushed seed left an impression in the lead plate.

Data tabulated below indicate that the I-125 Seeds maintain their integrity under the conditions of the percussion test.

TABLE 3. Results of Percussion Testing of I-125 Seeds, Model 6711

Sample No.	Lot no.	Activity (mCi comp.)	Removable activity
1	53250-13	0.55 - 0.59	$<2.0 \times 10^{-6}$ µCi
2	53250-13	0.55 - 0.59	$<2.0 \times 10^{-6}$ µCi
3	53250-13	0.55 - 0.59	5.8×10^{-6} µCi

D. Bend Test

A bend test was performed on I-125 Seeds, model 6711, to determine source integrity under use conditions, inasmuch as reports from the field indicate a certain likelihood that a seed could be bent by certain devices used to implant them. The bend test procedure is described below.

One end of each I-125 Seed was positioned in the jaws of a 4" long needle-nose pliers. A special groove (1/2 the diameter of the seed) was cut into the jaws to facilitate holding the seed. The seed was inserted to half its length and held in this position by gripping the handles of the pliers. The other half of the seed was gripped with a similar pliers. Both pliers were "backed off" to allow about 1 mm spacing between jaws.

Manipulating both pliers, the seed was bent to approximately 45°. This resulted in a bend in the middle of the seed and stretched the titanium tubing on the surface opposite the bend. The bent seed was then placed into a 1 dram vial containing 3 ml of wash solution and assayed for removable radioactivity according to the soak test procedure described above.

Data tabulated below indicate that the I-125 Seeds maintain their integrity under bend test conditions.

TABLE 4. Results of Bend Testing of I-125 Seeds, Model 6711

Sample No.	Lot No.	Activity (mCi comp.)	Removal activity
1	53250-13	0.55 - 0.59	5.0×10^{-6} µCi
2	53250-13	0.55 - 0.59	9.9×10^{-6} µCi
3	53250-13	0.55 - 0.59	$<2.0 \times 10^{-6}$ µCi

In addition to these prototype tests described above, non-radioactive seeds (which were identical in structure to the I-125 Seeds except for radioactivity) were evaluated for structural integrity at several temperatures to 1000° C, which would not be encountered under normal use conditions. The test procedures, including a description of the observations and test data recorded at various high temperatures, are presented below.

High Temperature Test

Each non-radioactive seed was placed into a covered ceramic crucible, which was then placed into a furnace. Temperatures were monitored using a Chromel-Alumel thermocouple attached to a digital voltmeter. Seeds were heated to respective temperatures for one hour, removed from the furnace, cooled, then observed, as summarized below.

600° C - The titanium can appeared to be porous, having shiny end welds, and no change in shape. As the source was bent in half 90°, the can did not break but sloughed a dark gray ash-like material.

On the basis of similar temperature tests of radioactive I-125 Seeds models 6701 and 6702 (submitted to NRC as part of license amendment application, dated March 15, 1979), we have observed that the structural integrity of the titanium can is affected by this temperature, such that contained I-125 has been lost to the atmosphere. Similarly, a leak in the titanium can containing I-125 adsorbed as silver iodide would result in loss of the radioactive iodine, due either to volatilization of iodine (I_2) or as silver iodide (AgI).

700° C - The seed appeared more porous, but no change in shape occurred. The titanium can cracked as the seed was bent 90°.

800° C - The seed resembled burned aluminum foil. No change in shape occurred, but the titanium can was easily broken with applied pressure.

1000° C - Titanium can was pale yellow in color and fragile. The silver wire had melted into a spherical shape and attached to a fragment of the titanium.

(iv) For devices containing byproduct material, the radiation profile of the prototype device.

Dose rates for I-125 Seeds, model 6711, have been determined on the basis of data gathered for the models 6701 and 6702 seeds, inasmuch as the output activities for all models are measured in "mCi comp.". Specifically, maximum radiation levels were measured at 5 and 30 cm from the external surface of the source, as described below.

Films (Kodak Type II) were contained within plastic holders (2-1/4 by 3/4") during exposure. Background radiation was maintained at <1% of the film exposure with appropriate radiation shielding. Two films were added as a control to measure background radiation levels and to check the manufacturer's film developing process.

Six (6) I-125 Seeds, ranging in activity from 0.30 mCi comp. to 19.25 mCi comp., were used to ascertain exposure at 5 cm. Four (4) seeds (3.29 to 19.25 mCi comp.) were used to measure exposure at 30 cm. Exposure times ranged from 0.4 to 43 hours. Exposed films were developed and read by R. S. Landauer, Jr. & Company (Glenwood Science Park, Glenwood, Illinois). Results of these measurements, tabulated below, were corrected to Average Dose Rate (in mr/hr·mCi) and averaged. An accuracy of ± 15% was assured by the testing laboratory.

Distance from source	Average dose rate
5 cm	25 mr/hr·mCi
30 cm	0.53 mr/hr·mCi

On the basis of these data, the following dose rates can be expected for I-125 Seeds of minimum (0.1 mCi comp.) and maximum (40 mCi comp.) activity.

I-125 Seed activity	Average dose rates (mr/hr) at 5 cm	at 30 cm
0.1 mCi comp.	2.5	0.053
40 mCi comp.	1000	21.2

(v) Details of quality control procedures to assure that production sources and devices meet the standards of the design and prototype tests.

All model 6711 I-125 Seeds are subjected to quality control tests prior to their transfer to a licensed recipient. In-process tests include the following procedures, which are described in detail in Appendix B of this submission.

Procedure name	Sample size	Specification
Visual inspection	100%	Uniform welds, no holes. Seed length 4.20-4.90 mm. Seed diameter 0.775-0.960 mm.
Initial leak test	100%	<0.005 μCi removable radioactivity.
Second leak test and autoclave	100%	<0.005 μCi removable radioactivity
Assay for Radioactivity	100%	≥0.10 mCi comp. I-125 activity

Any I-125 Seeds not meeting the specifications described above are rejected.

Control tests, in addition to those listed above, are performed as a final quality control check. These tests include the following procedures.

Procedure name	Sample size	Specification
Final leak test	100%	<0.005 μCi removable radioactivity.
Visual inspection	According to Mil. Std. 105*, Level II, AQL 0.15	Length and width as specified above.
	According to Mil. Std. 105, Level II, AQL 1.0	Uniform welds, no holes.

*A copy of Mil. Std. 105 was submitted to NRC in correspondence dated May 30, 1979.

(vi) Procedures and Standards for calibrating sources and devices.

Currently there is no National Bureau of Standards (NBS) standard for Iodine-125 from which I-125 Seeds may be calibrated, nor is the NBS prepared at this time to provide one. (Communication with Thomas Loftus, Radiation Physics Division, Center for Radiation Research, National Measurement Laboratory, 301-921-2361, on 10/2/78). As a result, I-125 Seeds will be calibrated according to the procedure described below.

Each model 6711 I-125 Seed is assayed using a meter equipped with either a sodium iodide crystal or a plastic scintillation crystal. In the case of the sodium iodide (NaI) crystal (Figure 2), the source is held in a fixed geometry with its long axis parallel to the face of the crystal. In using a plastic scintillation crystal (Figure 3), the source is held in a fixed geometry with its long axis parallel to the internal face of a slot (5/16" wide by 1-3/4" deep) machined within the plastic crystal.

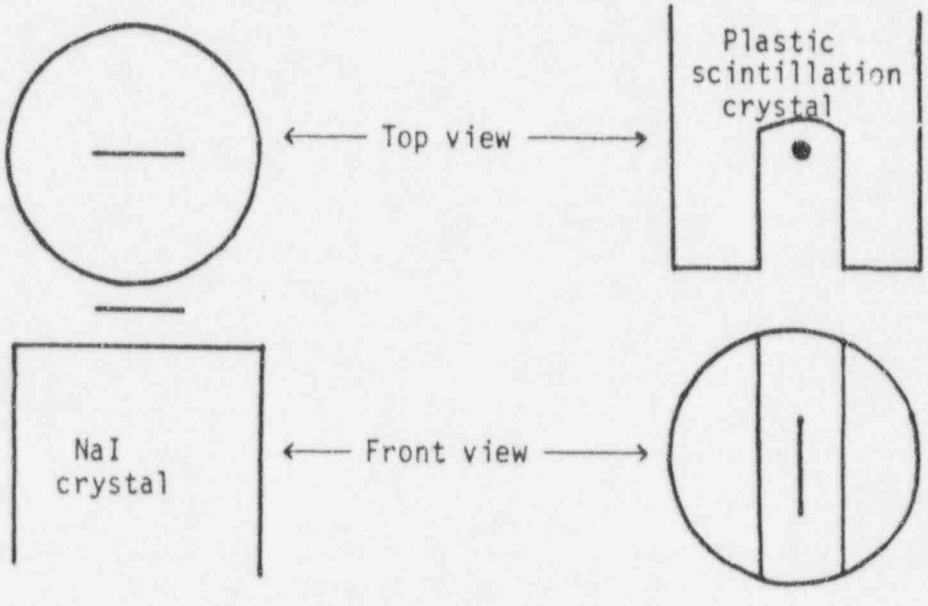


FIGURE 2

FIGURE 3

Both assay meters are calibrated using three standard sources (the maintenance and use of which is described in Appendix C), which bracket the activity range of the sources being sold.

The Model 6711 I-125 Seeds are assayed and then classified into logarithmically-arranged groups to allow for uniform decay accounting methods based on seven-day time increments. The activity ranges specified below are an example of typical ranges calculated in this manner.

Activity range (mCi comp.)

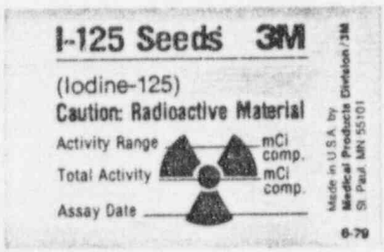
1.05+
.97 - 1.04
.89 - .96
.82 - .88
.76 - .81
.70 - .75
.65 - .69
.60 - .64
.55 - .59
.51 - .54
.47 - .50
.43 - .46
.40 - .42
.37 - .39
.34 - .36
.31 - .33

These listed ranges were based on the arithmetic mode selling range of 0.55-0.59 mCi comp. These activity ranges may be changed due to a shift in this arithmetic mode, as demonstrated by customer demand. Seeds with activities greater than 1.05 mCi comp. are assayed after appropriate decay intervals and grouped into the selected ranges as listed.

The subscript "comp." stands for "compensated", and is added to indicate that the assay allows for self-attenuation of radioactivity through the wall of the source. This allows the physicist to make dosimetry calculations based upon the "mCi comp." assay as though the seed were an unshielded source.

(vii) Legend and methods for labeling sources and devices as to their radioactive content.

Because of the small size of I-125 Seeds, it is not possible to label each source as to its radioactive content. I-125 Seeds supplied as a group of seeds with an assay within a stated range on the assay date, are packaged in a 1 dram, screw cap glass vial, onto which is affixed a label stating radioactive content, a sample of which is attached below. This label displays the caution symbol and is printed in colors to comply with the provisions of 10 CFR 32.72 and 10 CFR 20.203.



(viii) Instructions for handling and storing the source or device from the radiation safety standpoint; these instructions are to be included on a durable label attached to the source or device or attached to a permanent storage container for the source or device; provided, that instructions which are too lengthy for such label may be summarized on the label and printed in detail on a brochure which is referenced on the label.

The labeled vial containing I-125 Seeds is placed in either one of two lead storage/shipping containers, schematic diagrams for which are presented on the following pages as Figures 4 and 5. Instructions for handling and storing the I-125 Seeds are summarized on a label affixed to the lead containers, a sample of which is presented below for the model 6711. This label displays the caution symbol and is printed in colors to comply with the provisions of 10 CFR 32.72 and 10 CFR 20.203. Detailed instructions for handling and storing seeds are presented in the I-125 Seed package insert, which is referenced on the lead container label. One copy of the package insert, which is presented on pages 22-27, is supplied for each vial of I-125 Seeds in a shipment.

I-125 Seeds **3M**

Therapeutic For Interstitial Brachytherapy No. 6711

Made in U.S.A. by
Radiation Therapy Products
Medical Products Division/3M
St. Paul, MN 55101

DESCRIPTION: I-125 Seeds consist of a welded titanium capsule containing Iodine-125 adsorbed onto silver rod.

Activity range _____ mCi comp.

Total activity this vial _____ mCi comp.

Number of seeds _____ Assay Date _____

Lot no. _____

See package insert for instructions on handling and storage of I-125 Seeds.

Caution
Radioactive
Material

WARNING 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. **CAUTION** Federal law restricts this device to sale by or on the order of a physician. Maintain proper radiation safety precautions at all times.

2X80

Label for Lead Storage/Shipping Container - Model 6711

The labeled lead container is then placed in a U.S.A. DOT 7A, Type A cardboard shipping container, lined with styrofoam. One certification sheet (page 29) and the appropriate number of package inserts are included with each shipment, and the box is sealed with suitable packaging tape.

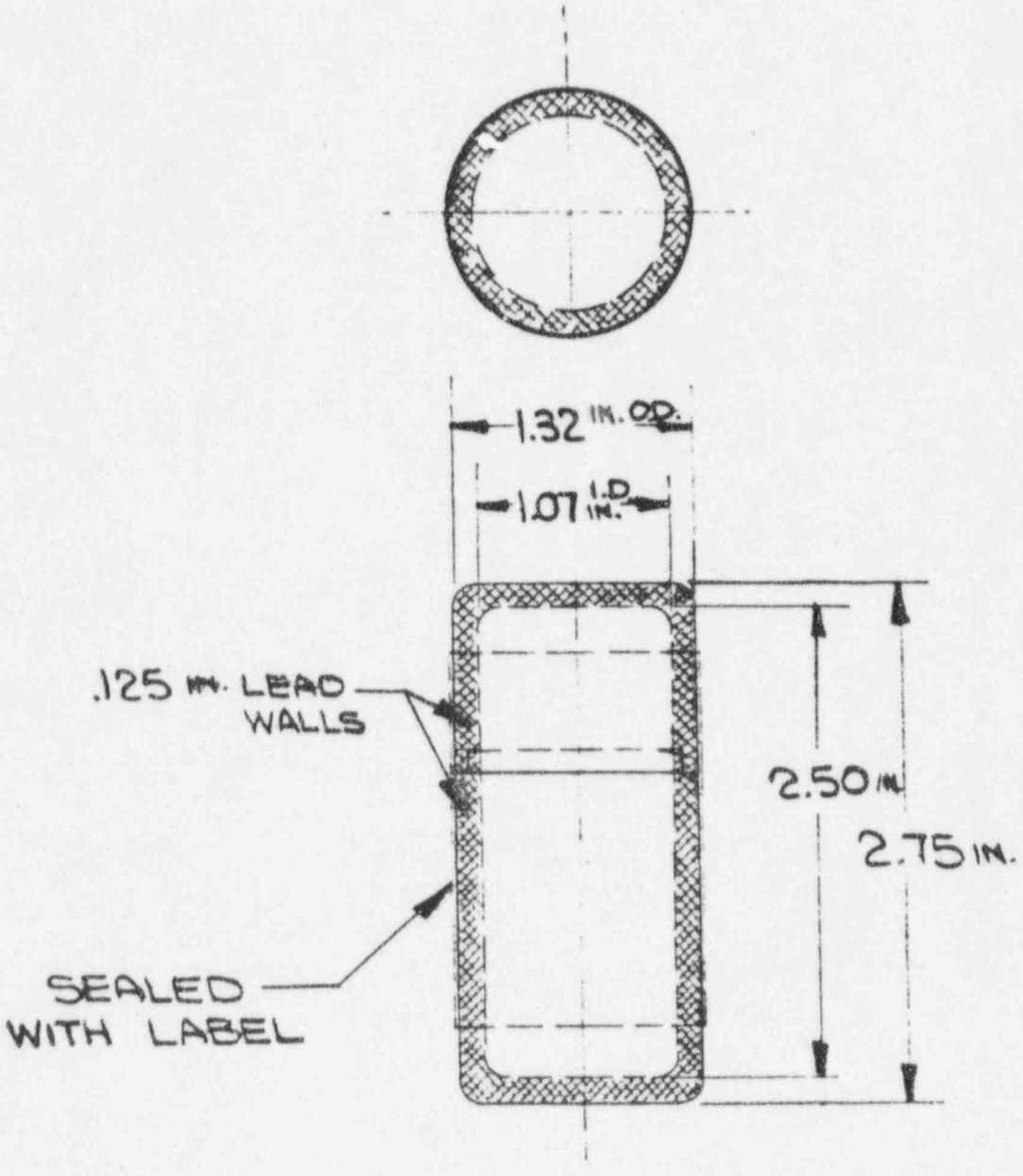


FIGURE 4. Lead Storage/Shipping Container - I-125 Seeds

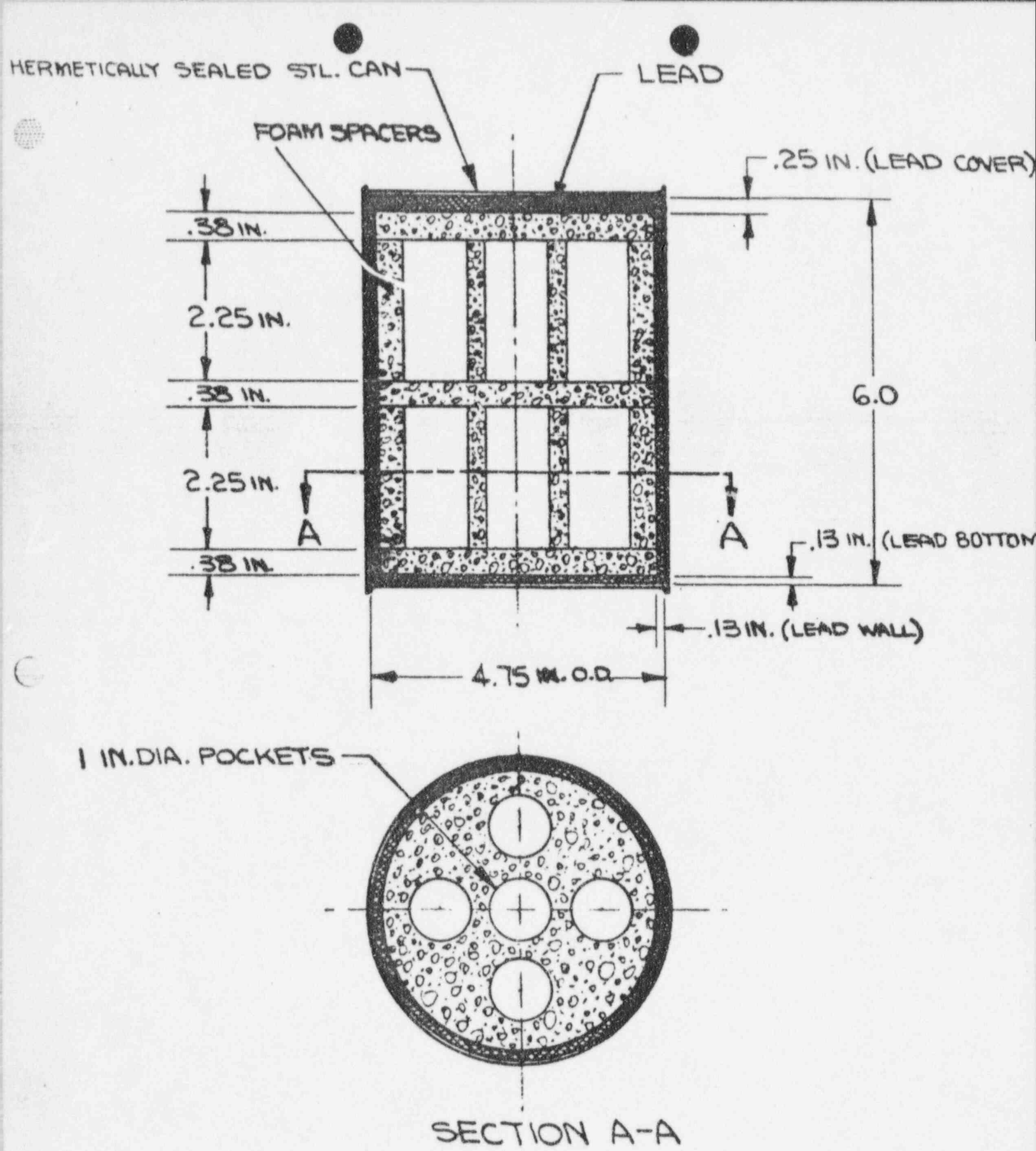
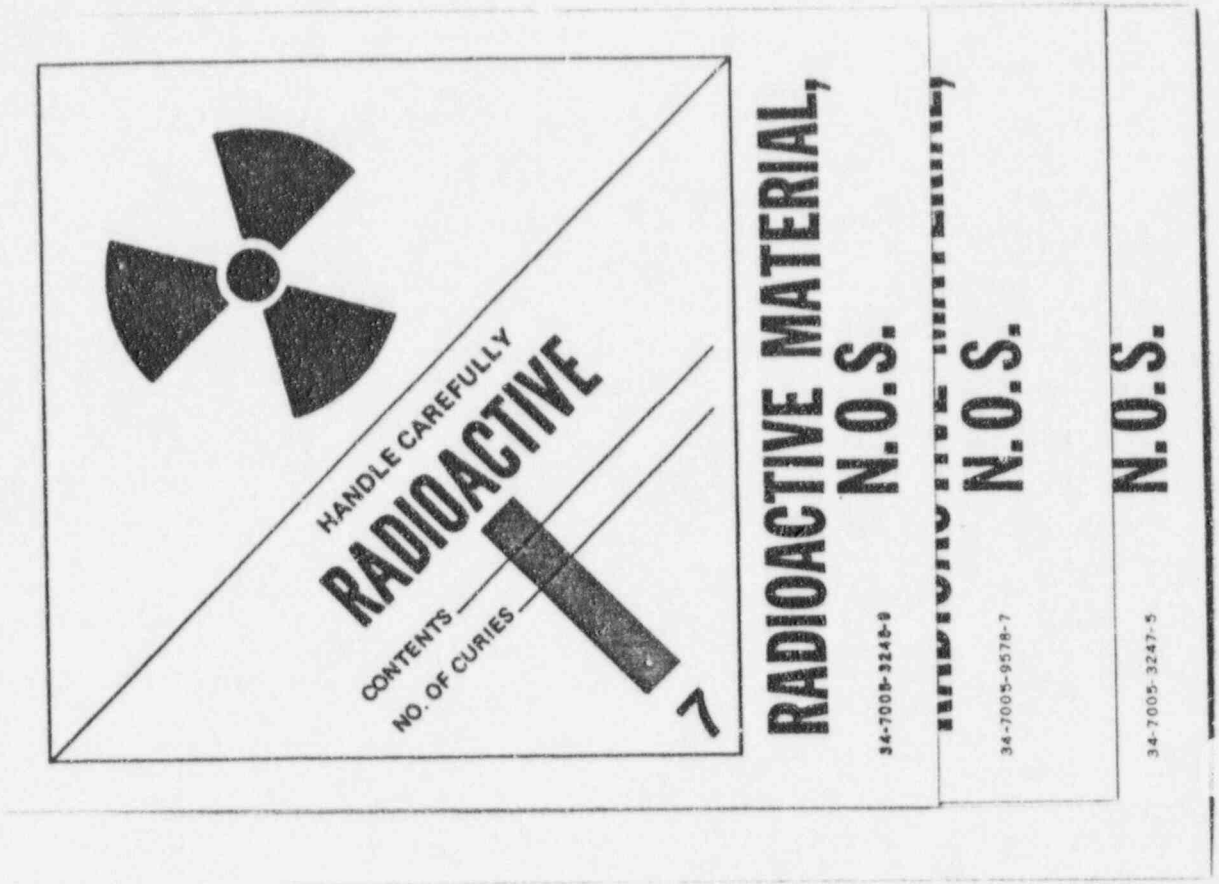


FIGURE 5. Lead-lined Storage/Shipping Container - I-125 Seeds

The sealed shipping carton, identified with the phrases "U.S.A. DOT 7A Type A" and "Radioactive Material N.O.S.", is then labeled with one of the three labels attached below.



The sealed shipping carton is labeled with the label attached below.

From **Diagnostic Products/3M**
TCAAP 590
New Brighton, Minnesota 55112

3M

Form 6550 225-A PWO

Lastly, a standard Shipper's Certification for Radioactive materials, Form 13906-2, is affixed to the outside of each shipping carton. A sample of this form is presented on the following page.

Form 13906-4

SHIPPER'S CERTIFICATION FOR RADIOACTIVE MATERIALS

Two completed and signed copies of this certification shall be handed to the carrier.
(Use block letters)

WARNING: Failure to comply in all respects with the IATA Restricted Articles Regulations may be a breach of the applicable law, subject to legal penalties. This Certification shall in no circumstances be signed by a Consolidator, a forwarder, or an IATA Cargo Agent.

This consignment is within the limitations prescribed for: *(mark one)*

☐ both passenger and cargo aircraft ☐ only cargo aircraft

NATURE AND QUANTITY OF CONTENT				PACKA -			
RADIONUCLIDE	GROUP	FORM	ACTIVITY	Number of Packages	CATEGORY	TRANSPORT INDEX	TYPE
NAME OR SYMBOL OF PRINCIPAL RADIOACTIVE CONTENT	GROUP NUMBER OF GROUPS I TO VII	CHEMICAL FORM AND PHYSICAL STATE (GAS/ LIQUID/SOLID), or SPECIAL FORM, or SPECIAL ENCAPSULATION	NUMBER OF CURIES, or MILLI-CURIES		I – WHITE or II – YELLOW or III – YELLOW LABEL	FOR YELLOW LABEL CATEGORIES ONLY	INDUSTRIAL or TYPE A, or TYPE B

ADDITIONAL INFORMATION REQUIRED FOR FISSILE MATERIALS ONLY

EXEMPTED FROM THE ADDITIONAL REQUIREMENTS FOR FISSILE MATERIALS SPECIFIED IN 7.1. OF PART 2 OF THE IATA RESTRICTED ARTICLES REGULATIONS ☐

NAMES, PLUS QUANTITY IN GRAMS, OR CONCENTRATION OR ENRICHMENT IN U235:

NOT EXEMPTED: FISSILE CLASS I ☐ FISSILE CLASS II ☐ FISSILE CLASS III ☐

Additional certificates obtained by the Shipper when necessary:

Special Form Encapsulation Certificate(s) ☐
Type "B" Packaging Certificate(s) ☐
Certificate(s) for Fissile Material ☐
Certificate(s) for Large Radioactive Source ☐
Government Approvals/Permits ☐

Special Handling Information

I hereby certify that the contents of this consignement are fully and accurately described above by Proper Shipping Name and are classified, packed, marked, labelled and in proper condition for carriage by air according to the current Edition of the IATA Restricted Articles Regulations and all applicable carrier and governmental regulations. I acknowledge that I may be liable for damages resulting from any misstatement or omission and I further agree that any air carrier involved in the shipment of this consignment may rely upon this Certification.

Name and full address of Shipper	Name and title of person signing Certification
Date	Signature of the Shipper (see **WARNING** above)

Air Waybill No.*	Airport of Departure*	Airport of Destination*

* This box is optional for completion by issuing carrier.

Form 13906-4

SHIPPER'S CERTIFICATION FOR RADIOACTIVE MATERIALS

Two completed and signed copies of this certification shall be handed to the carrier.
(Use block letters)

WARNING: Failure to comply in all respects with the IATA Restricted Articles Regulations may be a breach of the applicable law, subject to legal penalties. This Certification shall in no circumstances be signed by a Consolidator, a forwarder, or an IATA Cargo Agent.

This consignment is within the limitations prescribed for: *(mark one)*

☐ both passenger and cargo aircraft ☐ only cargo aircraft

NATURE AND QUANTITY OF CONTENT				PACKAGE			
RADIONUCLIDE	GROUP	FORM	ACTIVITY	Number of Packages	CATEGORY	TRANSPORT INDEX	TYPE
NAME OR SYMBOL OF PRINCIPAL RADIOACTIVE CONTENT	GROUP NUMBER OF GROUPS I TO VII	CHEMICAL FORM AND PHYSICAL STATE (GAS/LIQUID/SOLID), or SPECIAL FORM, or SPECIAL ENCAPSULATION	NUMBER OF CURIES, or MILLI-CURIES		I – WHITE or II – YELLOW or III – YELLOW LABEL	FOR YELLOW LABEL CATEGORIES ONLY	INDUSTRIAL or TYPE A, or TYPE B

ADDITIONAL INFORMATION REQUIRED FOR FISSILE MATERIALS ONLY

EXEMPTED FROM THE ADDITIONAL REQUIREMENTS FOR FISSILE MATERIALS SPECIFIED IN 7.1. OF PART 2 OF THE IATA RESTRICTED ARTICLES REGULATIONS ☐

NAMES, PLUS QUANTITY IN GRAMS, OR CONCENTRATION OR ENRICHMENT IN U235:

NOT EXEMPTED: FISSILE CLASS I ☐ FISSILE CLASS II ☐ FISSILE CLASS III ☐

Additional certificates obtained by the Shipper when necessary:

Special Form Encapsulation Certificate(s) ☐
Type "B" Packaging Certificate(s) ☐
Certificate(s) for Fissile Material ☐
Certificate(s) for Large Radioactive Source ☐
Government Approvals/Permits ☐

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Name and full address of Shipper	Name and title of person signing Certification
Date	Signature of the Shipper (see WARNING above)

Air Waybill No.*	Airport of Departure*	Airport of Destination*

* This box is optional for completion by issuing carrier.

19

Form 13906-4

SHIPPER'S CERTIFICATION FOR RADIOACTIVE MATERIALS

Two completed and signed copies of this certification shall be handed to the carrier.
(Use block letters)

WARNING: Failure to comply in all respects with the IATA Restricted Articles Regulations may be a breach of the applicable law, subject to legal penalties. This Certification shall in no circumstances be signed by a Consolidator, a forwarder, or an IATA Cargo Agent.

This consignment is within the limitations prescribed for: *(mark one)*

☐ both passenger and cargo aircraft ☐ only cargo aircraft

NATURE AND QUANTITY OF CONTENT				PACKAGE			
RADIONUCLIDE	GROUP	FORM	ACTIVITY	Number of Packages	CATEGORY	TRANSPORT INDEX	TYPE
NAME OR SYMBOL OF PRINCIPAL RADIOACTIVE CONTENT	GROUP NUMBER OF GROUPS I TO VII	CHEMICAL FORM AND PHYSICAL STATE (GAS/ LIQUID/SOLID), or SPECIAL FORM, or SPECIAL ENCAPSULATION	NUMBER OF CURIES, or MILLI-CURIES		I – WHITE or II – YELLOW or III – YELLOW LABEL	FOR YELLOW LABEL CATEGORIES ONLY	INDUSTRIAL or TYPE A, or TYPE B

ADDITIONAL INFORMATION REQUIRED FOR FISSILE MATERIALS ONLY

EXEMPTED FROM THE ADDITIONAL REQUIREMENTS FOR FISSILE MATERIALS SPECIFIED IN 7.1. OF PART 2 OF THE IATA RESTRICTED ARTICLES REGULATIONS ☐

NAMES, PLUS QUANTITY IN GRAMS, OR CONCENTRATION OR ENRICHMENT IN U235:

NOT EXEMPTED: FISSILE CLASS I ☐ FISSILE CLASS II ☐ FISSILE CLASS III ☐

Additional certificates obtained by the Shipper when necessary:

Special Form Encapsulation Certificate(s) ☐
Type "B" Packaging Certificate(s) ☐
Certificate(s) for Fissile Material ☐
Certificate(s) for Large Radioactive Source ☐
Government Approvals/Permits ☐

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Date	Signature of the Shipper (see WARNING above)

Air Waybill No.*	Airport of Departure*	Airport of Destination*

* This box is optional for completion by issuing carrier.

19

PACKAGE INSERT

FOR

I-125 SEEDS[R]

MODEL 6711

Medical Products Division/3M

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

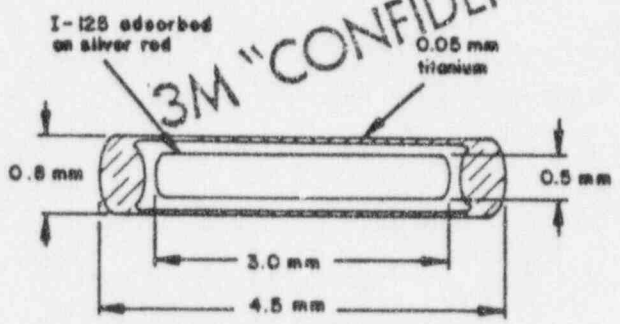
January, 1980

I-125 SEEDS®

No. 6711

DESCRIPTION

I-125 Seeds 6711 consist of a welded titanium capsule containing iodine-125 adsorbed onto a silver rod.



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 factors at selected days after the assay date are shown in table below.

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
20	0.794	44	0.603	68	0.457
22	0.776	46	0.589	70	0.447

Radiation Protection

The half value thickness of lead for iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% 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 together with the silver rod, results in a total self-absorption of approximately 35%.

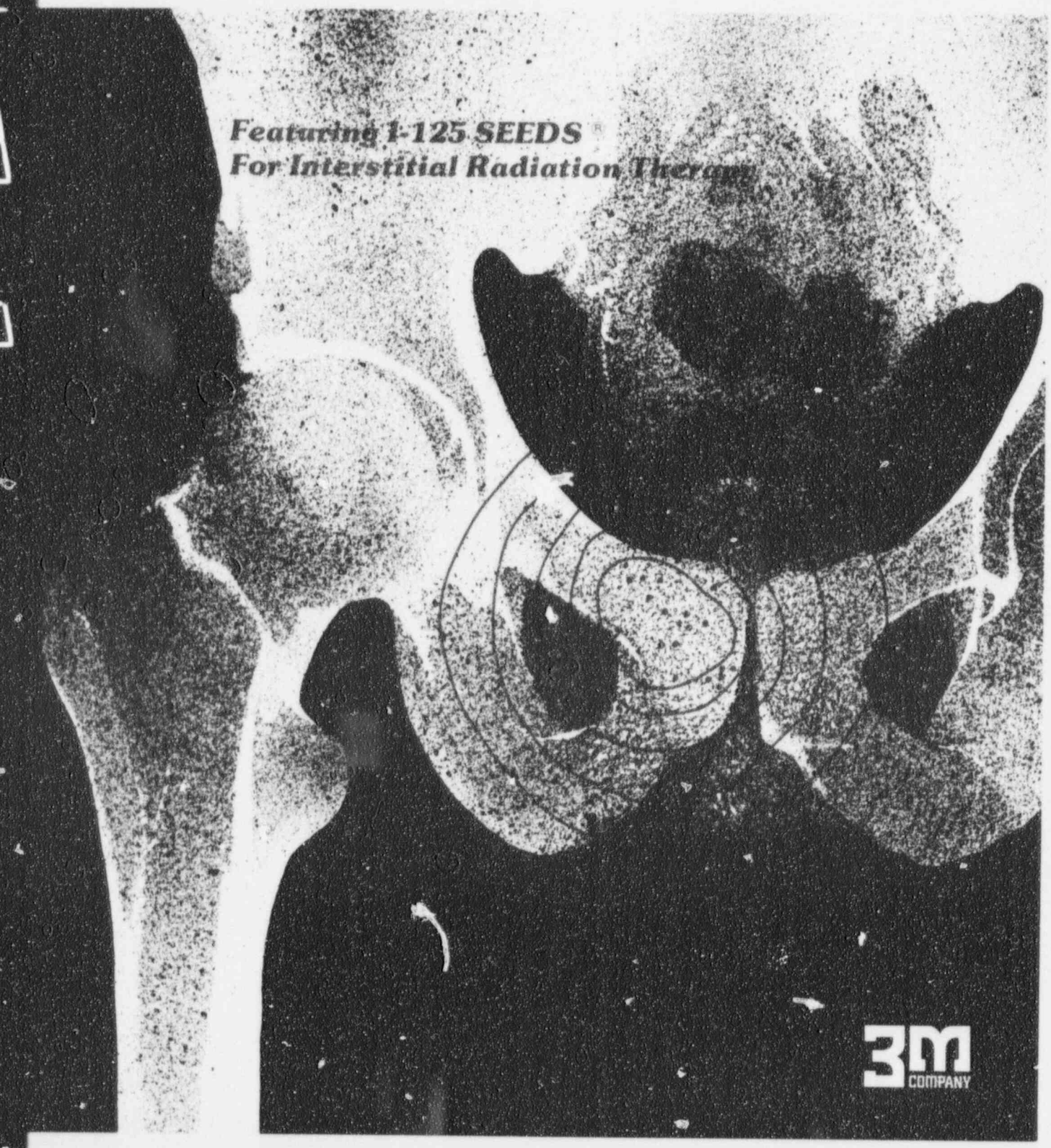
INDICATIONS

I-125 Seeds with activities from 0.1 to 1.0 mCi comp. are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, slow growth rate, and low to moderate radiosensitivity. Seeds in this activity range may be used to treat superficial, intraabdominal, and intrathoracic tumors. Tumors of the head, neck, lung, pancreas, and prostate (early stages) are commonly treated.

I-125 Seeds with activities greater than 1.0 mCi comp. are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, and moderate radiosensitivity. These seeds may be used for selected radiation applications as removable implants.

EMI BRAND

RADIATION THERAPY PRODUCTS



Featuring I-125 SEEDS®
For Interstitial Radiation Therapy

3M COMPANY

3M BRAND I-125 SEEDS®

- An ideal source for permanent interstitial implants
- Provides intense localized x-radiation
- Unique handling convenience

Development

3M Brand I-125 Seeds have been developed as a superior source for permanent interstitial implants[1]. Earlier sources, such as gold grains or radon seeds, have been limited by radiation exposure and scheduling restrictions due to their penetrating radiations and short half lives[2]. The soft x-rays from Iodine-125 Seeds are easy to shield, the dose rate is low and the shelf life is approximately 5 weeks (Table 1).

The availability of a safe, convenient brachytherapy source meets the critical requirements for a treatment technique which can be applied where surgery, chemotherapy or external beam irradiation are insufficient or inappropriate.

Clinical experience, dating from 1965, has shown that I-125 Seeds are an extremely effective method of delivering radiation to a tumor. The potential for obtaining 80% tumor control rate has been demonstrated for several tumor types when the minimal effective tumor dose of 16,000 rads is delivered[3,4].

I-125 Seeds can extend the capability of a radiation therapy department.

Design

Active Source	Iodine-125
Radiation Emitted	27-35 keV x-rays
Half Life	60 days
Protection-Lead HVL	0.025 mm
Range-Tissue HVL	2 cm
Format	Titanium capsules

Titanium encapsulation assures good tissue compatibility, and reduces the total self-absorption to approximately 25%. The gold x-ray marker is included to improve visualization on radiographs (Figure 1).

I-125 Seeds are small enough to be implanted with a minimum of tissue trauma (they will pass through a #17 gauge needle).

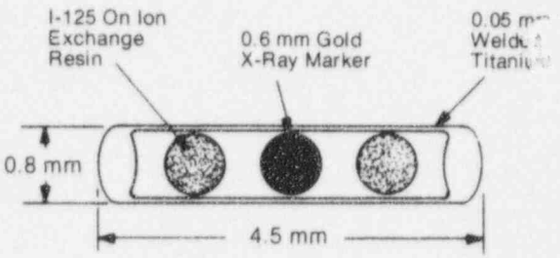


Figure 1. I-125 Seed design

Indications for Use

I-125 Seed implants may be indicated when a tumor has the following characteristics:

- Unresectable
- Localized
- Size less than 7 to 3 cm
- Slow growth rate
- Low to moderate radiosensitivity

The tumor may be superficial, intraabdominal or intrathoracic. I-125 Seeds are commonly used to treat tumors of the lung, pancreas and prostate. The prostate protocol should be used for stage B and early stage C[5] (Figure 2).

I-125 Seeds are widely used to treat residual tumors following the completion of a course of external radiation. Similarly, many recurrent tumors may be i[illegible]

Patient tolerance of the p[illegible]ent proc[illegible]ally good. The treatment is ther[illegible]e frequen[illegible]plied to tumors which might otherwise be managed by more traumatic modalities.

Table 1. Radionuclides for interstitial implants

Isotope	Half Life (days)	Emitted Energy Alpha	Beta (Max.)	Gamma	Half Value Layer (lead)	Half Value Layer (tissue)
Iodine-125	60.0	none	none	27-35 keV	0.025 mm	2 cm
Iridium-192	74.4	none	670 keV	300-610 keV	4.5 mm	6 cm
Gold-198	2.7	none	960 keV	410 keV	4.5 mm	6 cm
Radon-222	3.8	yes	70-3260 keV	50-2440 keV	13.0 mm	10 cm

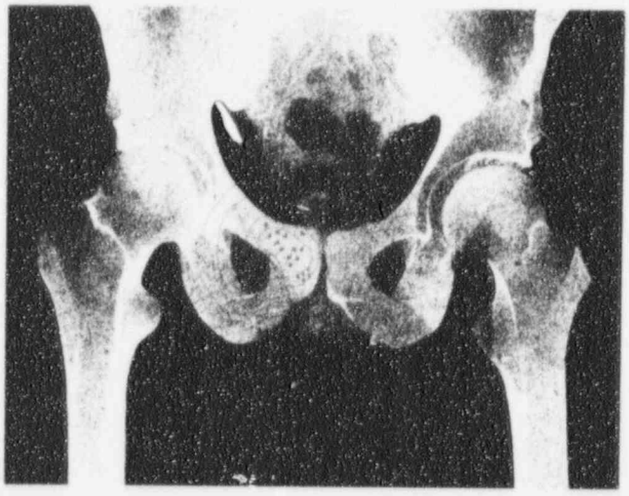


Figure 2. Computer-calculated isodose curves for prostate implanted with 19 I-125 Seeds.

Patient Benefits

Permanent implants require only a single simple surgical procedure. Many implants are performed under local anesthesia. Hospitalization is minimized and patients avoid the expense, inconvenience and emotional burden of a long hospital stay or daily visits to radiation therapy clinics. Hospitalized patients also benefit because the simplified radiation protection requirements frequently eliminate the necessity for expensive isolated accommodations[6].

A major benefit of I-125 Seed implants is the reduced morbidity. The procedure is usually quick, seeds are well-tolerated by the implanted tissue and the volume of irradiated tissue is small due to the rapid fall-off outside the implanted tumor. Consequently, patient discomfort is minimized and complications are considerably less frequent than for other modalities[3].

Permanent implants are usually simpler and faster to execute than removable implants. The risk of infection, surgical complications and radiation exposure are proportionally reduced[10].

Medical Personnel Benefits

The primary reason for the development of I-125 Seeds was the need to reduce the radiation exposure being accumulated by medical personnel who were performing implants using Radon-222 or Gold-198 sources[1]. Both of these isotopes emit a high energy gamma and generate a relatively high dose rate. It was not practical to provide sufficient shielding to protect the physicians or the nursing staff involved in these implant procedures. At many institutions, the accumulated exposure to the staff gave cause for concern.

Iodine-125 was selected as the best available isotope to minimize the risks of exposure. The 30 keV x-ray could be easily shielded. Technicians preparing the I-125 Seeds for an implant could safely work with thin metal shields and lead glass screens providing 99% protection. Lead-impregnated gloves are available and afford more than 70% protection even when handling unshielded sources.

Iodine-125 has a 60-day life, and the 0.55 mCi nominal activity seeds produce a low dose rate. As a result, even when the physician finds it necessary to be in close proximity to an unshielded source, the total exposure is minimal.

Another advantage of I-125 Seeds is that the patient represents very little hazard to either nursing staff or the patient's associates. The release of patients from the hospital is normally controlled according to the recommendations in the handbook NCRP 37. These recommendations are based upon the exposure rate at one meter from the patient, and for I-125 Seeds there are fewer restrictions than for most other isotopes.

The net effect of the introduction of Iodine 125 has been to eliminate the personnel exposure hazard as a limitation in the utilization of permanent implants in radiation therapy.

Implant Techniques

The use of I-125 Seeds does not require complex or expensive equipment. I-125 Seeds will pass through a #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 (the Royal Marsden Gold Grain Gun will *not* accept I-125 Seeds).

Individual seeds may be implanted using the familiar radon seed implanters.

Surface Applicators

The success of I-125 Seeds in permanent implants has led to investigations of Iodine-125 in surface applicators, particularly for treatment of intraocular tumors[8].

Radiation Protection

I-125 Seeds were developed specifically to minimize radiation exposure to medical personnel during implant procedures. The 30 keV x-rays of Iodine-125 are highly absorbed by any high Z material while simultaneously maintaining a desirable penetration in low Z tissue. In addition, exposure is limited by the low specific output due to the 60-day half life.

Lead	HVL =	0.025 mm
Gold	HVL =	0.01 mm
Tissue	HVL =	20.0 mm

A thin lead sheet of only 0.25 mm (0.01 in.) provides a 99.9% reduction in exposure. Lead-impregnated vinyl is available for gloves or bandages which may be used when handling the seeds or for shielding incorporated in the dressing of an implanted superficial tumor.

When reasonable precautions are taken using thin lead wrapping, i.e., forceps to handle the sources, etc., the physician can anticipate receiving very little exposure during an I-125 Seed implant[1].

Radiobiology

Recent studies suggest that I-125 Seeds have a higher therapeutic ratio than Radon-222 or Iridium-192[14]. The radiobiological basis for such a superiority is not clearly understood. Among many factors, three principal explanations might be advanced to account for the effectiveness of the Iodine implants: low dose rate, a sustained continuous irradiation, and a possible high RBE of low energy gamma radiation from the Iodine seeds[10].

Low energy x-rays produce secondary electrons with ionizing density characteristics similar to high LET sources[9]. This should result in an RBE close to 1.3[15].

Tumor Regression

The 60-day half life produces another phenomenon which enhances clinical effectiveness. Most implanted tumors regress some 50% during the first 30 days[14]. As the seeds are contained within the tumor, the seeds are drawn closer together. The dose to the remaining viable tumor and previously anoxic cells may thus be increased despite the isotope's decay.

Dosimetry

The percent depth dose within 4 cm of an I-125 Seed follows closely to the inverse square law[1]. In the regions more than 4 cm from the seed, tissue attenuation becomes more important and the dose falls off rapidly[1]. Most treatment planning computer systems provide a program specifically for I-125 Seeds. These typically incorporate a look-up table.

The rapid fall-off of dose beyond 4 cm from the periphery of an implant minimizes the volume of surrounding healthy tissue which is irradiated. The volume irradiated at the 10% level is less than half the volume irradiated by an equivalent gold grain implant[1,10].

A comparison of an I-125 implant with external beam dosimetry shows that an optimum 6 MV, 360° rotation treatment of a prostate would irradiate 10 times the tissue volume that receives 25% or more of a given tumor dose (Figure 3).

The small irradiated volume explains why high tumor doses have been prescribed for I-125 Seed implants with minimal tissue complications.

It has been noted that the angular distribution of radiation around each seed is anisotropic due to the presence of the gold-x-ray marker and the weld ends[11]. Crossfiring, tumor regression, and tissue movement combine to reduce the effect of this shadowing.

Implant Calculation – "Dimension Averaging"

A simple but effective empirical formula has been developed to calculate the activity required to treat a given tumor.[12] Clinical experience has shown that the mCi (comp.) implanted is proportional to the average of the three mutually perpendicular dimensions of the tumor d_a

$$\text{Average Dimension } d_a = \frac{(A+B+C)}{3} \text{ cm}$$

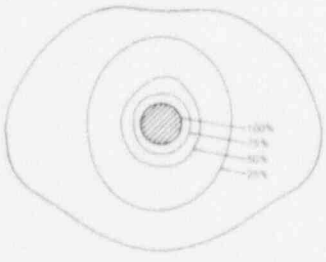
Activity Required

$A = 5\, d_a$ where $d_a \leq 2.4$ cm

$A = 3.87\, d_a^{1.293}$ where $2.4 \text{ cm} < d_a \leq 3.24$ cm

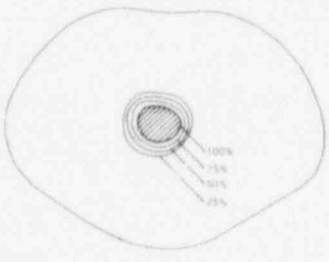
$A = 2.76\, d_a^{1.581}$ where $3.24 \text{ cm} < d_a$

External Beam Prostate Treatment



6 MV, 360° rotation, external beam. Rectum receives 65% tumor dose.

I-125 Seed Prostate Treatment



I-125 Seed implant. Rectum receives only 30% tumor dose.

Figure 3. Comparison of prostate treatment with external beam vs I-125 Seed implant

Seed Spacing Nomograph

To permit rapid calculation of the preceding formulas, a simple nomograph has been developed. Using the tumor volume (average dimension) and the average seed strength, one can approximate directly from the nomograph the number of seeds needed and the seed spacing required to carry out the implant. The nomograph is shown in Figures 4a and 4b.*

Example

A 3 x 4 x 2 cm tumor (Average Dimension is [3 + 4 + 2]/3 = 3 cm) is to be implanted with I-125 Seeds of 0.5 mCi comp. activity. The spacing along the needle is to be 1.0 cm.

In Figure 4a, a line connecting 0.5 mCi on the Seed Strength scale with 3.0 cm on the Average Dimension scale intersects at 32 for the Number of Seeds.

In Figure 4b, a line connecting 0.5 mCi on the Seed Strength scale and 3.0 cm on the Average Dimension scale is extended to intersect the Tie Line. A second line is drawn between the Tie Line intersection and the 1.0 cm point on the Spacing Along Needle scale. Extension of this line allows the needle spacing to be read at the point of intersection on the Spacing Between Needles scale, 0.6 cm.

By using the nomograph, one can determine total recommended activity, desired number of seeds and spacing between needles.

Definition of "mCi" Comp.

The assay of I-125 Seeds is now stated in mCi comp. (compensated). This indicates that the seed behaves equivalent to a point source of the stated activity. This compensated assay allows the user to ignore self-absorption of approximately 25% within the seed.

Specific Dose Rate Factor

The bulk of published clinical data on the use of I-125 Seeds originates from Memorial Hospital for Cancer, New York. The clinical doses described in all publications between 1965-1978 are based upon an absorbed dose factor of 1.68 rads cm^2/mCi hr at 1 cm. This figure has been revised by recent measurements.

Krishnaswamy[13] has shown that the specific dose rate factor at 1 cm for a point transverse to the axis of the seed is 1.32 rads cm^2/mCi hr. This figure does not take into account the attenuation of exposure along the axis of the seed due to the gold x-ray marker and the weld ends. Integrating over 4π results in a 14% reduction in integral dose. Consequently, in order to calculate dose to the tumor volume a Specific Dose Rate Factor of 1.1 rad cm^2/mCi hr at 1 cm should be used[14]. Clinical dosimetry reported from Memorial Hospital after 6/15/78 will use the revised specific dose rate factor.

If dosimetry calculations are made using any revised values for the specific dose rate factor, it is important that the prescribed doses equivalent to Memorial Hospital protocols are proportionately reduced.

I-125 Seed Spacing Nomograph[12]

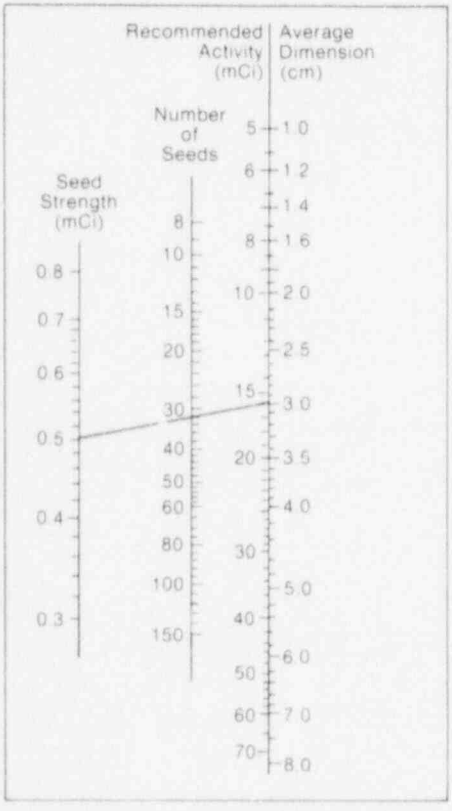


Figure 4a

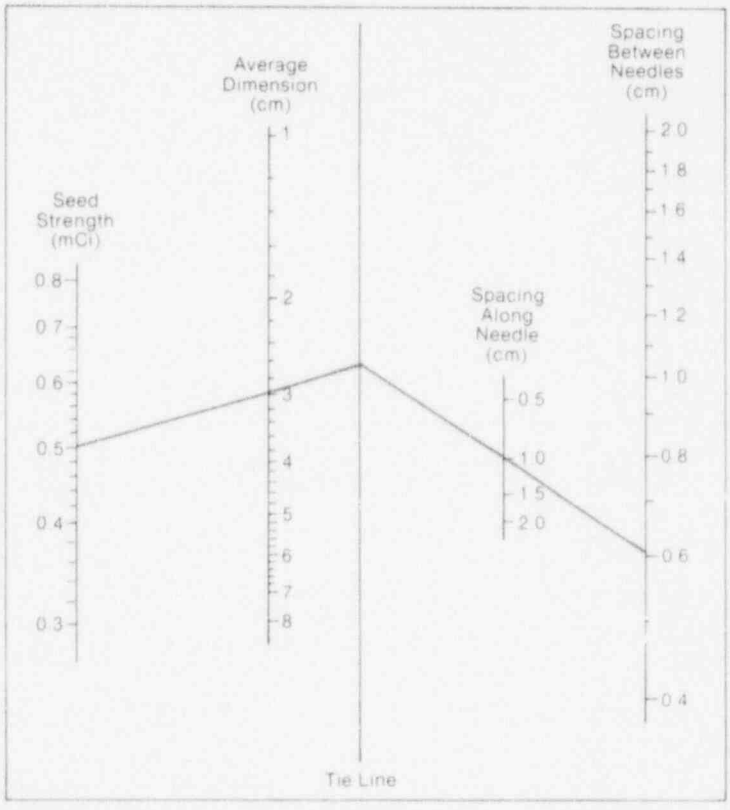


Figure 4b

*The determinations made from the Nomograph must be considered to be approximations only.

Licensing

In June, 1975, the U.S. Nuclear Regulatory Commission classified I-125 Seeds as a well-established clinical procedure and added the seeds to Group VI of 10 CFR, 35.100. Most Agreement States have similar regulations.

Before a shipment of I-125 Seeds can be made, 3M (Sunnyvale) must have a copy of your NRC (or Agreement State) license and amendments on file.

Sterilization

I-125 Seeds are **NOT** sterile when shipped. It is recommended that autoclave or ethylene oxide (EtO) sterilization be employed.

Quality Assurance

All seeds receive x-ray and microscope inspection and are individually assayed before shipment. Seeds are leak-tested to assure no significant removable contamination. All seeds are autoclaved prior to final leak test.

Storage

A principal feature of I-125 Seeds is that a physician can order a quantity of seeds and store them at the hospital. Iodine-125 has a 60-day half life and the seeds have a nominal activity of 0.55 mCi comp. when shipped. Their shelf life is approximately 5 weeks. This eliminates requirements for precise patient scheduling and allows a busy department to hold seeds ready for an urgent implant.

Delivery

Shipments are made within 10 days after receipt of an order. (Emergency supplies may be available on 48 hours' notice.) Shipment is via airfreight, both domestic and international.

Prices*

All prices quoted are FOB 3M, Sunnyvale, California.

Specifications*

I-125 Seeds:	
Nominal activity	0.55 mCi comp/seed
Seed dimension	4.5 mm × 0.8 mm
Emission energy	27-35 keV x-rays
Iodine-126 content	less than 0.5%

*Specifications and prices are subject to change without notice.

References

1) *Use of Iodine-125 for Interstitial Implants*, Govt. Print Office, No. 017-015-00094-0, 1975.
2) B. S. Hilaris et al: Cancer 22 p. 745–751, 1968, "Techniques of Interstitial and Intracavitary Radiation."
3) B. S. Hilaris et al: Am J Roentgenol Radium Ther Nucl Med 126 (No. 1) p. 171–178, 1976, "Low Energy Radionuclides for Interstitial Implantation."
4) B. S. Hilaris et al: Annals Thoracic Surgery 20 (No. 5) p. 491–500, 1975, "Interstitial Irradiation for Unresectable Carcinoma of the Lung."
5) B. S. Hilaris et al: Am. J. Roentgenol 121 (No. 4) p. 832–838, 1974, "Radiation Therapy and Pelvic Node Dissection in the Management of Cancer of the Prostate."
6) National Council on Radiation Protection (NCRP) Report No. 37.
7) C. G. Orton et al: Int. J. Radiation Oncology Biol. Phys. 2 p. 55–60, 1977, "Time-Dose Factor (TDF) Analysis of Dose Rate Effects in Permanent Implant Dosimetry."
8) R. Sealy et al: Br. J. Radiol. 49 p. 551–554, 1976, "The Treatment of Ophthalmic Tumors with Low-Energy Sources."
9) Bondura et al: Int. J. Radiat. Biol. 28 p. 539–548, 1975, "RBE of 50 kVp Xrays."
10) The Handbook of Interstitial Brachytherapy, edited by B. S. Hilaris, M.D., published by Publishing Sciences Group Inc., Acton, Mass. 1975.
11) C. Ling: Private Communication, Massachusetts General Hospital, 1976.
12) L. L. Anderson: Private Communication—to be published. Presented at International Endocurietherapy Meeting, LAC/USC, Los Angeles, 6/30/78 - 7/2/78.
13) V. Krishnaswamy: Radiology 126 p. 489–491, 1978, "Dose Distribution around an I-125 Seed Source in Tissue."
14) J. H. Kim et al: Am. J. Roentgenol 123 (No. 1) p. 163–169, 1975, "Iodine 125 Source in Interstitial Tumor Therapy."
15) L. Zeitz et al: Radiat. Res. 70 p. 552–563, 1977, "Determination of Relative Biological Effectiveness (RBE) of Soft X-rays."

Patents

U.S.	Patent No. 3,351,049
British	Patent No. 1,133,219
Canadian	Patent No. 830,573

For further information, write or call:

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Medical Products Division/3M
1246 Birchwood Drive*
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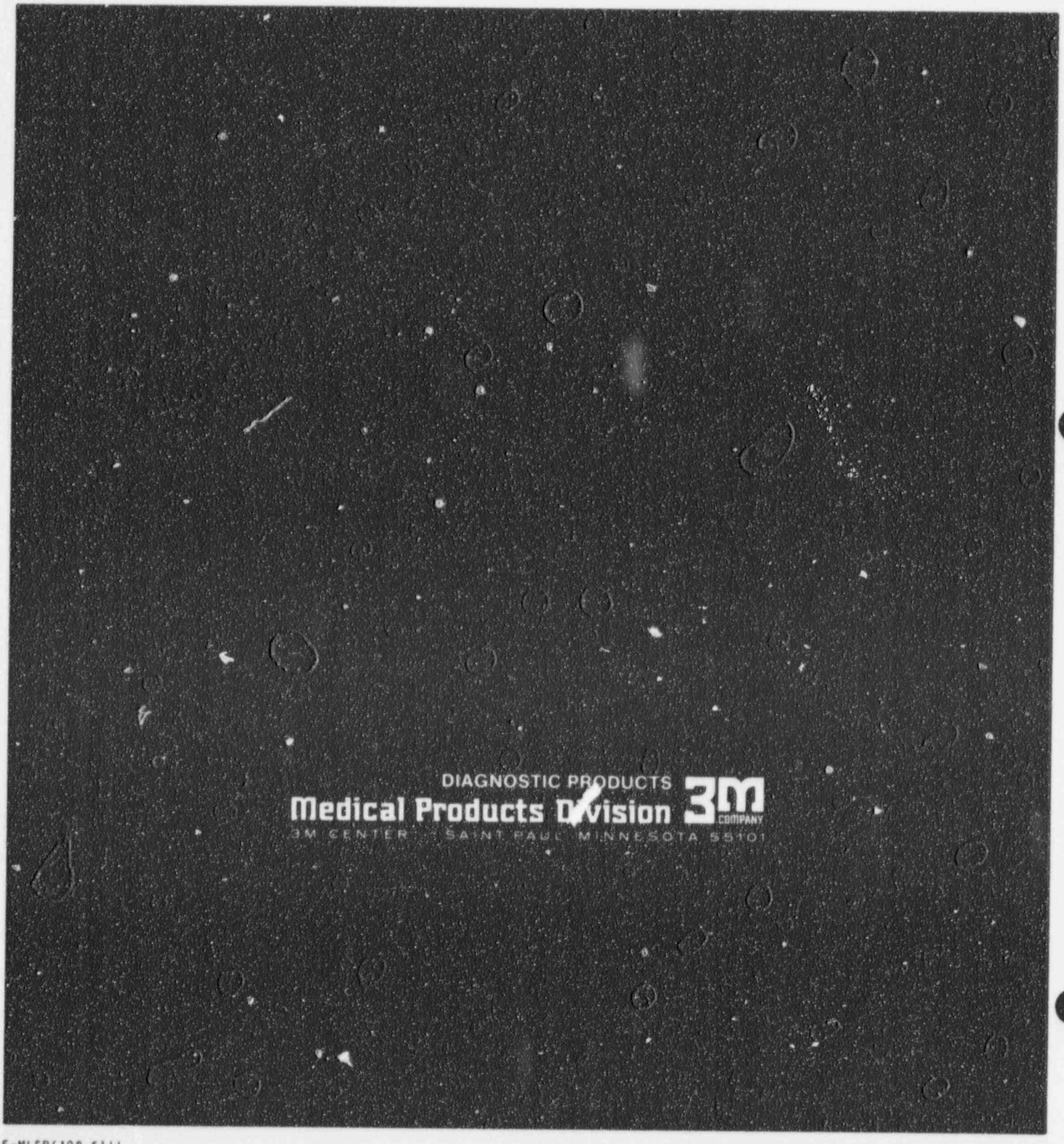
(408) 734-8911

*formerly Lawrence Soft Ray Corporation



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Litho in U.S.A. with 3M BRAND Photo Offset Plates, Film and Chemicals.

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

June 14, 1990

MEMORANDUM FOR: William Adam
Material Licensing Section,
Region III

FROM: Steven Baggett
Medical, Academic and Commercial
Use Safety Branch, NMSS

SUBJECT: SSD TECHNICAL ASSISTANCE REQUEST DATED 10/13/89-3M's REQUEST FOR RENEWAL OF LICENSE NUMBER 22-00057-59MD, CONTROL # 87687

Based on the information provided by the applicant, we have revised the Registry sheets for the brachytherapy sources. Please find enclosed copes of the registration certificates for those sources that 3M will continue to distribute. Certificates for those sources that are being discontinued will be forthcoming.

Please forward a copy of the enclosed registration certificates to the licensee and request that they read over the certificates and notify us immediately if there are any errors.

If you have any questions please call me at FTS 492-0542.

Steven Baggett
Medical, Academic and Commercial
Use Safety Branch, NMSS

Enclosure:
Registration Certificate numbers NR-460-S-137-S
NR-460-S-151-S
NR-460-S-166-S
NR-460-S-167-S
NR-460-S-169-S

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