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

NO.: NR-0220-D-131-S DATE: March 13, 2018

DEVICE TYPE: Glass Microsphere

MODEL: TheraSphere Y-90 Glass Microsphere System

MANUFACTURER/DISTRIBUTOR: Nordion (Canada), Inc.
(formerly MDS Nordion, A division of MDS (Canada), Inc.)
447 March Road
Ottawa, Ontario
Canada K2K 1X8

ISOTOPE:	MAXIMUM ACTIVITY:
Yttrium-90	20 GBq (540 mCi)

LEAK TEST FREQUENCY: None

PRINCIPAL USE: (AF) Other Medical Uses

CUSTOM USER: _____ Yes __X__ No

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DESCRIPTION:

TheraSphere is a therapeutic device consisting of insoluble glass microspheres in which the radionuclide yttrium-90(Y-90)is an integral constituent. TheraSphere is used to treat cancerous liver tumors via a catheter inserted into a tumor site through the patients' blood vessels. The Administration Set (to be used with the TheraSphere device) and Administration Accessory Kit (supplied to new user sites) facilitate the transfer of the radioactive microspheres from their container into the tumor. The microspheres become embolized in the tumor vasculature and are retained within the tumor. Microspheres are not biodegradable and once lodged into the tumor the microspheres are not expected to redistribute to other organs of the body. Y-90 is an integral component of the glass matrix in the microspheres. The beta particle emitted by Y-90 has an average tissue penetration of 2.5 mm (0.1 inch) and a maximum tissue penetration of approximately 8 mm (0.3 inch). Therefore, this application delivers highly localized radiation doses to tumors, while minimizing the damage to surrounding healthy liver tissue. Y-90, which has a physical half life of 64.1 hours (2.67 days), is a pure beta emitter that decays to zirconium-90. The microspheres have a mean diameter of 25 μm ($\pm$ 10 μm), with less than 5% below 15 μm and less than 10% above 35 μm. Each milligram of TheraSphere contains between 22,000 and 73,000 microspheres. TheraSphere Y-90 glass microspheres have a radionuclidic purity profile of $\leq$ 30 µCi total gamma impurities/50 mg at 60 days post calibration.

The TheraSphere dose is supplied in up to 0.60 mL of sterile water in a 1.0 mL vee-bottom vial, secured within a 12 mm clear lucite vial shield. TheraSphere is available in various dose sizes up to a maximum of 20 GBq (540 mCi). A pre-assembled single use Administration Set is required for use (consistent with the FDA approval) with each dose.

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DESCRIPTION (Cont.):

The Administration Set is a single use delivery system designed to deliver the microspheres to the target tissue. The Administration Accessory Kit is designed to minimize radiation exposure to administering personnel.

A single use Administration Set is used with each dose. The pre-assembled Administration Set has an injector assembly with two integrated needles, one for inlet and the other for outlet. These needles are used to transport saline to and from the TheraSphere vial and outlet lines that facilitate the infusion of the microspheres from the dose vial.

Throughout the administration procedure, the TheraSphere dose vial remains sealed within the clear acrylic vial shield in which it was supplied. A removable plug at the top of the vial shield provides access to the septum of the dose vial. The injector assembly permits proper placement of the inlet and outlet needles during TheraSphere priming and administration steps.

The product is shipped with a package insert detailing the directions for administration. The Administration Set and dose vial are stored at room temperature until use. The TheraSphere dose is shipped in a F390 Type A package (Attachment 1). The Administration Set is shipped separately from the radioactive material.

The TheraSphere Administration Set is to be used with the Administration Accessory Kit. The Administration Accessory Kit constitutes the equipment which provides the layout for the Administration Set, facilitates the infusion process, and provides the medical team with beta radiation shielding. The Administration Accessory Kit is an assembly of re-usable components. Attachment 2 shows the Administration Set and the Administration Accessory Kit.

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DESCRIPTION (Cont.):

Before administering the first procedure with the TheraSphere device, all institutions must undergo the TheraSphere training Program, as provided by the manufacturer or equivalent. All clinical and technical support staff, such as radiation safety personnel, physicians, medical physicists, technicians, and nurses, are required to be trained both in academic knowledge and clinical skills in their respective areas, as it applies to the clinical use of the system. The training program addresses such topics as the indication for use, description of available doses, device description, patient preparation, dose calculation, radiation monitoring, and administration. The radiation safety aspects of the training program include licensing, radiation safety overview, expected dose rates, and detection of microspheres.

The shelf life of the Administration Set sterilized by gamma is one year, and the shelf life of the Administration Set sterilized by ethylene oxide is three years. The shelf life of the dose vial is twelve days after calibration.

LABELING:

Because of their small size, individual microspheres cannot be labeled; therefore, each shipping container is labeled.

The lead pot/Lucite shield container label indicates the date of calibration, activity level (in GBq and mCi), amount of microspheres (in mg), specific activity (in GBq/mg and mCi/mg), and displays a yellow/black radiation symbol with the words "Caution Radioactive Material." The label designates the content as "TheraSphere Yttrium-90 Glass Microspheres." On the labels, the designation "Lot" and "Lot Number" are used to identify the individual TheraSphere doses and Administration Sets, similarly to the use of serial numbers.

All shipping boxes have a standard Nordion (Canada) Inc. shipping label attached.

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DIAGRAMS:

See Attachments 1 and 2.

CONDITIONS OF NORMAL USE:

TheraSphere Y-90 glass microspheres are designed for use in hospital or clinical environments for the treatment of cancerous liver tumors. TheraSphere Y-90 glass microspheres should be used only by physicians who are qualified by specific training in the safe use and handling of brachytherapy radionuclide sources. Adequate shielding and precautions for handling radioactive material must be maintained.

The TheraSphere dose vial is supplied with a clear acrylic vial shield to limit production of bremsstrahlung and radiation exposure to personnel. Because of the dose rate at the vial shield surface, the manufacturer requires caution including the use of tongs and a lead shielded container when possible. The vial should always be stored in a shielded location away from personnel.

PROTOTYPE TESTING:

Prototype testing of individual microspheres has not been performed, due to the limitations of their microscopic size. Traditional physical/mechanical prototype tests cannot be performed on a microsphere. The manufacturer provided test data on lots of bulk microspheres regarding chemical durability and stability.

The manufacturer subjected the F390 type A transport container to a series of tests which included a water spray test, a 9 m (354 in.) drop test, and two sequential penetration tests. The container maintained its integrity following the tests. The F390 lead pot and the TheraSphere acrylic shield were drop-tested from 1 m (39.4 in.) in various configurations onto a concrete floor and demonstrated that the containment could

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PROTOTYPE TESTING (Cont.):

withstand normal handling accidents which might occur in a hospital environment.

EXTERNAL RADIATION LEVELS:

The manufacturer reported the following external measured radiation levels for a device containing an activity of 20 GBq:

Distance from Source (cm)	Dose Acrylic Vial Shield (mR/hr)	Dose Acrylic Vial Shield in Lead Pot (mR/hr)
0	810	85
5	230	33
30	20	2.7
100	2.2	0.6

The level of ambient radiation in the vicinity of the Administration Accessory kit is a function of the activity being administered. The manufacturer reported that for a delivered dose of 10 GBq (270 mCi), the radiation fields are typically as listed below:

	Location		
Time	Top of Acrylic Shield	Catheter Inlet	Operator Position
Start	< 50 mR/hr	0	Background
During Infusion	Not Relevant	< 60 R/hr (beta)*	Background
End of Infusion	< 1 mR/hr	< 100 mR/hr (beta)	Background

*Instantaneous high reading, duration less than 10 seconds

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QUALITY ASSURANCE AND CONTROL:

Nordion (Canada), Inc. employs a quality assurance and quality control program to insure that each component is manufactured to the specifications furnished to the NRC. The quality assurance program has been assessed and registered as meeting the requirements of ISO 9001. The quality assurance program has been deemed acceptable for licensing purposes by the NRC. A copy of the program is on file with the NRC.

Nordion (Canada), Inc. provided quality assurance specifications which are maintained for microspheres production. The specifications address physical and chemical attributes, purity requirements, inspection requirements, handling and storage instructions.

LIMITATIONS AND/OR OTHER CONSIDERATIONS OF USE:

- The Model TheraSphere with the Administration Set and Administration Accessory Kit shall be manufactured and distributed according to the requirements of Section 32.74, 10 CFR Part 32, and distributed only to persons specifically licensed by the NRC or an Agreement State.

- This registration sheet and the information contained within the references shall not be changed without the written consent of the NRC.

- Handling, storage, use, transfer, and disposal: To be determined by the licensing authority. The devices shall be handled only in accordance with the manufacturer's instructions and with appropriate equipment (e.g., due to the activity level, forceps are recommended).

- REVIEWER NOTE: Please ensure the safety procedures outlined in 10 CFR Part 35, or equivalent Agreement State regulations, are adhered to, especially as they pertain to the handling of the devices.

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LIMITATIONS AND/OR OTHER CONSIDERATIONS OF USE (Cont.):

- REVIEWER NOTE: The clinical staff who administer TheraSphere must complete a training program that is specific to the TheraSphere administration procedure, as described above.

- REVIEWER NOTE: TheraSphere disposal should be handled in accordance with Information Notice (IN) 2007-10, "Yttrium 90 TheraSphere® and SIRSpheres® Impurities."

- REVIEWER NOTE: The TheraSphere Y-90 glass microspheres, Administration Set, and Administration Accessory Kit are distributed by Nordion (Canada), Inc. for Biocompatibles UK Ltd., a BTG International Ltd. group company.

SAFETY ANALYSIS SUMMARY:

Based on our review of the information and test data cited below and the past history of similar designs, we conclude that the Nordion (Canada), Inc., Model TheraSphere with the Administration Set and Administration Accessory Kit devices are acceptable for licensing purposes.

Furthermore, we conclude that these devices would be expected to maintain their integrity for normal and accidental conditions of use which might occur during the uses specified in this registration sheet.

REFERENCES:

The following supporting documents for the MDS Nordion, Model TheraSphere Yttrium-90 glass microsphere device are hereby incorporated by reference and are made a part of this registry document.

- MDS Nordion application, dated June 6, 2007, with enclosures thereto.

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REFERENCES (Cont.):

- MDS Nordion Letter dated August 28, 2008, with enclosures thereto.
- MDS Nordion e-mails dated September 16 and 17, 2008, and enclosure thereto.
- MDS Nordion e-mail dated October 1, 2008.
- Nordion (Canada), Inc. letter dated November 16, 2010.
- Nordion (Canada), Inc. letters dated March 10, 2016 (ML16082A135), March 23, 2016 (ML16095A298), and April 12, 2016 (ML16105A400).
- Nordion (Canada), Inc. emails dated December 8, 2016 (ML16344A318) and February 6, 2017 (ML17038A456), with enclosures thereto.
- Nordion (Canada), Inc. letter dated August 3, 2017 (ML17219A380) and email dated August 25, 2017 (ML17241A014), with enclosures thereto.
- **Nordion (Canada), Inc. email dated February 2, 2018 (ML18052A010), with enclosures thereto.**

ISSUING AGENCY:

U.S. Nuclear Regulatory Commission

Date: March 13, 2018 Reviewer: Tomas Herrera
Tomas Herrera

Date: March 13, 2018 Concurrence:
Celimar Valentin-Rodriguez

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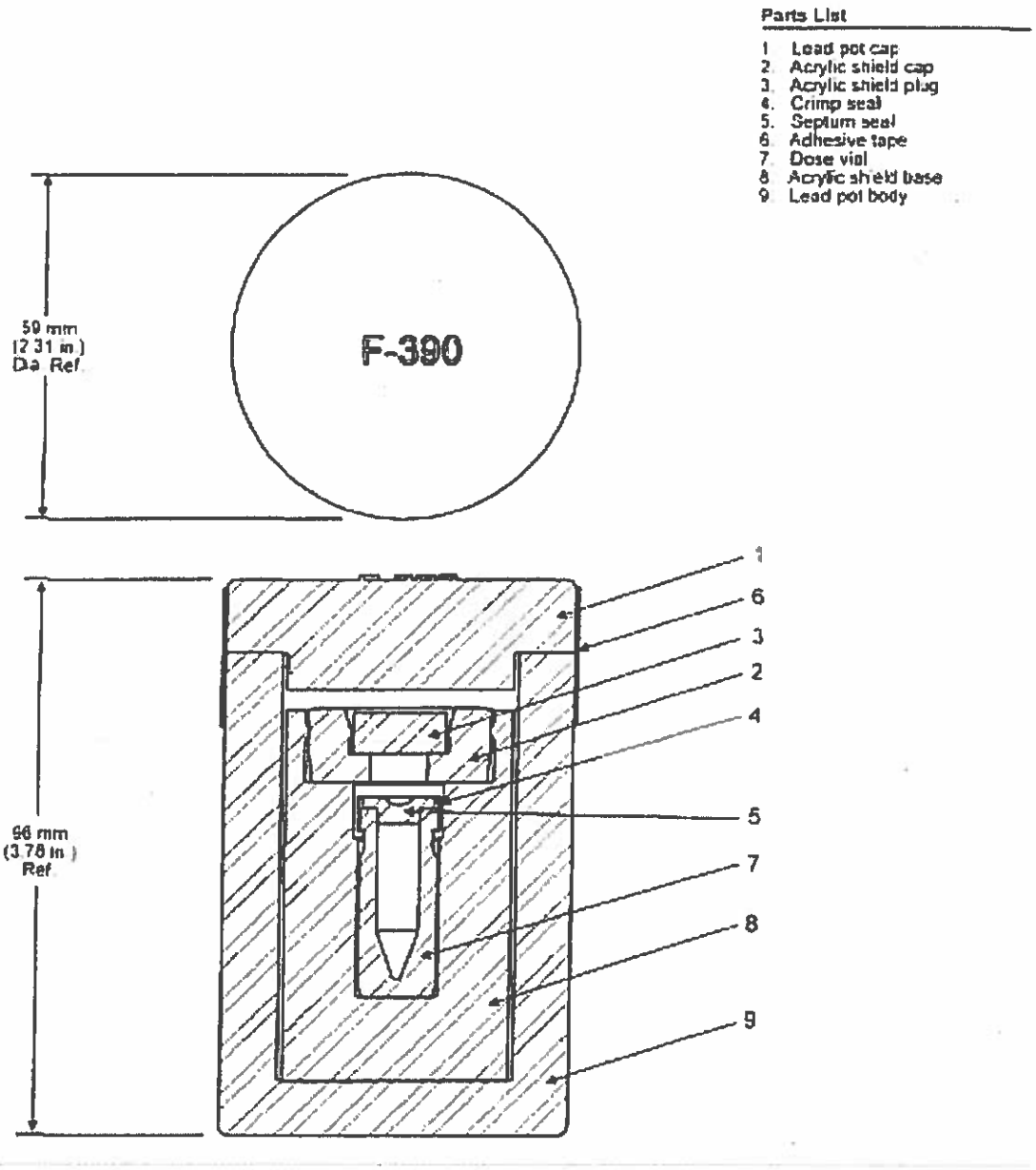

F390 Lead Pot

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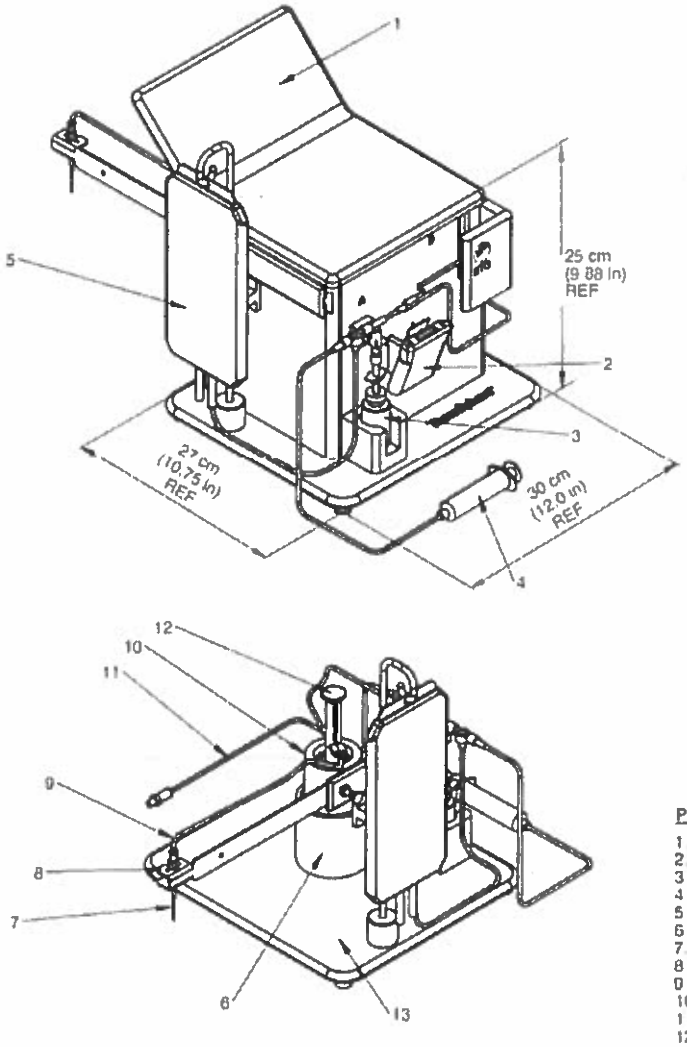

Parts List

1. Kit Lid
2. Electronic dosimeter
3. Empty sterile vial
4. Flushing syringe
5. Bagged sterile solution
6. Pot holder
7. Catheter
8. Catheter connection
9. Active line
10. Pot and vial
11. Disconnected priming line
12. Plunger assembly
13. Kit base

TheraSphere Administration Set and Administration Accessory Kit