



April 15, 2008

US-Nuclear Regulatory Commission, Region III
2443 Warrenville Road, Suite 210
Lisle, IL 60532-4352

Subject: Amendment of License Number 24-01041-04 for Cesium-131 Brachytherapy Seeds

Dear Sir/Madam:

Please consider this letter and any enclosed supplemental material an official request for amendment of our current radioactive material license for additional use of the IsoRay Cesium-131 Brachytherapy Seed.

Line 6 (Radioactive Material): Cesium-131

Line 7 (Chemical and/or Physical Form): Sealed Source, IsoRay Cs-131 Brachytherapy Seed

Line 8 (Maximum Possession Quantity): 185 GBq (5000 millicuries), no single source to exceed 370 MBq (10 millicuries or 65 millicuries for high activity)

Purpose for licensed materials: Treatment of malignant disease or similar to 10 CFR Part 35.400 Manual Brachytherapy

Location of use for licensed materials: St. Anthony's Medical Center, 10010 Kennerly Road, St. Louis, MO 63128

Authorized Personnel for material use: Eric J. Sutphen, MD; James E. Marks, MD

Patient Release Criteria: 10 CFR Part 35.75 or equivalent state regulations

Source Name/Model Number: Lawrence CSERION Cs-131 Brachytherapy Seed (also known as Cs-131 Seed), Model CS-1

Sealed Source Registry Number: WA-1220-S-101-S (Date October 5, 2003)

FDA 510(k) Clearance Number: K030162 (Date March 28, 2003)

Source Manufacturer: IsoRay Medical, Inc., 350 Hill Street, Suite 106 Richland, WA 99354, Phone: 509-375-1202

Additional Sealed Source Information: 4.5 mm x 0.8 mm, titanium-encased ceramic with gold wire $T_{1/2} = 9.7$ d, $E \sim 30$ KeV X-rays, HVL = 0.025 mm Pb Radiation energy is similar to I-125 and Pd-103 seeds Cs-131 is reactor-produced from Ba-130 neutron capture

Thank you for your time and assistance with this matter. If there is anything else you require, please contact me directly at 314-525-1688 or the address and telephone number listed above.

Sincerely,

A handwritten signature in black ink that reads "David J. Keys". The signature is written in a cursive, flowing style.

David J. Keys, Ph.D.
Radiation Safety Officer
Enclosures

RECEIVED APR 28 2008

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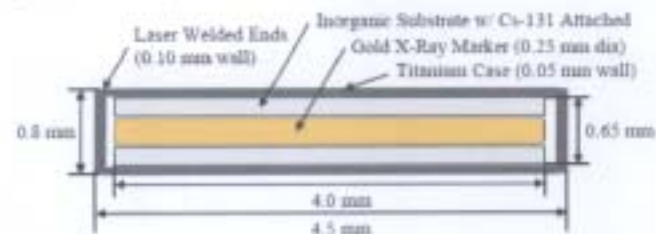
For Single Use, R₁ ONLY

Description

IsoRay Medical, Inc. Cesium-131 Brachytherapy Seed

Model No. CS-1

The IsoRay Medical, Inc. Cs-131 Brachytherapy Seed consists of a welded titanium capsule containing the low energy gamma (X-ray) emitting isotope, Cesium-131, adsorbed onto an internal inorganic substrate. The seed configuration is designed to generate near isotropic emission of therapeutic radiation.



Physical Characteristics

Principle Radionuclide:	Cesium-131 (Cs-131)
Half-life of Cs-131:	9.69 days (232.6 hr)
Radiation Energy:	29.5, 29.8, 33.6 keV
Half Value Thickness ⁽¹⁾ :	0.025 mm of Lead
Decay Mode:	Cs-131 decays by electron capture with the emission of characteristic low-energy X-ray photons and electrons. The electrons are absorbed by the titanium wall of the seed.
Radionuclide Purity:	> 99.85% Cs-131 < 0.10% Cs-132 < 0.05% All other radionuclides

Indications

IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds are indicated for the treatment of malignant disease (e.g., head and neck, brain, breast, prostate, etc.) and may be used in surface, interstitial, and intracavitary applications for tumors with known radiosensitivity. The seeds may be used as a primary treatment or in conjunction with other treatment modalities, such as external beam radiation therapy, chemotherapy or as treatment for residual disease after excision of primary tumors⁽²⁾.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (e.g. ulcerated) is not recommended with IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds due to the potential for source migration.

Warnings

Warning: IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds are supplied non-sterile, in a tamper-evident container and are indicated for single use only.

IsoRay Medical, Inc. Cs-131 Seeds must be sterilized prior to implantation using a qualified sterilization procedure such as steam or ethylene oxide (EPO). DO NOT USE DRY HEAT OR CHEMICAL STERILIZATION. Some cold chemical sterilization solutions may leave a residue which can interfere with seed loading and implantation. IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds should be sterilized in an adequately shielded container which is compatible with and allows for sterlant penetration. When in doubt about compatibility of steam heat with various seed containers, load them with non-radioactive seeds to determine the effect of steam on the container material and on seed recovery.

Warning: Never implant visibly damaged Cs-131 Brachytherapy Seeds.

IsoRay Medical, Inc. Cs-131 Seeds should not be handled roughly or forced into (or from) any implant tube, needle, or cartridge; since this may breach the external casing, potentially releasing free Cs-131 into the environment and/or body fluids if implanted. If this should happen, close off the area, seal the seeds in a shielded

container, restrict personnel movement to avoid spread of any radioactive contamination, and survey/decontaminate the area and personnel according to established radiological procedures.

Precautions

Caution: IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds contain radioactive Cesium-131.

IsoRay Medical, Inc. Cs-131 Seeds should only be handled in authorized, licensed facilities by experienced personnel who are fully trained and qualified in the safe use of radioactive materials by the appropriate regulatory agency. The seeds are quite small and are visually difficult to locate when dropped. All radiation and contamination surveys should be performed using calibrated equipment that is capable of detecting 30 keV photons (low energy X-rays). Personnel monitoring for radiation exposure is required (e.g., film badge, thermal luminescent dosimeter, finger rings, etc.). The half-value thickness of lead for Cesium-131 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide ~99.9% reduction of exposure.¹

Caution: IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds exhibit a high surface dose rate.

Appropriate precautions must be taken during handling (e.g., keep sources shielded, away from personnel, and minimize exposure time). Plan the implantation procedure to minimize radiation exposure to personnel⁽³⁻⁶⁾. The seeds should be handled behind shielding of adequate thickness. Forceps, either reverse or normal action, should be used to maintain operator to seed distance. If normal action forceps are used, gentle pressure should be applied so that seeds are not damaged. SEEDS SHOULD NOT BE PICKED UP WITH THE FINGERS.

Caution: Do not expose seeds to extreme conditions.

The outer titanium shell of the IsoRay Medical, Inc. Cs-131 Brachytherapy Seed has excellent biocompatibility and stability under normal use. Seeds are not affected by moderate pressure, vacuum, or temperature, common solvents (e.g., acetone, alcohol, etc.), or mild detergents. Do not expose the seeds to strong acids or bases. Do not expose seeds to excessive temperatures (greater than 300°C) or pressures (greater than 100 psi).

Instructions For Use

IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds may be implanted using any appropriate, FDA-cleared device (e.g., 18 gauge brachytherapy needle, seed applicator, tubing, etc.). Radiological protection devices should be utilized during implantation procedures. When protective barriers are not practical (e.g., certain surgical stages), the user must rely on time and distance to minimize radiation exposure.

Determination of Source Shelf-Life

IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds contain Cesium-131 with a 9.69 day half-life and must be corrected for decay in order to properly calculate activity at the time of implantation as is shown in the table below:

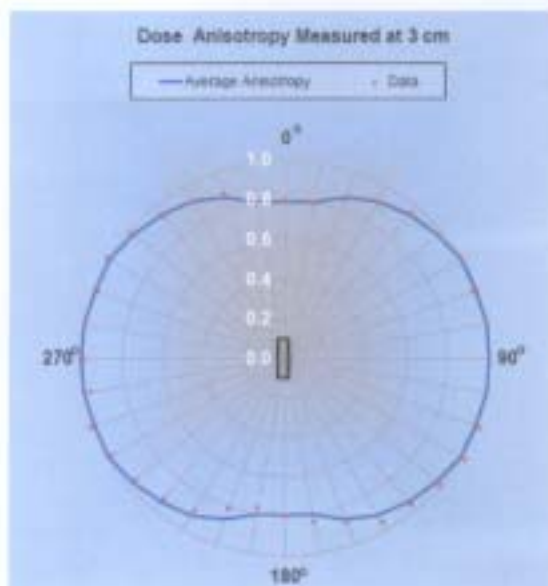
Day	Factor	Day	Factor	Day	Factor
0	1.0000	11	0.4553	22	0.2073
1	0.9310	12	0.4238	23	0.1930
2	0.8667	13	0.3946	24	0.1796
3	0.8069	14	0.3673	25	0.1672
4	0.7512	15	0.3420	26	0.1557
5	0.6993	16	0.3184	27	0.1449
6	0.6510	17	0.2964	28	0.1349
7	0.6061	18	0.2759	29	0.1256
8	0.5643	19	0.2569	30	0.1170
9	0.5253	20	0.2392	31	0.1089
10	0.4890	21	0.2226	32	0.1014

Dosage and Administration

The total activity and placement of IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds required for any given treatment depends upon a number of well-established

factors (e.g., treatment goals, tumor location/volume/shape, radiation history of the tumor site, concurrent treatment(s), etc.). Established practice should be followed for the proper placement of the sources within the tissue, and for evaluation of the radiation dose distribution achieved during implantation. ⁽²⁻¹²⁾

The IsoRay Medical, Inc. Cs-131 Seed is designed to produce a nearly isotropic dose distribution. The radiation dose contour of the Cs-131 Seed at a radius of 3 cm from the source, taken from actual measurements, appears in the figure below.



The dose characteristics of the Cs-131 Seed have also been confirmed through extensive Monte Carlo evaluations in accordance with American Association of Physicists in Medicine (AAPM) Task Group 43 (TG-43) guidelines⁽¹³⁾. The Cs-131 Seed has an anisotropy factor of 1.01 at 0.5 cm from the source and an average anisotropy factor of 0.97. ⁽¹²⁾

IsoRay Medical, Inc. Cs-131 Seeds are available with apparent activities from 0.20 to 50.0 mCi [Air-Kerma strength 0.13 to 33 microGy meter squared per hour ($\mu\text{Gy m}^2/\text{h}$)] ⁽¹²⁻¹⁴⁾. AAPM guidelines for brachytherapy should be followed for independent verification of source output. ⁽²⁻⁵⁾ A certificate of analysis is provided with each shipment that includes: customer order number, lot number, number of seeds, reference date, implant date, and average and total activities expressed as apparent activity (mCi) and Air Kerma strength ($\mu\text{Gy m}^2/\text{h}$) traceable to NIST (National Institute of Standards and Technology). Additional information, including patient and physician names, may be provided upon request.

Adverse Reactions

The potential for, and symptoms of, adverse events related to radiation exposure will vary depending on the radiosensitivity of the exposed tissue, the amount of radiation delivered, and the placement of the seeds themselves. The following information has been derived from articles published in the medical literature.

Immediately subsequent to transperineal seed implantation for prostate brachytherapy, there is often procedure-related bleeding or burning beneath the scrotum or passage of blood in the urine. ⁽¹⁵⁾ These symptoms are usually treated supportively. Short-term urinary symptoms (e.g., frequent urination, discomfort, or difficulty voiding), may be experienced after implantation, and may last for several weeks. ⁽¹⁶⁻¹⁸⁾ These effects are generally mild and resolve spontaneously as seed radiation levels decrease. Impotence has been noted as a possible long-term adverse effect with an incidence ranging from 6-30%, which may be age-related. ⁽¹⁹⁾ Long-term incontinence is uncommon, ^(18,20) although patients who have previously undergone transurethral resection of the prostate (TURP) may be at a higher

risk. ^(18,21) Urethral stricture has been reported in a small percentage of cases. ^(18,21) Incidents of asymptomatic seed embolization to the lungs have been reported. ⁽²²⁾

Patient Counseling Information

All patients should be informed of the nature of IsoRay Medical, Inc. Cs-131 Brachytherapy Seed implants and the expected period of time during which radiation precautions will be necessary. Patients, their close associates and associated medical personnel should be instructed in the necessary radiation safety procedures required for someone who has received an IsoRay Medical, Inc. Cs-131 Seed implant. Guidelines for necessary precautions and patient release have been established. ⁽²³⁻²⁵⁾

All patients should be advised of the possibility that, during a course of treatment, one or more seeds may be released into the urine or semen. Bandages or liners which come into contact with the implant site should be scrutinized for small metallic seeds (1/4 of an inch long). Patients should be advised that whenever seeds are found, they should be picked up with a spoon, placed in a jar or other container, and stored in an uninhabited area in the home. Patients should notify their health care provider as soon as possible after such an occurrence.

Accountability

IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds may only be distributed to persons licensed pursuant to Washington State Department of Health (WDOH) regulations or under equivalent licenses of the U.S. NRC or an Agreement State, and outside the United States, to persons authorized by the appropriate authority.

As with all radioactive materials, seeds must be controlled in accordance with approved procedures by authorized personnel in licensed facilities. When not in use, seeds should be stored in shielded containers in a controlled area (additional user requirements may also apply). If any radioactive material cannot be accounted for, the loss must be reported to the appropriate state or federal licensing agency.

Immediately report to IsoRay Customer Service any discrepancies between ordered and received shipments or any damaged or misrouted shipments. Dispose of damaged or unused seeds in compliance with local, state and federal regulations. If seed disposal services are desired, contact IsoRay Customer Service for return authorization at 1-509-375-5329. Radioactive materials approved for return must comply with applicable U.S. Department of Transportation regulations (49 CFR 173) regarding packaging and labeling.

Leak Testing

IsoRay Medical, Inc. Cs-131 Brachytherapy Seeds are leak tested prior to shipment and have passed a leak test showing < 0.005 μCi of removable Cs-131 as required by Washington State Department of Health (WDOH) regulations. This leak test date and value are printed on the Certification of Analysis that accompanies each shipment. The user is not required to perform additional leak testing.

Literature Citations and References

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- Henschke, UK, Lawrence, DC. "Cesium-131 Seeds for Permanent Implants." Radiology. 85, 1117-1119 (1965).
- Protection of Radiation from Brachytherapy Sources. NCRP Report No. 40, Washington DC (1972).
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- Rivard MJ, Cooney BM, DeWerd LA, Hanson WF, Huq MS, Ibbot GS, Mitch MG, Nath R, and JP Williamson. "Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations." Med Phys. 31, 633-674 (2004).
- Nath R, Anderson LL, Meis JA, Olch AJ, Sitt JA, and Williamson JP. "Code of Practice for Brachytherapy Physics: Report of the AAPM Radiation Therapy Committee Task Group No. 56." Med. Phys. 24, 1517-1648 (1997).
- J F Williamson, B M Cooney, L A DeWerd, W F Hanson, and R Nath. "Dosimetric Prerequisites for Routine Clinical Use of New Low Energy Photon Interstitial Brachytherapy Sources." Med. Phys. 25, 2169-2170 (1998).
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Association of Physicist in Medicine Radiation Therapy Committee Subcommittee on Low-Energy Brachytherapy Source Dosimetry." *Med. Phys.* 28, 2129-2130 (1999).

10. Anderson, L.L. "Intracavitary Brachytherapy - Physical, Biological, and Clinical Considerations." *Intracavitary Collaborative Working Group*, Raven Press, New York, NY 1990.
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23. Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides. NCRP Report No. 33, Washington DC (1976).
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D. Statement of Indications for Use

Applicant: IsoRay, Inc.
510(k) Number: K030162
Device Name: Lawrence CSERION Model CS-1

Indications For Use (Page 1 of 1):

IsoRay, Inc. Lawrence CSERION seeds are indicated for the treatment of malignant disease (e.g., head and neck, brain, breast, prostate, etc.) and may be used in surface, interstitial, and intracavitary applications for tumors with known radiosensitivity. The seeds may be used as a primary treatment or in conjunction with other treatment modalities, such as external beam radiation therapy, chemotherapy or as treatment for residual disease after excision of primary tumors.

DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ or Over-The Counter Use
(Per 21 CFR 801.109)

 David A. Johnson
(Division Sign-Off)
Division of Reproductive, Abdominal,
and Radiological Devices
510(k) Number K030162

Confidential Until SE Determination



Food and Drug Administration
8200 Corporate Boulevard
Rockville MD 20850

MAR 28 2003

Mr. David J. Swanberg
Chief Operations Officer
IsoRay, Inc.
350 Hills Street, Suite 106
RICHLAND WA 99352

Re: K030162
Trade/Device Name: Lawrence CSERION
Model CS-1
Regulation Number: 21 CFR 892.5730
Regulation Name: Radionuclide
brachytherapy source
Regulatory Class: II
Product Code: 90 KXK
Dated: January 13, 2003
Received: January 16, 2003

Dear Mr. Swanberg:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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) that do not require approval of a premarket approval application (PMA). 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 (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (sections 531-542 of the Act); 21 CFR 1000-1050.


This letter will allow you to begin marketing your device as described in your Section 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), please contact the Office of Compliance at one of the following numbers, based on the regulation number at the top of the letter:

800.1xxx	(301) 594-4591
876.2xxx, 3xxx, 4xxx, 5xxx	(301) 594-4616
884.2xxx, 3xxx, 4xxx, 5xxx, 6xxx	(301) 594-4616
892.2xxx, 3xxx, 4xxx, 5xxx	(301) 594-4654
Other	(301) 594-4692

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 Part 807.97) you may obtain. Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer 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,



Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

ISORAY

350 Hills Street Suite 106
Richland Washington 99352

Attention: Garrett N. Brown, Ph.D.
Radiation Safety Officer

In accordance with amendment request information referenced in License Condition 32.D, Radioactive Materials License Number WN-L0213-1 is amended as follows:

License Condition 9.A is amended to read:


9A. Processing, manufacture, possession, storage, research and development, **sealed source distribution**, and waste.

License Condition 32.D is added:

32.D. Sealed source and device registration WA-1220-S-101-S.

FOR THE STATE OF WASHINGTON DEPARTMENT OF HEALTH

Date: 5 October 2004
(04-08-37; 04-08-62)

TS
By: 
Anine Grumbles
Radioactive Materials Licensing



STATE OF WASHINGTON
DEPARTMENT OF HEALTH
DIVISION OF RADIATION PROTECTION

7171 Cleanwater Lane, Bldg. 5 • P.O. Box 47827 • Olympia, Washington 98504-7827
TDD Relay 1-800-833-6388

October 5, 2004

Garrett N. Brown, Ph.D.
Radiation Safety Officer
ISORAY
350 Hills Street Suite 106
Richland, Washington 99352

Dear Dr. Brown:

Enclosed is the Sealed Source & Device registration for your CSERION CS 131 Brachytherapy Seed, SS&D registry number WA-1220-S-101-S. Also enclosed is Amendment No. 1 to License Number WN-L0213-1 authorizing distribution of the ¹³¹Cseed. In accordance with your letter of August 13, 2004, our evaluation of your SS&D application is subject to WAC 246-254-120, "Fees for Licensing and Compliance Actions." It is the purpose of this section of Title 246 of the Washington Administration Code to recover the cost to the department of staff activities, such as the review of your Sealed Source and Device evaluation. This portion of WAC provides that we charge a fee of \$100.00 per hour.

Our staff's time directly associated with your SS&D evaluation totals 21 hours. At \$100.00 per hour the fee is \$ 2,100.00.

Please return the lower portion of the enclosed billing with your remittance to Department of Health, within 30 days.

Your cooperation in this matter is appreciated.

Sincerely,

A handwritten signature in black ink, appearing to read "Arden C. Scroggs".

Arden C. Scroggs, Supervisor
Radioactive Materials Section

Enclosures: Sealed Source & Device Registration No. WA-1220-S-101-S
License Amendment No.1

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

NO.: WA-1220-S-101-S

DATE: 17 September 2004

PAGE: 1 of 8

SOURCE TYPE:

Sealed Brachytherapy Source

MODEL:

CS-1
Lawrence CSERION Cs-131 Brachytherapy Seed
(also known as ¹³¹Cseed)

DISTRIBUTOR:

IsoRay
Suite 106
350 Hills Street
Richland, WA 99352

MANUFACTURER:

IsoRay
Suite 106
350 Hills Street
Richland, WA 99352

ISOTOPE:

Cesium-131

MAXIMUM ACTIVITY:

65 mCi (2.41 GBq) Internal Activity
2-5 mCi Average Air Kerma Strength/Assay Activity

LEAK TEST FREQUENCY:

Not Required

PRINCIPAL USE:

(AA) Manual Brachytherapy

CUSTOM SOURCE:

YES NO

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

NO.: WA-1220-S-101-S

DATE: 17 September 2004

PAGE: 2 of 8

SOURCE TYPE: Scaled Brachytherapy Source

DESCRIPTION:

The IsoRay Model CS-1 brachytherapy seed is a small, cylindrical, sealed source that consists of a welded titanium capsule containing the low energy gamma (X-ray) emitting isotope, cesium-131 ($T_{1/2} = 9.7$ d), adsorbed onto an internal inorganic substrate. The nominal external seed dimensions (4.5 mm length and 0.8 mm diameter) and patient-contacting material (titanium) are identical to other commercially available brachytherapy sources for radiation oncology.

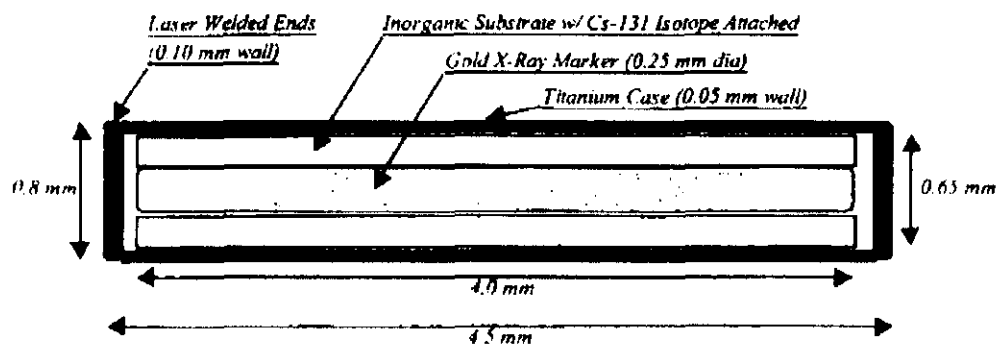
The brachytherapy seed contains a cylindrical inorganic substrate onto which a thin coating of radioactive cesium-131 is applied. A 0.25 mm diameter gold wire is placed within in the central annulus of the core. The gold wire serves as an X-ray marker for radiographic visualization of individual brachytherapy source locations. The internal core materials are inserted into a tube of commercially pure, grade 2 titanium (4.3 mm long, 0.8 mm OD, 0.7 mm ID). Titanium end caps (0.8 mm diameter, 0.1 mm thick) are precision laser welded in place.

LABELING:

Because of their small size, individual brachytherapy sources do not directly exhibit identifying marking, labeling or warnings. Multiple sources will be supplied in a primary container such as a glass vial or preloaded cartridges. The primary container will be placed inside a shielded storage container. The shielded storage container will be placed inside a shipping container meeting DOT requirements for shipment of radioactive materials. Examples of labels for each of these containers appear in Figures 1 - 3. The labels will be made of durable materials that remain legible during the expected conditions of transportation and use.

DIAGRAM:

A diagram of the IsoRay Model CS-1 brachytherapy seed showing components, dimensions, and the method of sealing appears below:



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

NO.: WA-1220-S-101-S

DATE: 17 September 2004

PAGE: 3 of 8

SOURCE TYPE: Sealed Brachytherapy Source

CONDITIONS OF NORMAL USE:

IsoRay Model CS-1 brachytherapy seeds are indicated for the treatment of malignant disease (e.g., head and neck, brain, breast, prostate, etc.) in a clinical setting and may be used in topical, interstitial, and intracavitary applications for tumors with known radiosensitivity. The seeds may be used as a primary treatment or in conjunction with other treatment modalities, such as external beam radiation therapy, chemotherapy or as treatment for residual disease after excision of primary tumors.

Seeds are typically supplied non-sterile in radiation shielded packaging. The sources are capable of withstanding autoclave conditions. Sources may be implanted using any appropriate, FDA-approved device (e.g., 18-gauge brachytherapy needle, seed applicator, tubing, etc.). Radiological protection devices should be utilized during implantation procedures. When protective barriers are not practical (e.g., certain surgical stages), the user must rely on time and distance to minimize radiation exposure.

PROTOTYPE TESTING:

IsoRay Model CS-1 Brachytherapy Seeds were classified and subjected to environmental test conditions and stresses as defined in ISO 2919-1999, "Radiation Protection – Sealed Radioactive Sources – General Requirements and Classification." The seeds successfully passed all of the required test conditions and are classified as ISO 99C53211, where the last five digits define the test conditions and requirements as shown in the following table. The cesium-131 isotope is classified as Group 3: Moderate Toxicity.

Test	Classification	Test Conditions
Low Temperature High Temperature	5	-40°C (20 min) w/ thermal shock to 20°C; +600°C (1 hr) w/ thermal shock to 20°C
External Low Pressure External High Pressure	3	Two 5 min periods at 25 kPa absolute; Two 5 min periods at 2 Mpa absolute
Impact	2	50 g steel weight dropped from 1 meter height
Vibration	1	No Test Required
Puncture	1	No Test Required
Bending	1	No Test Required
Steam Autoclave	Optional	121°C at 29.8 psig for 20 min

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

NO.: WA-1220-S-101-S

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SOURCE TYPE:

Sealed Brachytherapy Source

EXTERNAL RADIATION LEVELS:

The radiation dose rates in air at various distances from the Model CS-1 source were calculated using a gamma dose rate constant of 0.637 cGy/hr-mCi (637 mR/hr) at 1 cm. The dose rate constant is based on Air Kerma Rate measurements of actual seeds by the National Institute for Standards and Technology and has been confirmed using Monte Carlo calculations.

Distance from the source (cm)	Dose Rate (mR/hr) Maximum activity (50 mCi)	Dose Rate (mR/hr) Typical activity (3.3 mCi)
5	1300	84
30	35	2.3
100	3.2	0.21

QUALITY ASSURANCE AND CONTROL:

Prior to distribution, the following quality control tests will be completed:

Test	Method	Acceptance Criteria
Radionuclidic Purity	Gamma Analysis	> 99.9% Cs-131; < 0.01% Ba-131; < 0.1% Cs-132; < 0.05% all other radioisotopes
Weld Inspection	Visual – w/ Magnification	Silver in color, with no cracks or holes
Leak Test	ISO 9978	≤ 0.185 kBq (≤ 0.005 μCi) per seed
Radioassay	Dose Calibrator	0.2 to 50.0 mCi ± 5% apparent activity
External Dimensions	Gauging	0.8mm ± 10% OD; 4.5 mm ± 10% length
Seed Assembly	Visual	No foreign material, dents, or scratches
Labeling	Visual	Information is legible, accurate and complete

IsoRay maintains a quality assurance program that is based on ISO 9001 requirements and is designed to comply with US Food and Drug Administration Quality System Requirements for medical devices. Elements of the quality system that are directly applicable to this brachytherapy seed are included in the application for safety evaluation of this sealed source.

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

NO.: WA-1220-S-101-S

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SOURCE TYPE: Sealed Brachytherapy Source

LIMITATIONS AND OTHER CONSIDERATIONS OF USE:

- The sealed sources shall be distributed only to specific licensees of the Washington State Department of Health, the U.S. Nuclear Regulatory Commission, or an Agreement State.
- Handling, Storage, Use, Transfer and Disposal: To be determined by the licensing authority. Given that these sealed sources exhibit high surface dose rates when unshielded, these sources should be handled by experienced licensed personnel using adequate remote handling equipment and procedures.
- Leak testing beyond that performed by the manufacturer is not required due to the short half-life (9.7 days) of Cs-131.
- Since the seeds are non-sterile when shipped, they must be sterilized upon receipt prior to use using either steam (autoclave) or ethylene oxide (EtO). Dry heat sterilization must not be used.
- Sources shall not be exposed to conditions that exceed the ISO 2919 classification of 99C53211. Despite excellent corrosion resistance of titanium, seeds are not to be exposed to concentrated acids or bases.
- Licensees should observe the manufacturer's instructions for handling and using the Cs-131 sources which are provided with each shipment of seeds. When not in use, seeds should be stored in shielded containers in a controlled area.
- Any excess seeds must be disposed in accordance with applicable rules and regulations. Unused sources may be returned to the distributor.
- This registration sheet and the information contained with the references shall not be changed without the written consent of the Washington State Department of Health.

SAFETY ANALYSIS SUMMARY:

Based on review of the IsoRay Model CS-1 brachytherapy sealed source, its ISO 2919/ANSI N43.6/ANSI N44.1 classification, and the information and test data cited below, we conclude that the IsoRay Model CS-1 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 which might occur during uses specified in this certificate.

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

NO.: WA-1220-S-101-S

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SOURCE TYPE:

Sealed Brachytherapy Source

REFERENCES:

This Certificate of Registration is based on information contained in the following supporting documents which are hereby incorporated by reference and made a part of this registry document:

- Application for Safety Evaluation and Registration of IsoRay Model CS-1 Brachytherapy Sealed Source, dated May 20, 2004.
- Letter and attachment dated 24 August 2004.

ISSUING AGENCY: Washington State Department of Health, Office of Radiation Protection
Box 47827, Olympia, Washington 98504 360-236-3220.


Date: 17 Sept 04

REVIEWED BY:


for C. DeMaris

Date: 23 September 04

CONCURRENCE:


A. Grumbles

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

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SOURCE TYPE: Sealed Brachytherapy Source


Cs-131 Brachytherapy Seed Model CS-1	
IsoRay, Richland, WA 99352 USA	
Lot Number:	
Assay Date:	
Number of Sources:	
Total Activity: mCi	
NON-STERILE Caution: Cesium-131 Radioactive Material	

Figure 1. Example of primary seed container labeling


Cs-131 Brachytherapy Seed Model CS-1			
Manufactured By: IsoRay, Inc. 350 Hills Street, Suite 106 Richland, WA 99352 USA Phone: 509-375-1202	Certificate Number:		
	Lot Number:		
	Number of Seeds:	Reference Date:	Implant Date:
 Caution: Federal law restricts this device to sale by or on the order of a physician	Total Apparent Activity (mCi):		
	Total Air Kerma $\mu\text{Gy m}^2 \text{h}^{-1}$ (U):		
	Midpoint Apparent Activity (mCi):		
	Midpoint Air Kerma $\mu\text{Gy m}^2 \text{h}^{-1}$ (U):		
Caution: Radioactive Material Cesium-131	Patient Name or ID:		
	Physician Name:		
SINGLE USE ONLY		WARNING: NON-STERILE	

Figure 2. Example of shielded storage container labeling

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

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SOURCE TYPE:

Sealed Brachytherapy Source

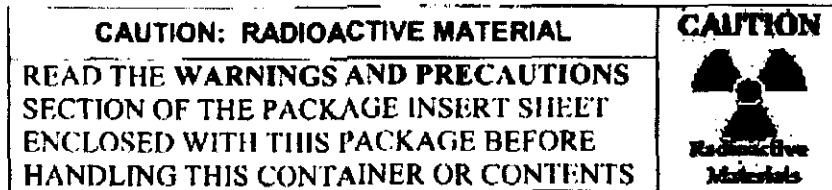


Figure 3. Example of package insert warning label



Date: October 30, 2006

To: Health Care Providers

From: IsoRay Medical, Inc.

Re: Patient Release Criteria for Cesium-131 Brachytherapy Seed Implants

The decision to release ^{131}Cs implant patients with documented instructions to limit exposure to family members can be determined by directly comparing ^{131}Cs with ^{125}I . The integrated dose to the patient is proportional to the half-life times the initial dose rate. Since ^{131}Cs has a 9.7 day half-life, and ^{125}I has a 60 day half-life the initial dose rate for a ^{131}Cs therapy would be 6.2 times as high as for ^{125}I if the prescribed dose were the same.

The prescribed dose for a prostate therapy is typically 145 Gy for ^{125}I and 115 Gy for ^{131}Cs . Therefore, the initial dose rate from a ^{131}Cs implant would be 5 times as high as for ^{125}I implanted in the same patient. Since ^{131}Cs and ^{125}I have nearly the same radiation energies, the external integrated dose will be approximately proportional to the prescribed dose.

While the Radioactive Materials License and Regulations place requirements on an institution to provide patient instructions to minimize dose to family and members of the public, patient compliance with the instructions cannot not be assured. The specific restrictions placed on a patient are between the health care provider and the patient. The health care provider can outline trade-offs to make compliance easier for the patient.

Examples of trade-offs may be one patient might choose to maintain separate sleeping arrangements, and maintain distance during the day for a month in exchange for no further restrictions afterwards. Another might find it easier to comply with being able to be within one meter of family members for up to six hours per day, and maintaining distance for the rest of the day.

In summary, while the initial dose rate of ^{131}Cs is higher, the integrated dose can be significantly lower. Moreover, the relatively short half life can permit a great deal more flexibility in determining the specific restrictions to minimize dose to family members.

For additional information or questions please contact Dale Boyce at 509-375-1202.

NUREG-1556 as Applied to Cesium-131 Seed Implants:

Patients who receive cesium-131 brachytherapy seed implants must be released following the applicable NRC guidance and regulations as referenced below. Patients may be released based on administered activity (U.1.1), measured dose rate (U.1.2) or patient-specific dose calculations (U.1.3), as described in NUREG-1556. The following equation provides a rational method for estimating the dose to the general public or an affected individual:

$$D(\infty) = \frac{34.6 \cdot \Gamma \cdot Q_0 \cdot T_p \cdot (0.25)}{(100\text{cm})^2} \quad \text{Equation U.2 from NUREG-1556}$$

$D(\infty)$ is the estimated dose to infinite decay that an affected individual is expected to receive. The specific gamma constant (Γ) is the dose rate at one meter per unit activity. Q_0 is the implanted activity. The physical half-life of cesium-131 (T_p) is 9.69 days. The one quarter factor (0.25) assumes that the affected individual is exposed for 6 hours per day.

Rearranging Equation U.2, converting 100 cm to 1 meter, inputting 500 mR for $D(\infty)$, and inputting 9.69 for T_p , the equation then simplifies to Equation (1) as follows:

$$Q_0 \cdot \Gamma = \frac{D(\infty) \cdot (100\text{cm})^2}{34.6 \cdot T_p \cdot (0.25)} = \frac{500\text{mR} \cdot (1\text{m})^2}{34.6 \cdot 9.69 \cdot (0.25)} = 5.96\text{mR/hr} \quad \text{Equation (1)}$$

The factor, $Q_0 \Gamma$, is the dose rate (mR/hr) at 1 meter for the entire implant at the time of patient release. In essence, if the patient is measured with a dose rate instrument and the reading is less than approximately 6.0 mR/hr at 1 meter, the NRC guidance/criteria for patient release is met.

As a comparison, Table U.1 in NUREG-1556 (which does not specifically list cesium-131) indicates that patients may be released at 1 mR/hr at 1 meter for iodine-125 (I-125). Since the half-life of Cs-131 is approximately 1/6th that of I-125, it makes sense that the dose rate could be six times greater at the time of patient release.

References:

- (1) <http://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-0075.html>
10 CFR 35.75 "Release of Individuals Containing Unsealed Byproduct Material or Implants Containing Byproduct Material." This regulation authorizes release of individuals who have been administered unsealed byproduct material or implants containing byproduct material if the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 500 mrem.
- (2) <http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr1556/v9/nureg-1556-9.pdf>
NUREG-1556 Vol. 9 "Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses." Appendix U of this guidance document describes methods for calculating doses to other individuals and contains tables of activities not likely to cause doses exceeding 500 mrem.
 - U.1.1 Release of Patients Based on Administered Activity
 - U.1.2 Release of Patients Based on Measured Dose Rate
 - U.1.3 Release of Patients Based on Patient-Specific Dose Calculations
 - Table U.1 Activities and Dose Rates for Authorizing Patient Release

Below is information from NUREG-1556 Volume 9 Appendix U.2.3.2.
<http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr1556/v9/nureg-1556-9.pdf>

U.2.3.2 Instructions Regarding Implants

For patients who have received implants, additional instructions may include the following:

A small radioactive source has been placed (implanted) inside your body. The source is actually many small metallic pellets or seeds, which are each about 1/3 to 1/4 of an inch long, similar in size and shape to a grain of rice. To minimize exposure to radiation to others from the source inside your body, you should do the following for _____ days.

- Stay at a distance of _____ feet from _____.
- Maintain separate sleeping arrangements.
- Minimize time with children and pregnant women.
- Do not hold or cuddle children.
- Avoid public transportation.
- Examine any bandages or linens that come into contact with the implant site for any pellets or seeds that may have come out of the implant site.
- If you find a seed or pellet that falls out:
 - Do not handle it with your fingers. Use something like a spoon or tweezers to place it in a jar or other container that you can close with a lid.
 - Place the container with the seed or pellet in a location away from people.
 - Notify _____ at telephone number _____.

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For international use affix customs declaration PS Form 2976.

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- 2. Payment Method**
Affix postage or meter strip to area indicated in upper right hand corner.



- 3. Acceptance**
Bring your Flat Rate Priority Mail envelope to a Post Office, or to schedule pickup of your postage paid envelopes visit us at usps.com/pickup.

From/Expéditeur:



From ST. ANTHONY'S - RADIATION INC.
10010 KENNERLY RD.
ST. LOUIS, MO 63128

TO US NUCLEAR REGULATORY COMMISSION
REGION III
2443 WARRENVILLE RD #210
LISLE, IL 60532-4352

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