NRC FORM 567
(1-1999)

U.S. NUCLEAR REGULATORY COMMISSION

REQUEST FOR A SEALED SOURCE OR DEVICE EVALUATION

INSTRUCTIONS: Send this rerquest AND a copy of all related letters/applications and drawings to the Chief, Sealed Source Safety Section, OWFN Mail Stop O-6 H3. Change the License Tracking System milestone to 19 and assign to reviewer code 1-5.
NOTE: Retain a copy of this request with the application and background files.

REQUESTER: **DraxImage**

TELEPHONE NUMBER:

DATE:

NAME OF APPLICANT: **Edward Bump**

MAIL CONTROL NUMBER(S):

LETTER/APPLICATION DATE: **04/20/2004**

LICENSE NUMBER(S):

REGION/LOCATION: ☐ I ☐ II ☐ III ☐ IV ☐ HQ ☐ LFARB

TYPE OF ACTION REQUESTED *(Check as appropriate)*

☐ SOURCE REVIEW
☐ DEVICE REVIEW
☐ CUSTOM REVIEW
☑ AMENDMENT OF REGISTRATION SHEET NUMBER(S) **NR-1121-S-101-S**

COMMENTS:

16751 Autoroute TransCanada Highway
Kirkland, Québec Canada
H9H 4J4

FOR SSSS USE ONLY

REVIEWER	MODEL NUMBERS	NUMBER ASSIGNED
Xiaosong Yin	LS-1	04-36
DATE RECEIVED	**DATE ASSIGNED**	**DATE TO FEES**
04/21/2004	04/26/2004	04/26/2004

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	☐ NEW	☐ NEW	☐ NEW
☑ AMENDMENT	☐ AMENDMENT	☐ AMENDMENT	☐ AMENDMENT

☑ NO SAFETY EVALUATION REQUIRED
NO FEES REQUIRED

☑ LICENSING ACTION REQUIRED (IF KNOWN) ☐ YES ☑ NO

☐ OTHER *(Specify)*

	TOTAL NUMBER OF REVIEW HOURS
	NUMBER OF DEFICIENCY LETTERS
	NUMBER OF DEFICIENCY CALLS

NOTES
Amendment request to registration NR-1121-S-101-S for brachytherapy LS-1.

FOR FEE USE ONLY

TYPE OF FEE:

FEE CATEGORY: ☐ 9A ☐ 9B ☐ 9C ☐ 9D

AMOUNT RECEIVED	CHECK NUMBER	DATE OF CHECK	LOG

APPROVED BY:

DATE OF RETURN:

COMMENTS:

DRAXIMAGE

VIA FedEx

April 20th, 2004

Mr. Ujagar S. Bhachu or
Mr. William R. Ward, P.E.
Materials Safety & Inspection Branch
Division of Industrial and Medical Nuclear Safety
Two White Flint North
11545 Rockville Pike
North Bethesda, MD 50852

Re: Amendment to the Registration Certificate for BrachySeed ™ – LS-1

Dear Mr. Bhachu,

In accordance with our discussion earlier this week, we are submitting an amendment to our registration certificate for BrachySeed™ LS-1 (NR-1121-S-101-S).

This amendment proposes the addition of our Williston, Vermont address on the outer label of this product, and an alternate outer label for the sterile product. Furthermore, the references to the NRC regulations located in the lower part of the label have been corrected as you suggested.

We hope the information provided is satisfactory. Please do not hesitate to contact me at (514) 630-7007 or fax (514) 694-9295 should you have any questions.

Sincerely yours,

Edward Bump, Ph D
Radiation Safety Officer

/ml

DRAXIMAGE Inc. • 16751 Autoroute TransCanada Highway • Kirkland • Québec • Canada • H9H 4J4
• Tel. 888-633-5343 • 514-630-7080 • Fax. 514-694-9295 • www.draximage.com

DRAXIMAGE LLC • 75 Talcott Road, Suite 50 • Williston • Vermont • USA • 05495
• Tel. 802-872-3536 • Fax. 802-872-3538

1. Table of Contents

2. Introduction

BrachySeed™ Model LS-1 is an Iodine I-125 brachytherapy source that has been registered for sale with the FDA and the NRC. The following registration information is provided:

- The NRC Registration Certificate for this product is NR-1121-S-101-S;
- This product is also licensed with the FDA under 510 (k) K000475.

A copy of the above certificate in included next and a copy of the 510(k) letter can be found on page 13.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

NO.: NR-1121-S-101-S DATE: **August 15, 2003** PAGE 1 OF 8

SOURCE TYPE: Brachytherapy Source

MODEL: LS-1

DISTRIBUTOR: **DRAXIMAGE, LLC.**
75 Talcott Rd.
Suite 50
Williston, VT 05495

MANUFACTURER: DRAXIMAGE, Inc.
16571 TransCanada Highway
Kirkland, QC
Canada H9H 4J4

ISOTOPE:	MAXIMUM ACTIVITY:
Iodine-125	75 mCi (2.75 GBq)

LEAK TEST FREQUENCY: 6 months

PRINCIPAL USE: (V) **For use in accordance with 10 CFR 35.400 through 35.491 (Subpart F) or the equivalent state regulations**

CUSTOM SOURCE: _____YES __X__ NO

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

NO.: NR-1121-S-101-S DATE: **August 15, 2003** PAGE 2 OF 8

SOURCE TYPE: Brachytherapy Source

DESCRIPTION:

The DRAXIMAGE, Inc. Model LS-1 seed is a titanium encapsulated radiation source containing the radioisotope iodine-125. It is a sealed brachytherapy source designed for radiation oncology applications.

The capsule consists of two end tubes, each with one end closed and with the open end press fitted onto a central plug (the annulus). Hermetic sealing of the source is achieved by a low profile laser weld around the central circumference that secures and joins the rims of the end tubes to each other and to the underlying annulus. The X-ray marker is a platinum/10% iridium rod which passes through the annulus. The radioisotope carrier consists of two hard ceramic beads containing about 10% silver which lie one at each end of the source. The core of the silver seed is a 0.5 mm ± 0.05mm (0.017" ± 0.0017") sphere. Each LS-1 seed's nominal external dimensions are 4.4 mm (0.173") in length and 0.8 mm (0.0315") in diameter. The end tube is titanium metal, grade 2, conforming to ASTM B-265, with a wall thickness of 0.048 mm (0.0019") ± 0.076 mm (0.0003") with radial end wall thickness of 0.0635 mm (0.0025") ± 0.005 mm (0.0002"). One end of the assembled source is inserted into a chuck rotating horizontally at 30 rpm. The source is a friction fit and, once inserted, rotates at the same speed. The positioning is such that the seam of the source is at the focus of a vertically aligned laser welder beam.

LABELING:

The physical size of the individual seed prevents direct labeling of the individual sources. A label is affixed to the shipping and storage pot stating: the trefoil radiation symbol, "Caution - Radioactive Materials" statement, model number, isotope, customer order number, total apparent activity, apparent activity per source, number of sources, average air-kerma strength, assay date, lot number, distributor name, and instructions to see the package insert and a statement for distribution to authorized persons. A label is attached to the primary container which includes: trefoil radiation symbol, "Caution Iodine-125 Radioactive Material" statement, model number, number of sources,

SOURCE TYPE: Brachytherapy Source

LABELING (Cont'd):

total activity, assay date, and distributor name. 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.

REVIEWER NOTE: The label shown in Attachment 2 is an example of the label. New labels must have the current wording of 10 CFR 32.74(a)(3) and should have the current address of the manufacturer or distributor.

DIAGRAMS:

See Attachments 1 and 2.

CONDITIONS OF NORMAL USE:

The DRAXIMAGE, Inc. Model LS-1 iodine-125 brachytherapy seed will be used in a hospital setting. It will be applied in multiple source implants for the treatment of localized tumors. The operating environment is within in tissue and body fluids at about 37° C (98.6° F) at about atmospheric pressure.

The working life of LS-1 is estimated to be one year based on the iodine-125 half-life of about 60 days.

The sources are not sterile when shipped. Before implantation, they must be sterilized in an adequately shielded container using ethylene oxide or steam at normal cycle (121° C [249.8° F] at 15 psi [103.43 kPa] for 15 to 30 minutes) or flash cycle (133° C [271.4° F] at 30 psi [206.85 kPa] for 3 minutes). Commercially available applicators and needles may be used.

The sources are not affected by common solvents such as acetone and alcohol or by mild detergents. However, they should not be exposed to acid or alkaline solutions exceeding one molar.

The sources should not be picked up with the fingers and ruptured, leaky, or damaged sources should never be used.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

NO.: NR-1121-S-101-S DATE: **August 15, 2003** PAGE 4 OF 8

SOURCE TYPE: Brachytherapy Source

PROTOTYPE TESTING:

The Model LS-1 Iodine-125 brachytherapy seed was classified and tested according to the standard ISO 2919:1999(E). The classification designation is ISO/98/C53211. Two sources with 2 mCi (74 MBq) were subjected to each of the five required stress tests followed by the immersion (hot liquid) leakage test as described in the standard ISO 9978:1992(E). After the tests, none of the ten sources showed any breach of the encapsulation upon visual inspection under the microscope and all showed leakage less than 0.01 nCi (0.37 Bq). Scaling up, this indicates the use of maximum 75 mCi (2.78 GBq) sources would have resulted in leakages of less than 0.4 nCi (14.8 Bq) which is less than the test failure criterion of 5 nCi (185 Bq).

The standard ANSI/HPS N43.6-1997 sets out the same tests as ISO 2919:1999(E), but also prescribes an additional drop test and requires a different leakage test. Therefore, two sources with 2 mCi (74 MBq) were subjected to the ANSI/HPS drop test followed by the immersion with boiling leakage test as required by this standard. After the test, neither source showed any breach of the encapsulation or any other damage upon visual inspection under the microscope and both showed leakage of less than 0.05 nCi (18.5 Bq). Scaling up, this indicates the use of maximum 75 mCi (2.78 GBq) sources would have resulted in leakages of less than 2 nCi (74 Bq) which is less than the test failure criterion of 5 nCi (185 Bq).

Subsequent to the immersion (hot liquid) leakage test, the ten seeds used for the ISO tests were combined in a single container and subjected together to the immersion with boiling leakage test of the ANSI/HPS standard. The combine sources showed leakage of 0.05 nCi (1.85 Bq).

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

NO.: NR-1121-S-101-S DATE: **August 15, 2003** PAGE 5 OF 8

SOURCE TYPE: Brachytherapy Source

EXTERNAL RADIATION LEVELS:

Calculated radiation levels using exposure rate constant of 1.45 R-cm^2/hr/mCi for iodine-125 provided in the Interstitial Brachytherapy, Raven Press, 1990, are tabulated below. The measurement system used was a Ludlum survey meter Model 14C with a pancake probe Model 44-9. It was last calibrated on July 31, 1999, using Cs-137. The due date for recalibration is one year later. The measurements were done on February 16, 2000.

Source-Director Distance	Calculated Field (mR/hr/mCi)	Measured Field (mR/hr/mCi)
100 cm (39.37")	0.15	0.15
30 cm (11.81")	1.61	1.45
5 cm (1.97")	58	50
Contact		440*

*The contact reading is not very meaningful but probably indicates an extremity exposure rate in excess of 500 mrem/hr/mCi if a person picks up a source with the fingers.

The radiation doses incurred by practitioners would be similar to implant, although an approximate further doubling could be expected because of the source removal procedure associated with temporary implants. Overall, a factor of four increase in radiation dose per procedure to hospital personnel relative to mainstream applications might be reasonably expected, although this could be offset by the fewer number of seeds involved and thus a reduction in overall exposure time.

QUALITY ASSURANCE AND CONTROL:

All manufacturing of the Model LS-1 iodine-125 sources and related operations are to be carried out in batch manufacturing processes consistent with the Current Good Manufacturing Practice Final Rule, Quality System Regulation, 21 CFR Part 820, under the supervision of the Quality Assurance group at DRAXIMAGE, Inc.

SOURCE TYPE: Brachytherapy Source

QUALITY ASSURANCE AND CONTROL (Cont'd):

All incoming materials will be quarantined under QA supervision, then appropriately tested against specifications before being released for source production purposes.

The following in-process quality control testing will be done on each source:

a) leak testing developed by the manufacturer to ensure conformance with 5 nCi (185 Bq) limit;
b) check of radiation intensity versus angle to ensure conformance with design specifications;
c) measurement of overall radiation output strength to ensure consistency within a batch and conformance with customer order; and
d) visual inspection using video magnification to check weld integrity and to ensure no mechanical damage or blemishes.

In addition, the following properties of finished sources will be quality control tested against acceptable quality limit by the QA department on samples from each lot:

e) visual appearance (damage, blemishes, shape, weld color, and weld integrity);
f) dimensions;
g) radiation output intensity (by means of a system whose calibration is traceable to NIST); and
h) leakage.

Batch release will include a review of batch manufacturing records. A certificate stating that all sources in a shipment have shown less than 5 nCi (185 Bq) leakage on a particular date will accompany each shipment.

Weld sectioning and microscope examination will be done periodically in non-radioactive sources welded under prevailing production conditions. Visual integrity, weld width, and weld depth will be checked and controlled.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

NO.: NR-1121-S-101-S DATE: **August 15, 2003** PAGE 7 OF 8

SOURCE TYPE: Brachytherapy Source

LIMITATIONS AND OTHER CONSIDERATIONS OF USE:

- These sources shall be distributed to specific licensees of the U.S. Nuclear Regulatory Commission or an Agreement State.
- 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.
- Handling, storage, use, transfer and disposal: To be determined by the licensing authority.
- 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 **F** are adhered to, especially as they pertain to the handling of the sources.

SAFETY ANALYSIS SUMMARY:

Based on our review of the information and test data cited below and the past history of similar source design, we **continue to** conclude that the Model LS-1 sources are acceptable for licensing purposes.

Furthermore, we **continue to** 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 August 22, 2000, Reference K00475)

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

NO.: NR-1121-S-101-S . DATE: **August 15, 2003** PAGE 8 OF 8

SOURCE TYPE: Brachytherapy Source

REFERENCES:

The following supporting documents for the DRAXIMAGE, Inc. Model LS-1 iodine-125 brachytherapy sealed sources are hereby incorporated by reference and are made part of this registration document.

- DRAXIMAGE, Inc. letters dated February 21, 2000, May 9, 2000, May 29, 2000, and June 12, 2000, with enclosures thereto.
- **DRAXIMAGE, Inc. letters dated February 16, 2003, February 18, 2003, May 7, 2003, and facsimile dated May 8, 2003, with enclosures thereto.**

ISSUING AGENCY:

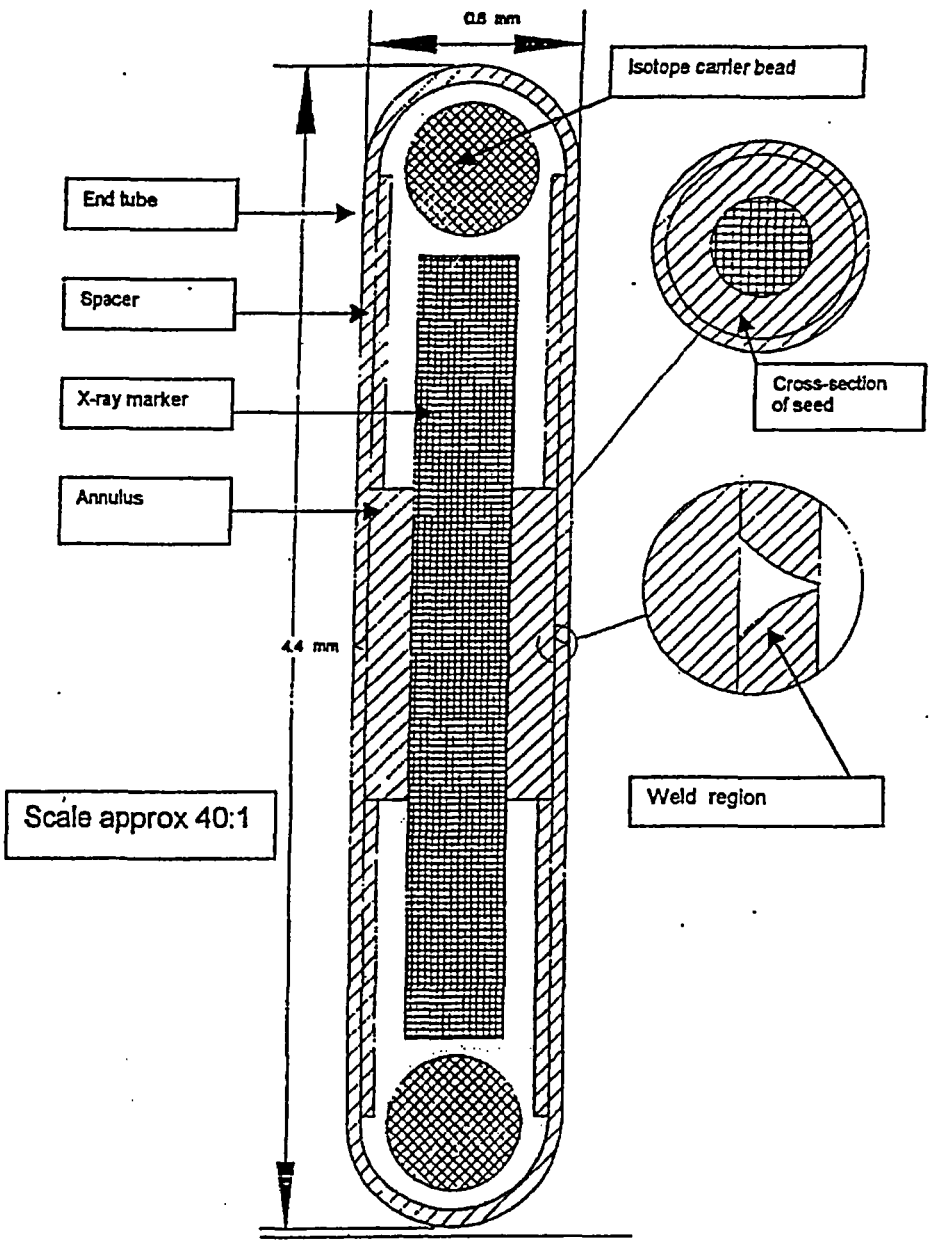
United States Nuclear Regulatory Commission

Date: August 15, 2003 Reviewer: Ujagar S. Bhachu

Date: August 15, 2003 Concurrence: John P. Jankovich

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

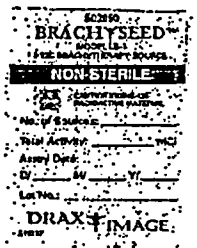
NO.: NR-1121-S-101-S DATE: August 15, 2003 ATTACHMENT 1



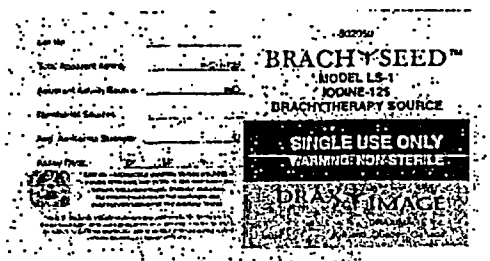
Cutaway view of LS-1 source

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF SEALED SOURCE
(AMENDED IN ITS ENTIRETY)

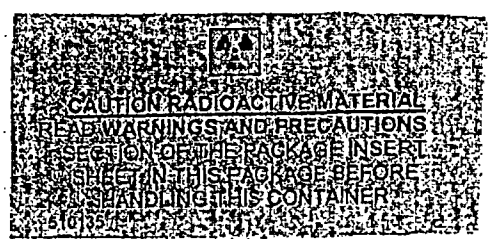
NO.: NR-1121-S-101-S DATE: **August 15, 2003** ATTACHMENT 2



Primary Container Label



Outer Container Label



Warning Insert

Example labels

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

AUG 22 2000

Richard J. Flanagan, Ph.D.
Executive Vice President
DraxImage Inc.
16751 Autoroute TransCanada Highway
Kirkland, Quebec
Canada H9H 4J4

Re: K000475
BrachySeed™ (I-25 Brachytherapy Source)
Dated: June 12, 2000
Received: June 15, 2000
Regulatory class: II
21 CFR 892.5730/Procode: 90 KXK

Dear Dr. Flanagan:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4591. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Daniel G. Schultz, M.D.
Captain, USPHS
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure(s)

3. Subject of the Amendment

This amendment proposes a change to the labels that are applied on the lead pot in which the brachytherapy sources are shipped. The change consists of the following:

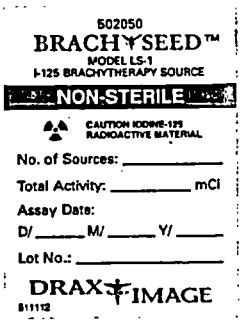
1) Addition of our United States address in Williston, Vermont;
2) Correction of the references to the applicable regulations;
3) Addition of an alternate outer label for BrachySeeds that are supplied sterile.

Please note that the inner container label will remain the same as per the current registration certificate.

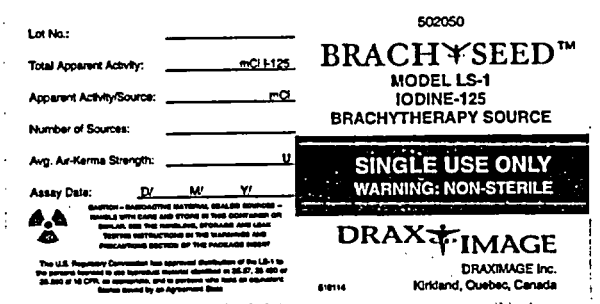
4. Labeling

4.1 Current Labels

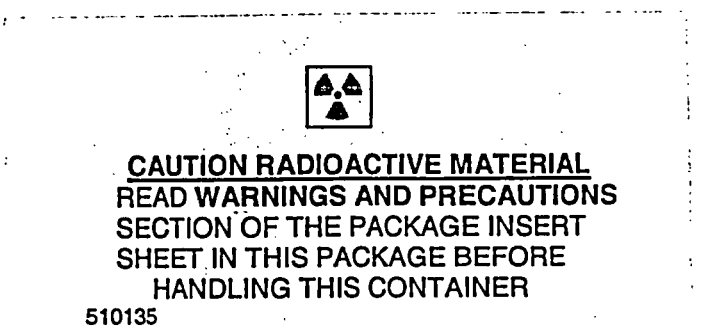
Primary Container Label



Outer Container Label

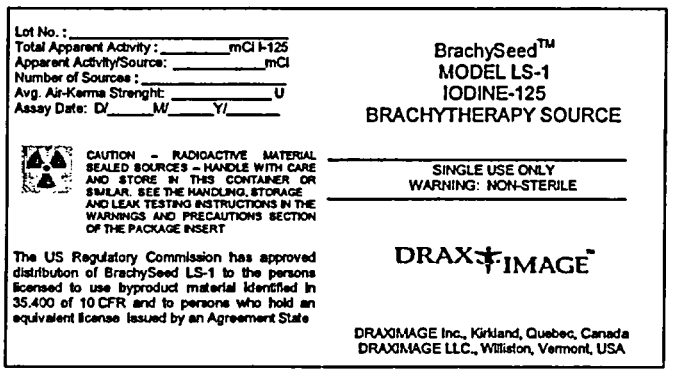


Warning Insert

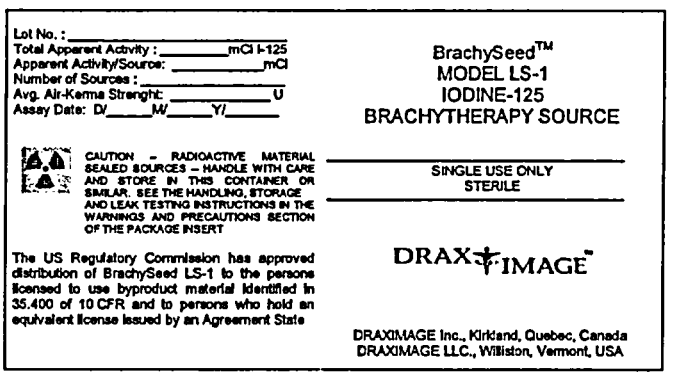


4.2 Proposed Draft Outer Label with Highlighted Changes

Proposed Outer Container Label (Non-Sterile)

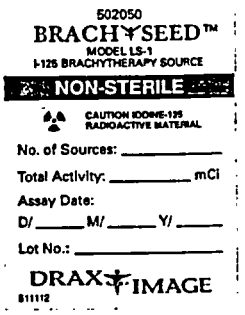


Proposed Alternate Outer Container Label (Sterile)

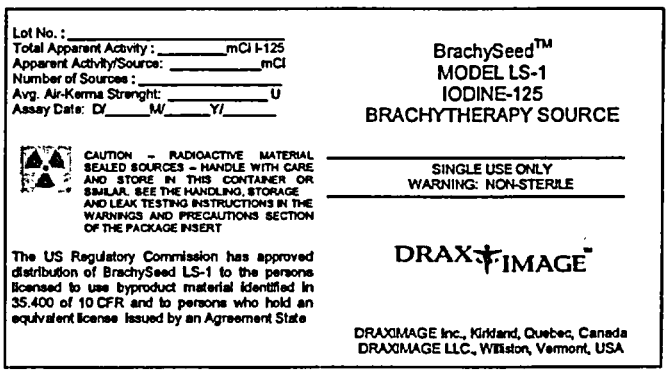


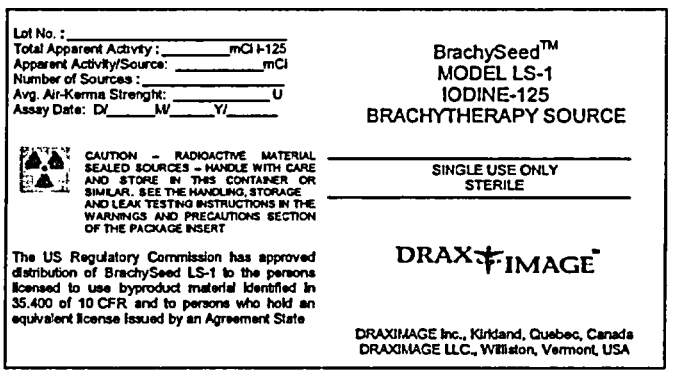
4.3 Proposed Labeling

Primary Container Labels



Proposed Outer Container Label





Warning Insert

CAUTION RADIOACTIVE MATERIAL
READ WARNINGS AND PRECAUTIONS
SECTION OF THE PACKAGE INSERT
SHEET IN THIS PACKAGE BEFORE
HANDLING THIS CONTAINER
510135

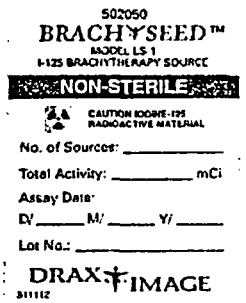
5. Implementation timelines

The proposed new primary outer labels will come in effect after approval from the NRC is granted, and once our current stock of labels is depleted.

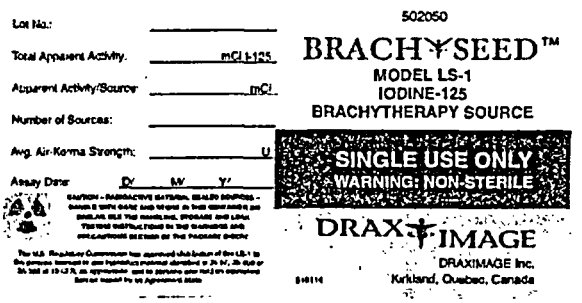
4. Labeling

4.1 Current Labels

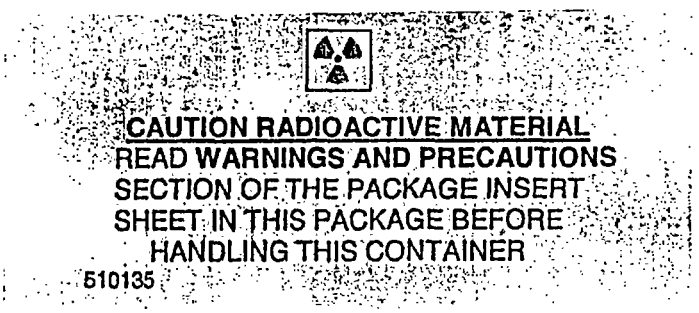
Primary Container Label



Outer Container Label

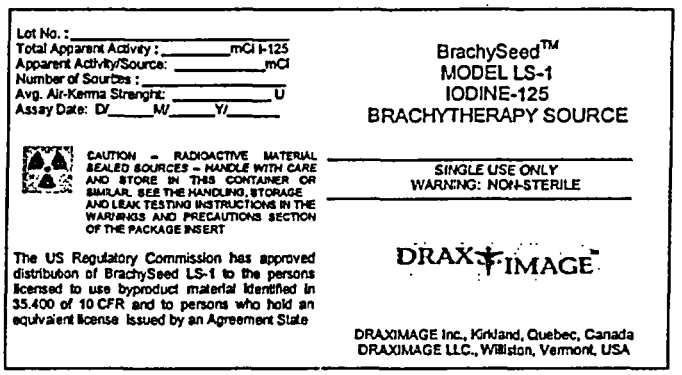


Warning Insert

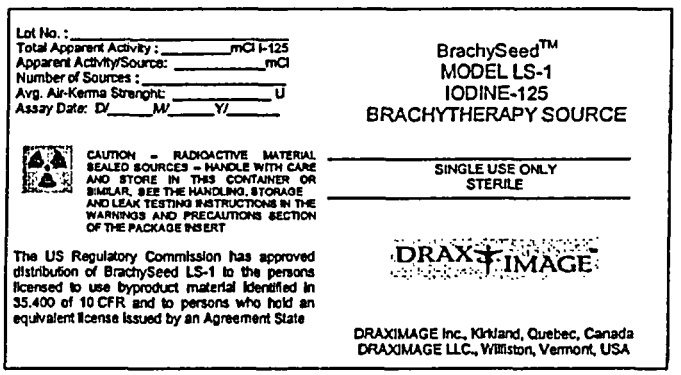


4.2 Proposed Draft Outer Label with Highlighted Changes

Proposed Outer Container Label (Non-Sterile)

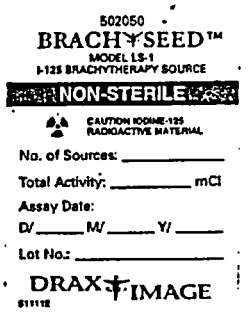


Proposed Alternate Outer Container Label (Sterile)

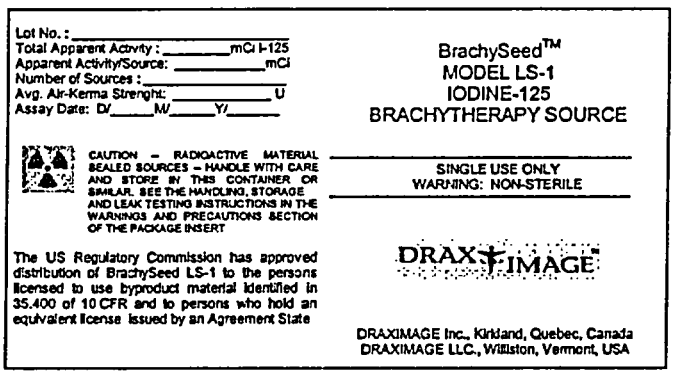


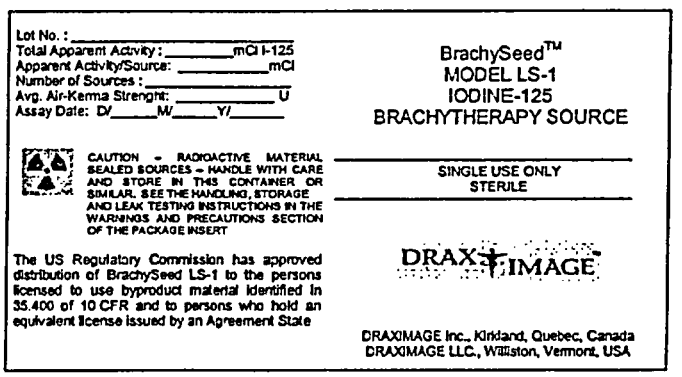
4.3 Proposed Labeling

Primary Container Labels



Proposed Outer Container Label





Warning Insert

CAUTION RADIOACTIVE MATERIAL
READ WARNINGS AND PRECAUTIONS SECTION OF THE PACKAGE INSERT SHEET IN THIS PACKAGE BEFORE HANDLING THIS CONTAINER
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