UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

December 1, 1999

Dr. Stanely L. Mills, President
Mills Biopharmaceuticals, Inc.
120 N.E. 26th Street
Oklahoma City, Oklahoma 73105

Dear Dr. Mills:

Based on the information and test data submitted with your application dated August 2, 1999, with enclosures thereto, we conclude that Mills Biopharamaceutical Therapeutic Seed Source Models I-125SL and I-125SH, are acceptable for licensing purposes in accordance with the conditions of the enclosed registration certificate (NR-1081-S-101-S).

Please be advised that you must manufacture and distribute the product in accordance with the statements and representations contained in your application, with enclosures thereto, and the information set out in the enclosed registration certificate. As a general rule, you must request and obtain an amendment to the certificate before you make changes or modifications to the information submitted to obtain the registration certificate.

You are obligated to notify us promptly in writing should you decide to no longer manufacture or offer service support for the product.

Please be aware that, as a holder of an NRC registration, you may be subject to the NRC's licensing fees in accordance with 10 CFR Part 170, and annual fees in accordance with 10 CFR Part 171. If you have any questions concerning the fee requirements, please contact the License Fee and Debt Collection Branch at (301) 415-7544.

Please read over the registration certificate in its entirety and notify us immediately of any errors or omissions. If you have any questions, please contact me at (301) 415-7894 or Mr. Seung Lee on (301) 415-5787.

Sincerely,

Ujagar S. Bhachu, PEng. CEng., Mechanical Engineer
Materials Safety and Inspection Branch,
Division of Industrial and
Medical Nuclear Safety
Office of Nuclear Material Safety
and Safeguards.

Enclosure: As stated
cc. w/encl: S. Kimberly, LFDCB

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

NO: NR-1081-S-101-S DATE: December 1, 1999 PAGE: 1 OF 6

SOURCE TYPE: Therapeutic Seed Source

MODEL: I-125SL and I-125SH

MANUFACTURER/DISTRIBUTOR: Mills Biopharmaceuticals, Inc.
120 N.E. 26th Street
Oklahoma City, Oklahoma 73105

ISOTOPE:	MAXIMUM ACTIVITY:
Iodine- 125	5.55 GBq (150 millicuries)

LEAK TEST FREQUENCY: 6 months

PRINCIPAL USE: (V) General Medical Use

CUSTOM SOURCE: _____YES __X__ NO

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

NO: NR-1081-S-101-S DATE: December 1, 1999 PAGE: 2 OF 6

SOURCE TYPE: Therapeutic Seed Source

DESCRIPTION:

The Mills Biopharmaceuticals, Inc. (MBI) Model I-125SL and I-125SH seeds contain sodium iodine-125 absorbed on solid silver spheres and encapsulated in a cylindrical titanium capsule. As indicated in Attachment 1, the core of the silver seed is a 0.5 mm ± 0.05mm (0.017" ± 0.0017") sphere. Each MBI I-125 seed's maximum external dimensions are 4.9 mm (0.193") in length and 0.96 mm (0.0378") in diameter. The cylindrical metal casing is A-40 (commercially pure) titanium, conforming to ASTM F-67-95, with a wall thickness of 0.06 mm (0.0024") ± 0.02 mm (0.0008") The titanium tubing is welded on one end, inverted, the spheres added, and the open end is closed with a weld. The welds are made in a vertical position in the presence of a gentle flow of high purity argon to consistently achieve good quality high strength welds.

Both the models have three to five silver sphere seeds. Each seed of model I-125SH contains maximum 150 mCi (5.55 GBq) and model I-125SL contains maximumly 1 mCi (37 MBq). The two models differ only in total radioactivity contained.

LABELING:

The physical size of the individual seed prevents direct labeling of the individual sources. 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 production lot is assigned a unique lot number. A label is affixed to the vial stating: "Caution - Radioactive Materials," distributor name, isotope, activity range, total activity, assay date, and the trefoil radiation symbol. 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 the package insert and a warning against distribution to unauthorized persons. The labels will comply with the provisions of 10 CFR 32.74, 20.1901, and 20.1904. The labels will be legible and made of durable material.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

SOURCE TYPE: Therapeutic Seed Source

DIAGRAMS:

See Attachments 1 and 2

CONDITIONS OF NORMAL USE:

The Mills Biopharmaceuticals, Inc. Iodine-125 brachytherapy seed is designed for use in the permanent interstitial treatment of cancerous tumors. The placement of Iodine-125 brachytherapy seeds in tissue under surgical conditions is assisted by the use of any one of several implant tools commercially available. In addition the sources are designed to be sterilized using ethylene oxide or autoclaves at normal autoclave temperature and pressure variations up to 138° C (280° F) and 35 psi (241.3 kPa). The titanium encapsulation should not be exposed to concentrated acids or sterilized by dry heat methods. Due to the high dose rates from the sources, appropriate handling equipment, such as forceps, must be used. Ruptured, leaky or damaged sources should never be used.

PROTOTYPE TESTING:

The Iodine-125 brachytherapy seed prototypes were subjected to tests to demonstrate that the sources will maintain their integrity under stresses of use and accidents that may occur. These tests included temperature, impact, percussion, autoclave temperatures and pressures for sources with wall thickness of 0.05 mm (0.00197").

The tests performed closely followed the recommendations of ANSI N44.1-1973. The only deviations from the standard's recommendations were an autoclave high temperature and limitations imposed on the minimum diameter requirements of the source tube. The manufacturer indicates the sources passed each of these tests.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

SOURCE TYPE: Therapeutic Seed Source

EXTERNAL RADIATION LEVELS:

Calculated radiation levels using gamma radiation constants provided in the Radiological Health Handbook are tabulated below. The value provided for I-125 is given as approximately 0.7 $Rcm^2/hr/mCi$. Containment of 1.0 mCi within a welded titanium capsule with corresponding wall thickness of 0.05 mm (0.00197") would attenuate the output by approximately 15%.

	1.97" (5 cm)	3.94" (10 cm)	11.8" (30 cm)
Unencapsulated:	28 mR/hr	7 mR/hr	0.8 mR/hr
Encapsulated:	24 mR/hr	6 mR/hr	0.7 mR/hr

Radiation levels for a maximum loading would be proportionately higher.

QUALITY ASSURANCE AND CONTROL:

Sources manufactured by Mills Biopharmaceuticals, Inc. are governed by its quality policy manual. A copy of the program is on file with NRC. The QC program contains provisions for design and procurement documentation reviews and includes elements for ensuring identity of incoming products, conducting receipt inspection, initial leak tests, autoclave and second leak tests, inspection of assembly and welds.

Any source found with more than 0.005 μCi (185 Bq) of removable contamination is rejected and relocated in locations away from the production and assembly areas.

Radioactivity: Activity levels of manufactured sources supplied shall be within $\pm$ 10%.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

NO: NR-1081-S-101-S DATE: December 1, 1999 PAGE: 5 OF 6

SOURCE TYPE: Therapeutic Seed Source

LIMITATIONS AND OTHER CONSIDERATIONS OF USE:

1. These sources shall be distributed to specific licensees of the U.S. Nuclear Regulatory Commission or an Agreement State.

2. These sources shall be tested for leakage at time intervals not to exceed 6 months. Leak testing shall be governed by individual license requirements from the U.S. Nuclear Regulatory Commission or an Agreement State.

3. Sources should not be exposed to temperatures in excess of 138° C (280.4° F) and pressures in excess of 35 psi (241.3 kPa)

4. Due to the high surface dose rates exhibited by these sources when unshielded, sources should be stored in the shielded container supplied with each source or set of sources.

5. The sources shall not be autoclaved in plastic tubing or plastic containers. Only autoclave in suitable materials such as stainless steel, glass, nylon, teflon, or tin should be used. The sources shall not be exposed to concentrated acids or alkaline fluids or sterilized by dry heat methods. These sources are designed for use in controlled laboratory or medical surgery conditions and should not be subjected to conditions exceeding those specified by the ANSI rating 77C64221 classification.

6. Handling, storage, use, transfer and disposal: To be determined by the licensing authority.

7. This registration sheet and the information contained within the references shall not be changed without the written consent of the U.S. Nuclear Regulatory Commission.

Reviewer Note: Please ensure the safety procedures outlined in 10 CFR Part 35 Subpart G are adhered to, especially as they pertain to the handling of the sources.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

NO: NR-1081-S-101-S DATE: December 1, 1999 PAGE: 6 OF 6

SOURCE TYPE: Therapeutic Seed Source

SAFETY ANALYSIS SUMMARY:

Based on our review of the information and test data cited below and the past history of similar source design, we conclude that MBI Models I-125SH and I-125SL are acceptable for licensing purposes.

Furthermore we conclude that these sources would be expected to maintain their containment integrity for normal and accidental conditions for use which might occur during the uses specified in this certificate.

The United States Food and Drug Administration (FDA) have determined the efficacy and granted authorizations for the application of therapeutic seed sources in humans. (FDA letter dated April 16, 1999, Reference K984446)

REFERENCES:

The following supporting documents for the Mills Biopharmaceuticals Inc. Models I-125SH and I-125SL brachytherapy sealed sources are hereby incorporated by reference and are made part of this registration document.

- Mills Biopharmaceuticals Inc. letters dated June 13, 1999, October 01, 1999, and November 12, 1999, with enclosures thereto.

ISSUING AGENCY:

United States Nuclear Regulatory Commission

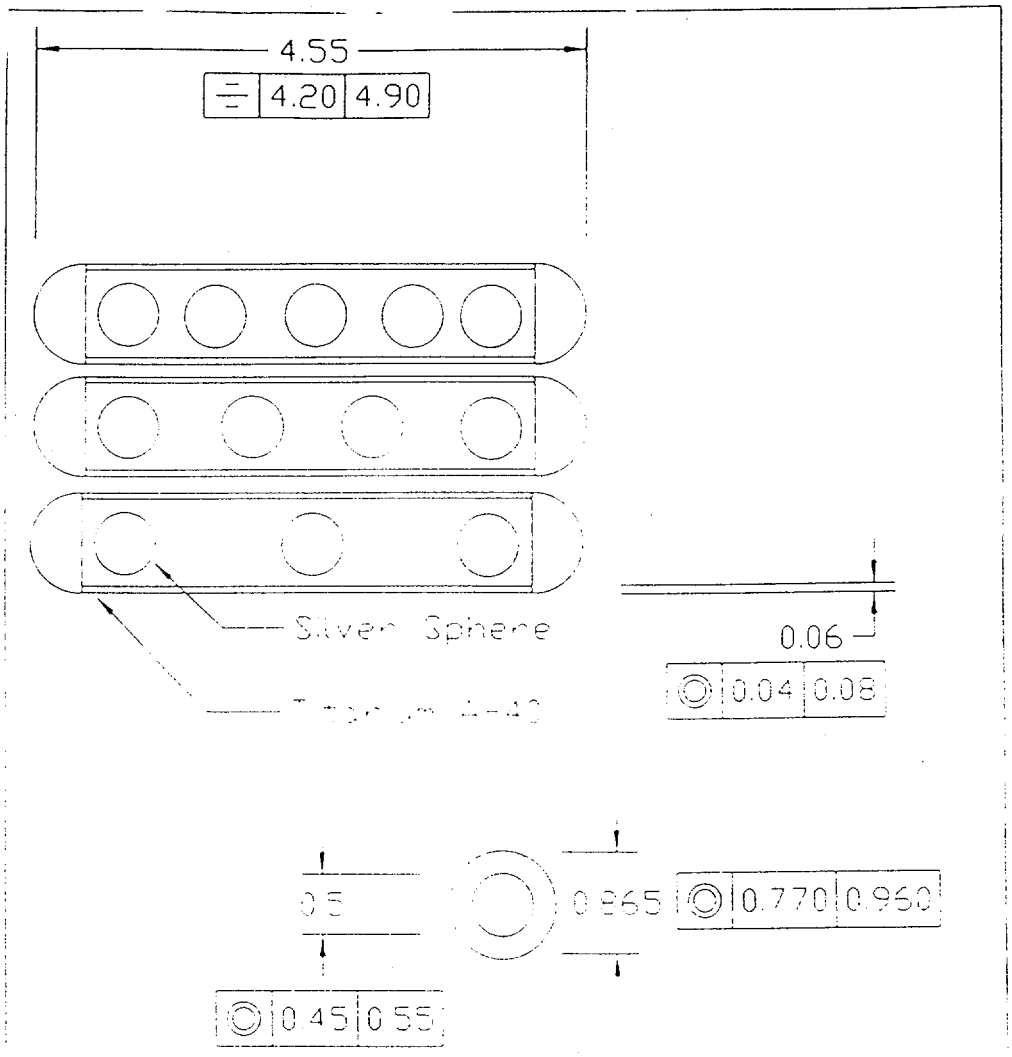
Date: December 1, 1999 Reviewer: Ujagar S. Bhachu

Date: December 1, 1999 Concurrence: Seung J. Lee

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

NO: NR-1081-S-101-S DATE: December 1, 1999 ATTACHMENT: 1

SOURCE TYPE: Therapeutic Seed Source

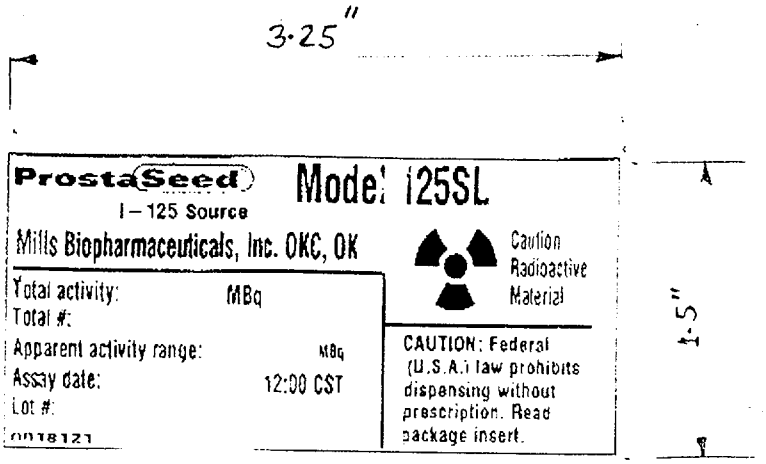


Models I-125SL & I-125SH
(Dimensions in millimeters)

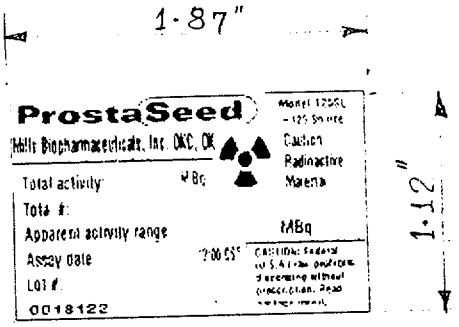
REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE

NO: NR-1081-S-101-S DATE: December 1, 1999 ATTACHMENT: 2

SOURCE TYPE: Therapeutic Seed Source



Lead Container Label



Vial Label

All shipments of sources and containers will include storage, receiving and handling instructions.

NRC FORM 567
(8-93)

U. S. NUCLEAR REGULATORY COMMISSION

REQUEST FOR A SEALED SOURCE OR DEVICE EVALUATION

INSTRUCTIONS: Send this request AND a copy of all related letters/applications and drawings to: The Sealed Source Safety Section, ATTN: Chief, OWFN Mail Stop 6 H3. Change the License Tracking System milestone to 19 and assign to reviewer code I-5.
NOTE: Retain a copy of this request with the application and background files.

REQUESTER: Mills Biopharmaceutical, Inc.
TELEPHONE NUMBER:
DATE:
APPLICANT'S NAME: Stanley Mills
MAIL CONTROL NUMBER(S):
LETTER/APPLICATION DATE: 8-11-99
LICENSE NUMBER(S):

REGION/LOCATION: ☐ I ☐ II ☐ III ☐ IV ☐ V ☐ HQ ☐ LFDCB

TYPE OF ACTION REQUESTED (Check as appropriate)

☐ SOURCE REVIEW
☒ DEVICE REVIEW
☐ CUSTOM REVIEW
☐ AMENDMENT OF REGISTRATION SHEET NUMBER(S) _____

COMMENTS:
120 N.E. 26th Street
Oklahoma City, OK 73105

FOR SSSS USE ONLY

REVIEWER	MODEL NUMBERS	NUMBER ASSIGNED
U. Bhachu	125SL & 125SH	99-50
DATE RECEIVED	**DATE ASSIGNED**	**DATE TO FEES**
8-11-99	8-11-99	8-11-99

TYPE OF ACTION (Indicate the number of each type)

☐ COMMERCIAL DISTRIBUTION (FORMAL)
☐ USE BY A SINGLE APPLICANT (CUSTOM)

SOURCE (9C)	DEVICE (9A)	SOURCE (9D)	DEVICE (9B)
☐ NEW ☐ AMENDMENT	☒ NEW ☐ AMENDMENT	☐ NEW ☐ AMENDMENT	☐ NEW ☐ AMENDMENT

☐ NO SAFETY EVALUATION REQUIRED
NO FEES REQUIRED

☐ LICENSING ACTION REQUIRED IF KNOWN ☐ YES ☐ NO

☒ OTHER *(Specify)* Fee has already been paid

TOTAL NUMBER OF REVIEW HOURS	NOTES: Application for use of I-125 Brachy therapy Seeds.
NUMBER OF DEFICIENCY LETTERS	
NUMBER OF DEFICIENCY CALLS	

FOR BILLING PURPOSES ONLY

☐ NAME CHANGE ☐ ADDRESS CHANGE ☐ NEW REGISTRATION – ADD TO BILLING ☐ PRODUCT INACTIVE – REMOVE FROM BILLING

FOR FEE USE ONLY

TYPE OF FEE: Appl.	FEE CATEGORY: ☐ 9A ☐ 9B ☐ 9C ☐ 9D	
AMOUNT RECEIVED: No fee required	CHECK NUMBER	☐ MATANN UPDATED AS REQUIRED
DATE OF CHECK: Admin Info	LOG: Aug 99 issued	☐ MATSYS UPDATED AS REQUIRED
APPROVED BY: ↓	DATE RETURN: 8/12/99	DATE
COMMENTS: Control # 9641699-24		

NRC FORM 567 (8-93)

ORIGINAL TO SSSS

NRC FORM 567
(8-93)

U. S. NUCLEAR REGULATORY COMMISSION

REQUEST FOR A SEALED SOURCE OR DEVICE EVALUATION

INSTRUCTIONS: Send this request AND a copy of all related letters/applications and drawings to: The Sealed Source Safety Section, ATTN: Chief, OWFN Mail Stop 6 H3. Change the License Tracking System milestone to 19 and assign to reviewer code I-5.
NOTE: Retain a copy of this request with the application and background files.

REQUESTER: Mills Biopharmaceutical, Inc.
TELEPHONE NUMBER:
DATE:
APPLICANT'S NAME: Stanley Mills
MAIL CONTROL NUMBER(S):
LETTER/APPLICATION DATE: 8-11-99
LICENSE NUMBER(S):

REGION/LOCATION: ☐ I ☐ II ☐ III ☐ IV ☐ V ☐ HQ ☐ LFDCB

TYPE OF ACTION REQUESTED (Check as appropriate)
☐ SOURCE REVIEW
☒ DEVICE REVIEW
☐ CUSTOM REVIEW
☐ AMENDMENT OF REGISTRATION SHEET NUMBER(S) _____

COMMENTS:
120 N.E. 26th Street
Oklahoma City, OK 73105

FOR SSSS USE ONLY

REVIEWER	MODEL NUMBERS	NUMBER ASSIGNED
U. Bhachu	125SL & 125SH	99-50
DATE RECEIVED	**DATE ASSIGNED**	**DATE TO FEES**
8-11-99	8-11-99	8-11-99

TYPE OF ACTION (Indicate the number of each type)

☐ COMMERCIAL DISTRIBUTION (FORMAL) ☐ USE BY A SINGLE APPLICANT (CUSTOM)

SOURCE (9C)	DEVICE (9A)	SOURCE (9D)	DEVICE (9B)
☐ NEW ☐ AMENDMENT	☒ NEW ☐ AMENDMENT	☐ NEW ☐ AMENDMENT	☐ NEW ☐ AMENDMENT

☐ NO SAFETY EVALUATION REQUIRED NO FEES REQUIRED
☐ LICENSING ACTION REQUIRED IF KNOWN ☐ YES ☐ NO
☒ OTHER *(Specify)* Fee has already been paid

TOTAL NUMBER OF REVIEW HOURS	NOTES: Application for use of I-125 Brachy therapy Seeds.
NUMBER OF DEFICIENCY LETTERS	
NUMBER OF DEFICIENCY CALLS	

FOR BILLING PURPOSES ONLY

☐ NAME CHANGE ☐ ADDRESS CHANGE ☐ NEW REGISTRATION – ADD TO BILLING ☐ PRODUCT INACTIVE – REMOVE FROM BILLING

FOR FEE USE ONLY

TYPE OF FEE: App).	FEE CATEGORY: ☐ 9A ☐ 9B ☐ 9C ☐ 9D	
AMOUNT RECEIVED: No fee required Addl Info	CHECK NUMBER	☐ MATANN UPDATED AS REQUIRED
DATE OF CHECK	LOG: Aug 99 / SSOD	☐ MATSYS UPDATED AS REQUIRED
APPROVED BY	DATE RETURN: 8/12/99	DATE
COMMENTS: Control # 9941699-24		

NRC FORM 567 (8-93)

ORIGINATORS COPY

Cover Page

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Aug-09-99

11:22

To:

Fax: 301 415 5369

From: M

Fax: 4055253143

Pages: 13 not including this page

MILLS BIOPHARMACEUTICALS INC.

120 N.E. 26th Street
Oklahoma City, OK 73105

Phone: (405) 525-3141
FAX: (405) 525-3143

FAX TRANSMITTAL

☐ *For your information, no response necessary* ☒ *Please respond/reply as soon as possible*

TO: Mr. Sudhamay Basu

COMPANY: U.S. N.R.C.

FROM: Ken Snow

DATE: 09 Aug 99

This is a fax transmission consisting of 12 page(s) and this cover page. If all pages were not received or you received this fax in error please contact this office immediately.

MESSAGE:

Please find the info you requested attached. A copy (2) will follow via FedEx for Tues. Am delivery.

Ken

faxcvsht.96