

MILLS BIOPHARMACEUTICALS INC.  
120 NE 26th St.  
Oklahoma City, OK 73105  
Phone: (405) 525-3141 Fax: (405) 525-3143

United States Nuclear Regulatory Commission  
Materials Safety Branch  
Division of Industrial and Medical Nuclear Safety  
Two White Flint North  
11545 Rockville Pike Mail Stop 8F5  
Rockville, Maryland 20814

April 30, 2001

Gentlemen:

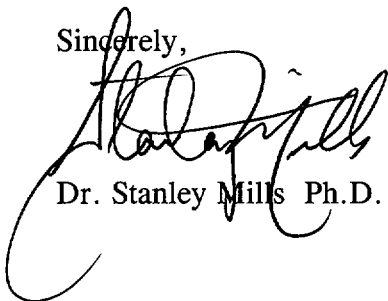
Enclosed is our amended Sealed Source and Device Evaluation and Registration to include a request for a "series" type product (using Palladium-103) which is equivalent to our original product that uses Isotope Iodine-125. We have highlighted the additional isotope for your convenience showing the changes in relationship to the original isotope (Iodine 125).

We have reduced our Leak Test from 18 hours to 4 hours and made corrections as necessary to support our amendment and updated our Quality Manual which is also enclosed.

There are no associated fees in relationship with this amendment and correction based on our discussions with your office.

If there are any questions please contact me.

Sincerely,



Dr. Stanley Mills Ph.D. R. Ph.

NM5512  
1/1

# **AMENDMENT and CORRECTION TO APPLICATION FOR REGISTRATION OF BRACHYTHERAPY SEED FOR MEDICAL USE**

## **10.1 SUMMARY INFORMATION**

Mills Biopharmaceuticals Inc.  
120 NE 26<sup>th</sup> Street  
Oklahoma City, Oklahoma 73105  
Telephone Number 405-525-3141  
Facsimile Number 405-525-3143  
e-mail [smills@ionet.net](mailto:smills@ionet.net)

The product is not intended for a Custom User, but for Brachytherapy Seed use.

Mills Biopharmaceuticals is the Manufacturer of these products.

Tradename: ProstaSeed™

Common Name: I-125 Brachytherapy Seed

Models: I-125 SL  
I-125 SH

Common Name: Pd-103 Brachytherapy Seed

Models: Pd-103, SL  
Pd-103 SH

## **10.2 CONDITIONS OF USE**

The maximum activity is 5.55 GBq (150 millicuries) + 10% for Iodine Model 125SH and 37 MBq (1.0 mCi) + 10% for Model 125SL. The maximum activity is 185 MBq (5.0 millicuries) + 10% for Palladium Model 103 SH and 78MBq (2.11mCi) + 10% for Model 103SL.

MBI I-125 Brachytherapy Seeds with apparent activities between 3.7 MBq (0.1 mCi) to 37 MBq (1.0 mCi) and MBI Pd 103 with apparent activities between 3.7 MBq (0.1 mCi) to 78 MBq (2.11 mCi) are indicated for permanent interstitial treatment of tumors which are unresectable or residual after excision of the primary lesion, localized, slow growing, and exhibit low to moderate radiosensitivity. Intra abdominal, intrathoracic and superficial tumors may be treated with seeds containing apparent activities within this range. Tumors commonly treated are prostate (early stage), pancreas, head, neck, and lung.

MBI I-125 and Pd-103 Brachytherapy Seeds containing apparent activities greater than 37 MBq (1.0 mCi) and 78 MBq (2.11 mCi) respectively are indicated for temporary interstitial treatment of tumors which are unresectable or residual after excision of the primary lesion, localized, and exhibit moderate radiosensitivity. Temporary implants are indicated in breast, brain and eye tumors.

MBI I-125 and Pd-103 Brachytherapy Seeds are indicated for treatment of residual tumors and recurrent tumors following external radiation therapy, hyperthermia, or chemotherapy or concurrent with these treatment modalities.

### 10.3 CONSTRUCTION OF THE PRODUCT

Each MBI I-125 and Pd-103 Brachytherapy Seed has external dimensions of  $4.5 \text{ mm} \pm 0.3 \text{ mm}$  in length and  $0.8 \text{ mm} \pm 0.1 \text{ mm}$  in diameter. The cylindrical metal casing is titanium having a wall thickness of  $0.05 \text{ mm} \pm 0.01 \text{ mm}$  laser welded at both ends. The laser welding process will be conducted in a steel sealed enclosure. The inert gas nozzles used are constructed and configured to prevent turbulence in the weld area preventing air from entering and contaminating the welds. The inert gas also supplies cooling to the weld after laser termination. The titanium used, A-40 (commercially pure), will be certified by the manufacturer as conforming to the ASTM specification F-67-95 (grade 2), A Standard Specification for Unalloyed Titanium for Surgical Implant Applications. The grade of titanium used and the inert atmosphere of the welds would ensure that there is little or no Oxygen and Nitrogen contamination of the welds. Titanium is a universal material for low energy brachytherapy seed due to its durability, low atomic number, and biocompatibility. (NR-460-S-165-S, NR-460-S-166-S, NR-187-S-103-S, GA-1061-S-101-S, TX-1068-S-101-S, IL-136-S-338-S and GA-645-S-101-S). The silver spheres/carrier for both Iodine-125 and Palladium-103 respectively as silver Iodine or silver palladium are dimensionally  $0.5 \text{ mm} \pm 0.1 \text{ mm}$ .

In brief, for the Iodine, the surface of the silver spheres will be coated with silver iodine by incubating activated silver spheres in NaI-125, rinsed with  $\text{H}_2\text{O}$ , acetone, and air dried. The basic solution of sodium iodine-125 will be used as supplied by the manufacturer.

In brief for the palladium, the surface of the silver spheres will be coated with palladium by a proprietary process, rinsed with  $\text{H}_2\text{O}$ , acetone, and air dried. The basic solution of ammonium hydroxide palladium-103 chloride will be used as supplied by the manufacturer. The titanium tubing is welded on one end, inverted, the spheres are added, and the remaining end is welded closed. All models have five silver spheres to provide x-ray contrast and support for the radioisotope. An Engineering design drawing is included in the appendix.

### 10.4 LABELING

The size of the individual seeds precludes any engraved, etched, or printed labeling. The seeds are supplied as a group of seeds with an activity within a stated range on the assay date and are packaged in a one-dram vial. Each distribution lot is assigned a unique lot number. A label is affixed to the vial stating: A Caution Radioactive Materials, isotope, activity range, total activity, assay date, and the trefoil radiation symbol, instructions to see package insert and a warning against distribution to unauthorized persons. An additional label is attached to the lead storage container which includes: a Caution - Radioactive Material statement, the trefoil radiation symbol, product description, activity range, total activity, number of seeds, assay date, lot number, instructions to see package insert and a warning against distribution to unauthorized

persons.

## 10.5 PROTOTYPE TESTING

See NRC REGISTRY NR-1081-S-101-S

The palladium 103 is the same as the iodine-125 brachytherapy seed prototypes.

Products of similar design have been used for over 30 years without known operational problems. Nycomed/Amersham (IL-136-S-337-S, IL-136-S-338-S), North American Scientific (CA-0510-S-126-S), Best Medical International (NR-187-S-103-S), Theragenics Corporation (GA-645-S-101-S), and Mills Biopharmaceuticals Inc. (NR-1081-S-101-S,) are currently manufacturing and distributing seeds in the U.S.

Manufacturer	Model	Capsule	Welding	Use	Isotope
Mills Biopharm. Inc.	125SL 125SH	Titanium	Laser	Interstitial Implant	I-125
International Isotope	IS 125	Titanium	Laser	Interstitial Implant	I-125
Amersham	6711/6702	Titanium	Tig	Interstitial	I-125
Best Medical	2300	Titanium	Laser	Interstitial	I-125
International Brachytherapy	1031 L	Titanium	Laser	Interstitial	Pd-103
Theragenics	200	Titanium	Laser	Interstitial	Pd-103
Mills Biopharm Inc	103SL 103SH	Titanium	Laser	Interstitial Implant	Pd-103

## 10.6 RADIATION PROFILES

See NRC Registry: NR-1081-S-101-S

Radiation profiles for Pd-103 will be less than I-125 of similar activity based upon a reduced specific gamma radiation constant from  $7.432 \times 10^{-5}$  mSv/h)/MBq @100 cm for I-125 to  $6.219 \times 10^{-5}$  (mSv/h)/MBq @100 cm for Pd-103 and an estimated palladium 103 attenuation of 55% for 0.05 mm of titanium.

## 10.7 QUALITY CONTROL AND QUALITY ASSURANCE

See NRC Registry : NR-1081-S-101-S

All Quality Control and Quality Assurance will be remain the same with the exception of Leak testing will be reduced in time to 4 hours from 18 hours for both I-125 and Pd-103 sources.

## 10.8 INSTALLATION, SERVICING, AND INSTRUCTIONS TO USERS

See NRC REGISTRY NR-1081-S-101-S

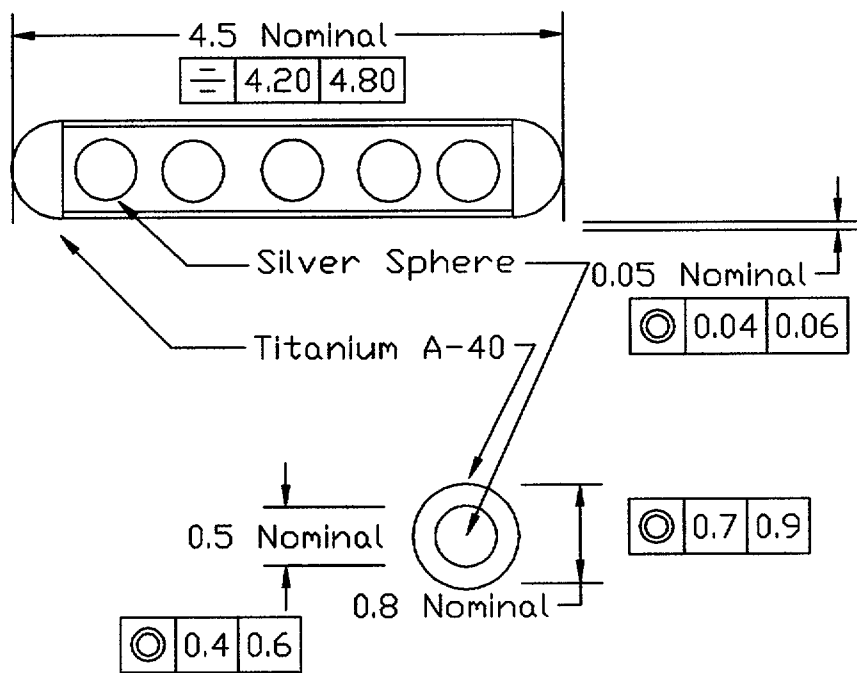
### **I-125 or Pd-103 Brachytherapy Seeds Intended for Permanent Implant**

See NRC REGISTRY NR-1081-S-101-S  
Pd-103 same as I-125.

### **I-125 or Pd-103 Brachytherapy Seeds Intended for Temporary Implant and Reuse**

See NRC REGISTRY NR-1081-S-101-S  
Pd-103 same as I-125.

**APPENDIX A**  
**Drawing of**  
**Mills Biopharmaceutical Sealed Source**  
**follows on next page**



# Appendix B Labels

A label will be affixed to the vial and the shield for Palladium 103 the same as I-125.

**MBI Pd-103 Brachytherapy Seed Model 103SL**  
**Pd-103 Source**  
**Mills Biopharmaceuticals, Inc. OKC, OK**

Total activity: XXXXXXX MBq  
 Total #: XXXXX  
 Apparent activity range: XXXXXXXXXX MBq  
 Assay date: XXXXXXXXXX 12:00 CST  
 Lot #: XXXXXXX  
 0021558 04180101



Caution  
Radioactive  
Material

**CAUTION: Federal  
 (U.S.A.) law prohibits  
 dispensing without  
 prescription. Read  
 package insert.**

**MBI Pd-103 Brachytherapy Seed**  
**Mills Biopharmaceuticals, Inc. OKC, OK**

Model 103SL  
Pd-103 Source



Caution  
Radioactive  
Material

Total activity: XXXXXXX MBq  
 Total #: XXXXX  
 Apparent activity range: XXXXXXXXXX MBq  
 Assay date: XXXXXXXXXX 12:00 CST  
 Lot #: XXXXXXX  
 0021558 04180101

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