

Mills
Biopharmaceuticals, Inc.

120 N.E. 26TH STREET
OKLAHOMA CITY, OKLAHOMA 73105
405-525-3141
405-525-3143 FAX

August 2, 1999

Mr. Sudhamay Basu
U.S. N.R.C.
Materials Safety Branch
Division of Industrial and Medical Nuclear Safety
Two White Flint North Rockville Pike
North Bethesda, MD 50852

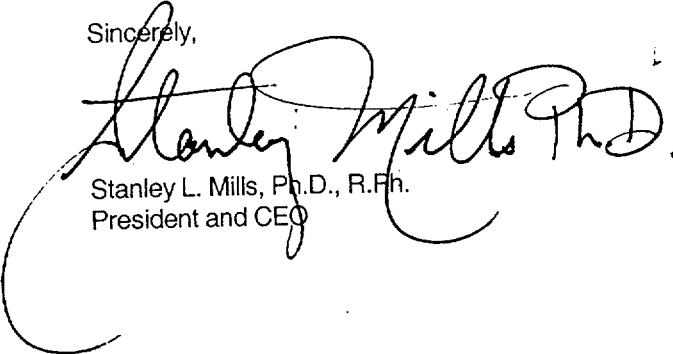
Dear Mr. Basu:

Pursuant to our telephone conversation enclosed are the raw material specification sheets for argon, silver spheres, sodium iodine-125, and titanium tubing. Following an extensive review of the literature brachytherapy sources containing iodine-125 have been used for almost 30 years and are considered safe and effective by the medical community.

MBI manufactures our brachytherapy sources by an automated proprietary process. In brief, the tubing is laser welded in the vertical position under a gentle flow of high purity argon to provide a consistent high strength weld. The process we developed replaces the more traditional process of hand welding the sources thus reducing the potential for human error and inconsistent welds.

As indicated in our original submission our source is similar to the current approved therapeutic seed source recently registered by International Isotope, Inc registry number TX-1068-S-101-S. MBI's seeds utilize silver to produce silver iodine, which is virtually water insoluble. Several silver spheres are encapsulated in medical grade titanium of similar dimensions by laser welding. Attached are two-product literature sheets provided by Imagyn and International Isotopes, Inc. describing their product and a NRC registry for Model IS 125.

Sincerely,



Stanley L. Mills, Ph.D., R.Ph.
President and CEO

Mills Biopharmaceuticals Inc.
Raw Material Specification Sheet

Material: Sodium Iodide I-125
Part Number: 0125
Grade: Radioactive

Acceptable Manufacturers: MDS Nordion

Appearance: Yellow-Orange Liquid

pH 8.0 - 11

Chemical Composition:

Iodates $\leq 2.0\%$

Radionuclidic Purity

I-125 $\geq 99.9\%$
I-126 $\leq 0.005\%$
Cs-137 + Cs-134 $\leq 0.001\%$

Approvals:

Quality Control: Armand **Date:** 8/2/99

Quality Assurance: RCL **Date:** 2 Aug 1999

Mills Biopharmaceuticals Inc.
Raw Material Specification Sheet

Material: Silver Spheres
Part Number: 0020
Grade: Equivalent to ASTM

Acceptable Manufacturers: Scientific Alloy Company

Size: Diameter 0.0195" to 0.0205"

Appearance: Spheres without burrs, Bright Silver Color

Chemical Composition:

Silver $\geq 99.99\%$

Not more than 0.01% total of the following impurities:

Gold	Silicon
Cadmium	Iron
Cobalt	Zinc
Copper	Nickel
Antimony	Aluminum
Arsenic	Palladium
Lead	Molybdenum
Mercury	

(Analysis by ASTM Method using ICP/MS or equivalent)

Approvals:

Quality Control: *[Signature]*

Date: 8/2/99

Quality Assurance: *[Signature]*

Date: 2 Aug 1999

Mills Biopharmaceuticals Inc.
Raw Material Specification Sheet

Material: Argon Gas
Part Number:
Grade: High Purity

Acceptable Manufacturers: Air Gas

Appearance: Clear, Colorless gas

Moisture: < 5 ppm

Chemical Composition:

Argon:	99.995%
Oxygen	< 5 ppm
Nitrogen	< 5 ppm

Approvals:

Quality Control:

Handwritten signature

Date:

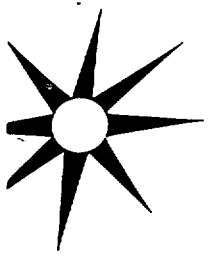
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Quality Assurance:

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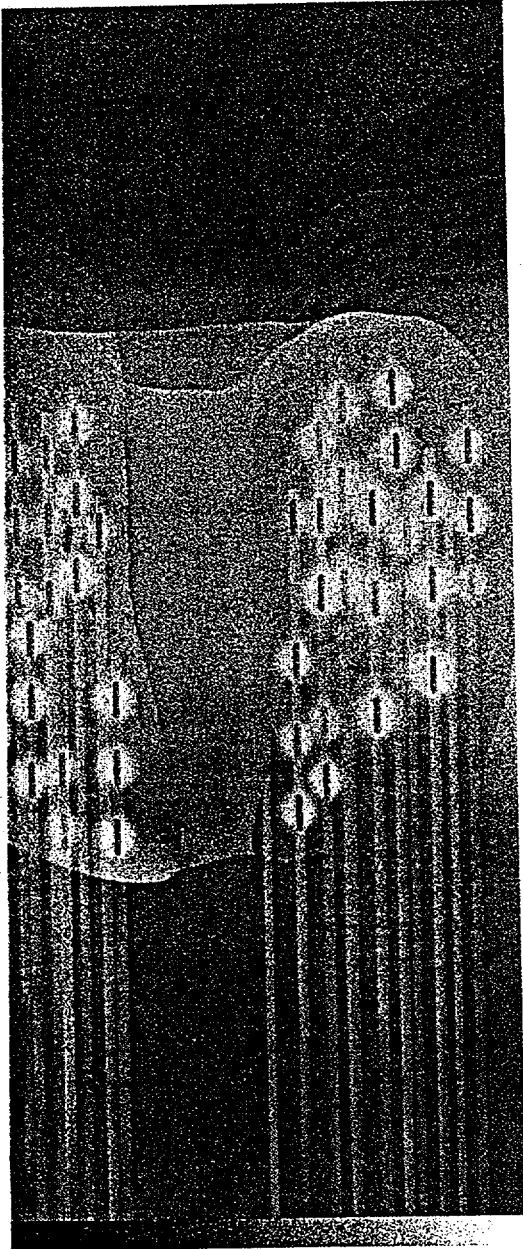
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2 Aug 1999

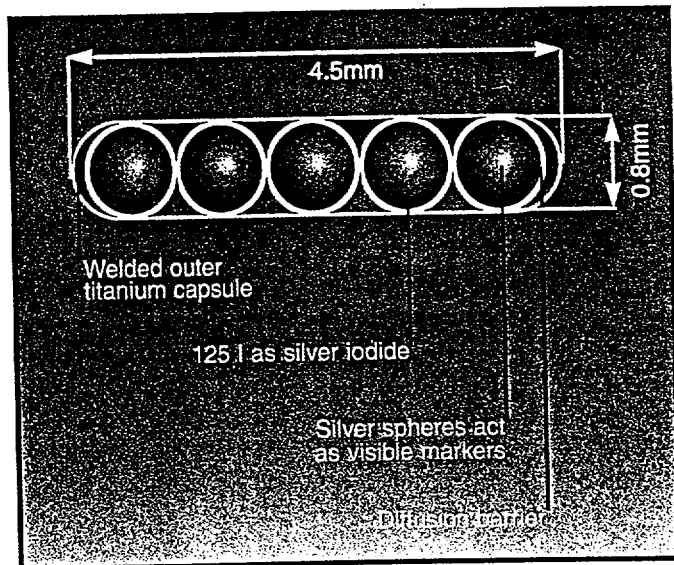


*isoSTAR*TM

Iodine-125 Interstitial Seed For Prostate Brachytherapy



- * Visualization of location and orientation under all commonly used imaging modalities
- * Silver spheres provide high contrast under x-ray and fluoroscopy
- * Laser-welded outer titanium capsule
- * Compatible with conventional brachytherapy needles and applicators
- * 1999 NIST Air Kerma Standard traceable



Calibration

Each IsoSTARTM Iodine-125 seed is measured by a detector that is calibrated by direct comparison against a standard source of the same model (i.e., identical configuration) which has been calibrated by the National Institute of Standards and Technology (NIST) utilizing the 1999 NIST Standard for Air Kerma Strength.



imagyn
MEDICAL TECHNOLOGIES

ISO STAR

Iodine-125 Interstitial Seed

TERMS AND CONDITIONS

Pricing

IsoSTAR™ I-125\$45.00 per seed
Calibration Seeds\$60.00 per seed

Note: pricing is subject to change.

Cancellation Policy

Customers may cancel an order up until 12:00 noon CST ten (10) business days prior to scheduled shipment date.

Returned Goods Policy

IsoSTAR™ I-125

Customers must request a Returned Materials Authorization (RMA) number from Imagyn no later than 5 p.m. CST on the original scheduled surgery date, which is indicated on the Imagyn sales order confirmation. Customers must receive an RMA number before returning a product. IsoSTAR™ I-125 sources must be returned in their original unopened shipping container via overnight delivery. If required, Imagyn will provide customers with the appropriate shipping container. An RMA number and a return address can be obtained by calling Imagyn Customer Service at (888) 242-7181.

Note: Customers must pay for all shipping costs. A returned-materials-processing fee equal to 100% of the original invoice will be charged.

Freight and Handling Policy

All orders will be shipped FOB Denton, Texas. The freight & handling charge of \$40.00 per shipment will be added to customers invoice.

Table 1

Apparent Activity In Millicuries	Air Kerma Strength ($\mu\text{Gy m}^2/\text{h}$)
0.28-0.30	0.36-0.38
0.31-0.33	0.39-0.42
0.34-0.36	0.43-0.46
0.37-0.39	0.47-0.50
0.40-0.42	0.51-0.53
0.43-0.46	0.55-0.58
0.47-0.50	0.60-0.64
0.51-0.54	0.65-0.69
0.55-0.59	0.70-0.75
0.60-0.64	0.76-0.81
0.65-0.69	0.83-0.88
0.70-0.75	0.89-0.95
0.76-0.81	0.97-1.03
0.82-0.88	1.04-1.12
0.89-0.96	1.13-1.22
0.97-1.04	1.23-1.32

Table 1 provides seed strength specifications in apparent activity and air kerma strength for some commonly used activities. To convert from apparent activity to air kerma strength multiply the activity by a factor of 1.27.

To Order Call Imagyn Toll Free At (888) 242-7181



Imagyn Medical Technologies Inc.
15365 W. 95th Street, Lenexa, KS 66219
888-242-7181 • Fax 888-332-2765

Manufactured for Imagyn Medical Technologies, Inc.
by International Isotopes Inc. Denton, TX 76207

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE

NO.: TX-1068-S-101-S

DATE: December 18, 1998

PAGE 1 OF 5

DEVICE TYPE: Therapeutic Seed Source

MODEL IS 125

DISTRIBUTOR: International Isotopes Inc.
3100 Jim Christal Rd.
Denton TX 76207-2600

MANUFACTURER: International Isotopes Inc.
3100 Jim Christal Rd.
Denton TX 76207-2600
Phone (940) 484-9492

ISOTOPE:

MAXIMUM ACTIVITY:

Iodine-125

1.0 mCi per source

LEAK TEST FREQUENCY:

6 months, if a seed's activity was in excess of 800 microcuries at distribution.

PRINCIPAL USE: (V) General Medical Use

CUSTOM DEVICE: YES _____ X _____ NO

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE

NO.: TX-1068-S-101-S

DATE: December 18, 1998

PAGE 2 OF 5

DEVICE TYPE: Therapeutic Seed Source

DESCRIPTION:

The International Isotope Inc. Model IS 125 seed consists of iodine-125 deposited on a silver coated titanium bead or sphere with subsequent metallic over-lays applied with vacuum sputtering and electroplating techniques. Finally, several (typically five) of these beads are loaded into a pure titanium tube and welded into a cylindrical, shiny, metallic-gray seed with an outer dimension of approximately 4.5 mm length and 0.8 mm diameter. The wall thickness of the tube or welded sleeve is 0.05 mm. The average thickness of each laser weld (located at both ends) is about 0.5 mm.

LABELING:

Because of their small size, individual seeds are not labeled. The seeds are supplied as a group of seeds with an activity within a stated range and are packaged in a screw cap glass, one-dram vial. Each production lot is assigned a unique lot number. A label is affixed to the vial stating: "Caution-Radioactive Material, isotope, total activity, activity range, assay date, lot number, the trefoil radiation symbol, non-sterile, manufacturer, and marketed by." An additional label is attached to the lead storage container which includes the same information on the glass vial and a warning that regulated distribution is limited to specific radioactive material licensees subsequent to a physician's order.

DIAGRAM:

See Attachment 1.

CONDITIONS OF NORMAL USE:

The model IS 125 brachytherapy source is intended to be used as a permanent interstitial implant in the treatment of selected localized tumors. Licensed physicians in a clinical environment (surgery) use the device. The placement of the seeds in the tumor is facilitated by the use of one of several commercially available implant tools. These tools are used solely for source placement and not designed either to store or hold the seeds. The seeds are designed to withstand normal autoclave temperatures and pressure variations not to exceed 135° C and 35 psi for 30 minutes. Steam sterilization instructions are provided in the Instructions-for-Use that accompanies the product.

PROTOTYPE TESTING:

Prototypes of the Model IS 125 seeds were subjected to tests for demonstration that the sources would maintain their integrity under stresses of use and accident. The tests performed were in accordance with ISO 2919-1980, Annex C (Medical: interstitial and intracavitary appliances), with a resulting classification of ISO/C53211. This model source has not been tested to satisfy the testing criteria to be declared "special form," as described in 49 CFR 173.469. The impact test was performed striking against the conical end of the seeds, in a manner determined as the source's most vulnerable area. The manufacturer provided additionally testing of the seeds to include autoclaving at 135° C at 34 psi for 30 minutes, without evidence of source failure. These autoclaving values are in excess of the manufacturer's recommendations, and were offered as the seeds are provided non-sterilized.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE

NO.: TX-1068-S-101-S

DATE: December 18, 1998

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DEVICE TYPE: Therapeutic Seed Source

EXTERNAL RADIATION LEVELS:

<u>1 millicurie seed at:</u>	<u>dose rate</u>
5 cm	3.9 mR/hr
30 cm	0.25 mR/hr
100 cm	0.05 mR/hr

QUALITY ASSURANCE AND CONTROL:

International Isotopes Inc., conducts quality control tests and inspection of the Model IS 125 sources prior to distribution, that include: visual inspection, leak testing, radioassay, and physical outer dimensions. Incoming inspections of raw materials includes: labeling, physical and chemical attributes. Manufacturing quality control includes measurements, radiochemical, and radioassay.

LIMITATIONS AND/OR OTHER CONSIDERATIONS OF USE:

- These sources shall be distributed only to persons specifically licensed by the United States Nuclear Regulatory Commission (NRC), an Agreement State, or a Licensing State.
- The licensing authority will have to obtain details on specific holders, measuring equipment, and any operational procedures from the license applicant to making a licensing determination. Based on exhibited, unshielded surface dose rates and the frequent number of sources handled during a typical procedure, these sealed sources should be handled by only experienced licensed personnel equipped with remote handling equipment and appropriate low-energy photon detection equipment.
- The source shall not be subjected to environmental or other conditions of use which exceed ISO 2919.
- This registration sheet and the information contained within the references shall not be changed without the written consent of the Texas Department of Health.
- In spite of the excellent corrosion resistance of titanium, exposure to strong acids and/or bases should be avoided.
- The sources are designed to withstand temperatures and pressures of 275° F (133° C) and 30 psi for 30 minutes. Higher temperatures and pressures are not recommended. Nominal autoclaving conditions are 250° F (121° C) at 15 psi for 15 minutes. Sources should not be sterilized by dry heat.

SAFETY ANALYSIS SUMMARY:

Based on our review of the information, test data cited below, we conclude that the International Isotopes Inc., Model IS 125 sealed source is acceptable for licensing purposes. Furthermore, we conclude that this source should maintain its integrity under normal conditions-of-use and accidental conditions plausible within the medical laboratory/surgery environment. The United States Food and Drug Administration (FDA) shall have determine the efficacy and granted authorization for the therapeutic use of these seeds in humans.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE

NO.: TX-1068-S-101-S

DATE: December 18, 1998

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DEVICE TYPE: Therapeutic Seed Source

REFERENCES: Supporting information for the creation of this summary was obtained from letters supplied by the manufacturer, dated: July 1, 1998, August 31, 1998, October 7, 1998, and December 14, 1998.

ISSUING AGENCY: Texas Department of Health's Bureau of Radiation Control

Date: 12/18/98

REVIEWED BY:

David M. Wood
David M. Wood

Date: 12/18/98

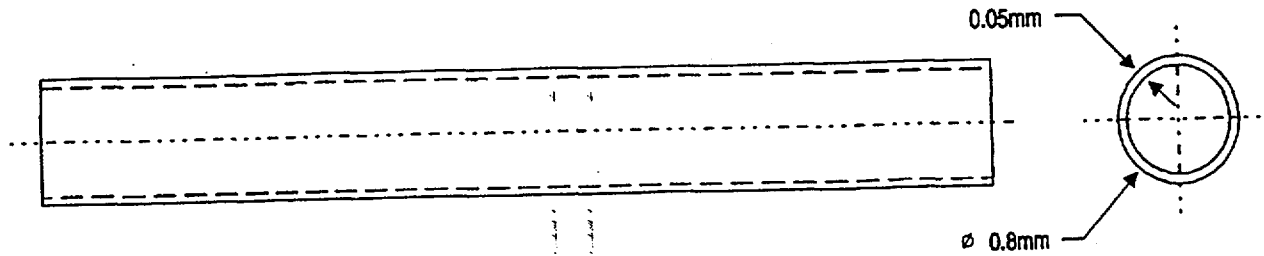
CONCURRENCE:

D. Ray Jisha
D. Ray Jisha

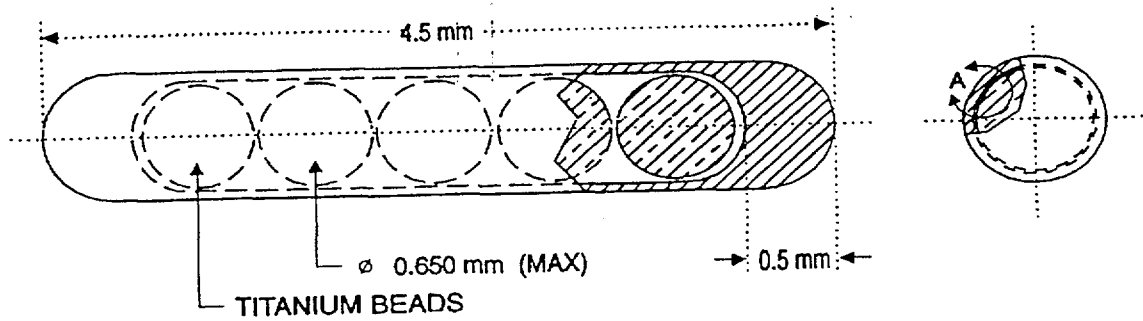
REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE
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ATTACHMENT 1

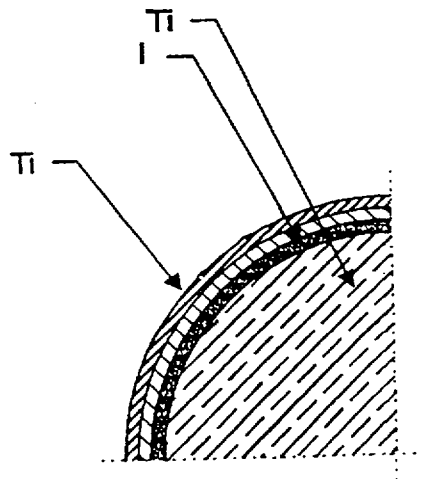
TITANIUM TUBE BEFORE WELD



TITANIUM TUBE AFTER WELD



SINGLE BEAD CUT-AWAY



DETAIL A OF BEAD
SCALE 4:1