



*Science Advancing Health*

August 13, 1999

John T. Yankovich Senior Engineer  
Office of Nuclear Materials Safety and Safeguard  
United States Nuclear Regulatory Commission  
Mail Stop: T-8F-5 2 White Flint North  
11545 Rockville Pike  
Rockville, MD  
20555

Dear Mr. Yankovich:

**RE: TheraSphere Application for USNRC Sealed Source and Device Registration**

Further to our telephone conference call on August 11, 1999, concerning the MDS Nordion application to the US NRC for sealed source and device registration for TheraSphere, the following additional information and comments are provided and addressed for your review:

1. **Provide a copy of the registration to meet the requirements of ISO 9001.**

**Response:**

See attachment 1: ISO 9001 registration.

2. **Provide a copy of the MDS Nordion quality program.**

**Response:**

See attachment 2: Nuclear Medicine Quality Manual.

3. **Please provide information to show that the test specimens used in 1993 to leach analysis are of the same composition as the product currently manufactured.**

**Response:**

The article "Chemical durability of  $Y_2O_3$ - $Al_2O_3$ - $SiO_2$  glasses for the in vivo delivery of beta radiation, J. Biomed. Materials Res. 27:1301-1308, 1993 provided the following information:

The most durable composition of YAS in the above reference is YAS-4 frit. The % mol stated for this formulation is 17%  $Y_2O_3$ , 19%  $Al_2O_3$  and 64%  $SiO_2$ . The molar mass of these compounds is  $Y_2O_3$  226 g/mol,  $Al_2O_3$  102 g/mol and  $SiO_2$  60 g/mol.

	g/mol	% mol	total mass	mass %
$Y_2O_3$	226	17	3842	40
$Al_2O_3$	102	19	1938	20
$SiO_2$	64	64	3840	40

The above formulation is the same mass % formula which MDS Nordion uses in the manufacture of their glass frit and which is subsequently made into spheres. The specification for the glass frit (990601.SPE) which references the purity of the glass and this information is cross-reference in the specification for glass microspheres (990602.SPE).

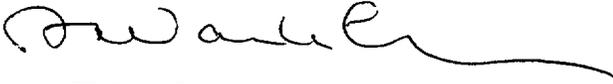
4. **Provide a copy of ISO 2919.**

**Response:**

See attachment 4: ISO 2919

Please do not hesitate to contact me if additional clarification is required. Thank you for the quick attention given to our application. It is much appreciated.

Yours sincerely,



Ann Warbick Cerone  
Manager, Regulatory Affairs  
Tel: 613 592-3400 extn. 2033  
Fax: 613 591-7481  
E:mail [awarbick@mds.nordion.com](mailto:awarbick@mds.nordion.com)

## REQUEST FOR A SEALED SOURCE OR DEVICE EVALUATION

**INSTRUCTIONS:** Send this request 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 <b>MDS Nordion</b>		REGION/LOCATION: <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> IV <input type="checkbox"/> HQ <input type="checkbox"/> LFARB	
TELEPHONE NUMBER	DATE	<b>TYPE OF ACTION REQUESTED (Check as appropriate)</b>  <input type="checkbox"/> SOURCE REVIEW <input type="checkbox"/> AMENDMENT OF REGISTRATION SHEET NUMBER(S) <input type="checkbox"/> DEVICE REVIEW <input type="checkbox"/> CUSTOM REVIEW	
NAME OF APPLICANT <b>Ann Warbick Cerone</b>			
MAIL CONTROL NUMBER(S)			
LETTER/APPLICATION DATE <b>01/19/2000</b>	LICENSE NUMBER(S)		

COMMENTS:  
**447 March Road  
 Kanata, Ontario, Canada K2K 1X8**

### FOR SSSS USE ONLY

REVIEWER <b>John Jankovich</b>	MODEL NUMBERS <b>TheraSphere</b>	NUMBER ASSIGNED <b>00-04</b>
DATE RECEIVED <b>01/24/2000</b>	DATE ASSIGNED <b>01/24/2000</b>	DATE TO FEES

### TYPE OF ACTION (Indicate the number of each type)

<input checked="" type="checkbox"/> <b>COMMERCIAL DISTRIBUTION (FORMAL)</b>		<input type="checkbox"/> <b>USE BY A SINGLE APPLICANT (CUSTOM)</b>	
SOURCE (9C)	DEVICE (9A)	SOURCE (9D)	DEVICE (9B)
<input type="checkbox"/> NEW <input type="checkbox"/> AMENDMENT	<input checked="" type="checkbox"/> NEW <input type="checkbox"/> AMENDMENT	<input type="checkbox"/> NEW <input type="checkbox"/> AMENDMENT	<input type="checkbox"/> NEW <input type="checkbox"/> AMENDMENT
<input type="checkbox"/> NO SAFETY EVALUATION REQUIRED NO FEES REQUIRED		<input type="checkbox"/> LICENSING ACTION REQUIRED (IF KNOWN)	
		<input type="checkbox"/> YES <input type="checkbox"/> NO	

OTHER (Specify)

	TOTAL NUMBER OF REVIEW HOURS	NOTES <b>Registration for a new TheraSphere device. Follow-up to 99-44.</b>
	NUMBER OF DEFICIENCY LETTERS	
	NUMBER OF DEFICIENCY CALLS	

### FOR FEE USE ONLY

TYPE OF FEE		FEE CATEGORY <input type="checkbox"/> 9A <input type="checkbox"/> 9B <input type="checkbox"/> 9C <input type="checkbox"/> 9D	
AMOUNT RECEIVED	CHECK NUMBER	DATE OF CHECK	LOG
APPROVED BY			DATE OF RETURN

COMMENTS

**LICENSE FEE REQUIREMENTS**

ATTN: Sandra Kimberley, MS T-9E10  
U.S. Nuclear Regulatory Commission  
License Fee and Accounts Receivable Branch  
P. O. Box 954514  
St. Louis, MO 63195-4514

**MDS Nordion**  
ATTN: Ms Ann Warbick Cerone  
Manager, Regulatory Affairs  
447 March Road  
Kanata, Ontario, Canada K2K 1X8

**TYPE OF ACTION**

- NEW LICENSE
- RENEWAL OF LICENSE
- AMENDMENT TO LICENSE

REQUESTED DATE

07/02/1999

LICENSE NUMBER

New

CONTROL NUMBER

99-44

**I. APPLICATION FEE DUE**

Your request for a licensing action is subject to the fee(s) in the category(ies) noted below in accordance with Section 170.31 of 10 CFR Part 170. Payment of the fee is required prior to the issuance of the license, renewal, or amendment.

FEE CATEGORY	APPLICATION	RENEWAL	AMENDMENT
9A	\$ 3,600.00	\$	\$
	\$	\$	\$
	\$	\$	\$
	\$	\$	\$
	\$	\$	\$
	\$	\$	\$
	\$	\$	\$
	\$	\$	\$
	\$	\$	\$
	\$	\$	\$

**II. FEE NOT REQUIRED**

- Check Number \_\_\_\_\_ Enclosed is your check which accompanied your request. The fee is not required because:
- Check Number \_\_\_\_\_ We received your check listed in payment of the fee.
- Date of Request \_\_\_\_\_ The Licensing staff has informed us that your request is to be considered as a continuation of the request listed.
- Control Number \_\_\_\_\_
- Date of Request \_\_\_\_\_ Your request was combined, prior to review, with the request listed.
- Control Number \_\_\_\_\_

FEE(s) DUE	\$ 3,600.00
PAYMENT RECEIVED	\$ 910.00
AMOUNT DUE	\$ 2,690.00

**III. CHECK RETURNED**

- Check Number \_\_\_\_\_ Enclosed is your check which was returned to us by the bank for:
- INSUFFICIENT FUNDS
- ACCOUNT CLOSED
- OTHER

- Your request was received without the prescribed application fee.
- We received your check listed below. Payment of the additional fee noted above is required.  
2047767 Check Number  
\$ 910.00 Amount

MAIL THE REPLACEMENT CHECK TO THE ADDRESS LISTED AT THE TOP OF THIS FORM AND REFERENCE THE ABOVE CONTROL NUMBER.

- Your request will increase the scope of your license program. Therefore, your request is subject to the application fee(s) noted above. Refer to Section 170.31 and Footnote 1(d)(2).
- Your license expired prior to the receipt of your application for renewal. Therefore, your request is subject to the application fee(s) noted above. Refer to Section 170.31 and Footnote 1(a).

**IV. LICENSE ISSUED WITHOUT THE REQUIRED FEE**

- License Number \_\_\_\_\_ Amendment Number \_\_\_\_\_ Date Issued \_\_\_\_\_ The listed license was issued without the required fee being collected. The fee required is noted in Section I of this form.
- The scope of your licensed program was increased. Therefore, your request is subject to the application fee(s) noted in Section 1 of this form. Refer to Section 170.31 and Footnote 1(d)(2).
- Because of the urgency of your request, the license was issued without remittance of the prescribed fee noted in Section 1 of this form.

MAKE PAYMENT OF THE FEE(S) TO THE U.S. NUCLEAR REGULATORY COMMISSION AND MAIL THE PAYMENT TO THE ADDRESS LISTED AT THE TOP OF THIS FORM. IF WE DO NOT RECEIVE A REPLY FROM YOU WITHIN 30 CALENDAR DAYS FROM THE DATE LISTED BELOW, WE SHALL ASSUME THAT YOU DO NOT WISH TO PURSUE YOUR APPLICATION AND WILL VOID THIS ACTION.

SIGNATURE -- LICENSE FEE ANALYST	LFDCB	LFDCB	Distribution: OC/DAF/LFARB S/F (LF-3.2.7) OC/DAF/LFARB RF OC/DAF R/F	Pending Cy	DATE
	slk				
Sandra Kimberley, 301-415-6096	7/12/99				

Safety review  
8/30-31/99 JPF

**SUMMARY DATA**

<b>Name and Complete Mailing Address of the Applicant:</b> Ann Warbird Cerone MDS Nordion 447 Maple Rd Kanata, Ontario, Canada		<b>Name, Title, and Telephone Number of the Individual to Be Contacted If Additional Information or Clarification Is Needed by the NRC:</b> Ann Warbird Cerone 613 592-3400/2033	
<b>The Applicant is (check one):</b> <input type="checkbox"/> Custom User <input type="checkbox"/> Manufacturer <input type="checkbox"/> Distributor <input checked="" type="checkbox"/> Manufacturer and Distributor		<b>If the Applicant Is Not the Manufacturer, Provide the Name and Complete Mailing Address of the Manufacturer:</b>	
<b>If the Applicant Is a Custom User, Provide the Name and Complete Mailing Address of the Distributor:</b> NA		<b>Provide the Name, Complete Mailing Address, and Function of Other Companies Involved:</b>	
<b>Model Number:</b> TheraSphere		<b>Principal Use Code (see Appendix F):</b> <input checked="" type="checkbox"/>	
<b>Name Used by the Industry to Identify the Product (e.g., Radiography Exposure Device, Teletherapy Source, Calibration Source, etc.):</b> Y-90 glass microsphere		<b>For Use by:</b> <input checked="" type="checkbox"/> Specific Licensees Only <input type="checkbox"/> General Licensees Only <input type="checkbox"/> Both Specific and General Licensees <input type="checkbox"/> Persons Exempt from Licensing	
<b>Leak-Test Frequency:</b> <input checked="" type="checkbox"/> Periodic Leak-Testing is Not Required <input type="checkbox"/> 6 Months <input type="checkbox"/> Attached is justification for a leak test frequency of greater than 6 months		<b>Principal Section of the 10 CFR that Applies to the User (e.g., General Licensees under 10 CFR 31.5):</b> 10 CFR 35	
		<b>Radionuclides and Maximum Activities (including loading tolerance):</b> Y-90, 20 GBq	

**CERTIFICATION:**

THE APPLICANT UNDERSTANDS THAT ALL STATEMENTS AND REPRESENTATIONS MADE IN THIS APPLICATION ARE BINDING UPON THE APPLICANT.

THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATION ON BEHALF OF THE APPLICANT, NAMED IN ITEM 2, CERTIFY THAT THIS APPLICATION IS PREPARED IN CONFORMITY WITH TITLE 10, CODE OF FEDERAL REGULATIONS, PARTS 30 AND 32 AND THAT ALL INFORMATION CONTAINED HEREIN IS TRUE AND CORRECT TO THE BEST OF THEIR KNOWLEDGE AND BELIEF.

WARNING: 18 U.S.C. SECTION 1001 ACT OF JUNE 25, 1948 62 STAT. 749 MAKES IT A CRIMINAL OFFENSE TO MAKE A WILLFULLY FALSE STATEMENT OR REPRESENTATION TO ANY DEPARTMENT OR AGENCY OF THE UNITED STATES AS TO ANY MATTER WITHIN ITS JURISDICTION.

**Certifying Officer — Typed Name and Title**

**Signature:**

**Date:**

**CHECKLIST**

**Registration Certificate Holder:** *MDS Nordion*

**Model:** *TheraSphere*

DESCRIPTION	OK/DEF	COMMENTS
DESCRIPTION/CONSTRUCTION		
If registration certificate holder is requesting to register more than one source/device on a certificate, are designs similar enough to do so?		<i>one only</i>
Device/source design with complete engineering drawings (dimensions, tolerances, list of materials)		<i>def. questions</i>
Assembly methods (screw, welds, etc.); verify integrity	✓	
Source mounting (size and integrity) and security	✓	
Is source ANSI classification sufficient (from ANSI N542-1977):		
Radiography - Unprotected . . . . . 43515	<i>N/A</i>	
Radiography - In Device . . . . . 43313		
Medical - Radiography . . . . . 32312		
Medical - $\gamma$ Teletherapy . . . . . 53524		
$\gamma$ Gauges - Unprotected . . . . . 43333		
$\gamma$ Gauges - In Device . . . . . 43232		
$\beta$ Gauges, Low Energy $\gamma$ Gauges, or X-ray fluorescence . . . . . 33222		
Oil Well Logging . . . . . 56522		
Portable Moist/Density . . . . . 43333		
Neutron Applications . . . . . 43323		
$\gamma$ Irradiators (II, III, IV) . . . . . 43424		
$\gamma$ Irradiators (I) . . . . . 43323		
Static Eliminators . . . . . 22222		
Smoke Detectors . . . . . 32222		
Definition of shutter operation (locked in Off position, not locked in On position), Fail safe, spacing and tolerances	<i>NA</i>	
On-Off indicators (description, qty., location)	<i>NA</i>	
Safety interlocks, guards, etc. to prevent access to beam or high radiation levels	<i>NA</i>	
Corrosion between unlike materials (e.g., aluminum & steel, depleted uranium & steel, etc.)	<i>NA</i>	
Shielding efficiency and integrity		<i>def. question</i>
For medical devices: Was a 510(k) provided? (provide written notification to FDA)		<i>still missing on 8/31/99</i>
Well logging sources must be nondispersible and nonsoluble. (see Appendix B for a list of approved well logging sources as of November 1991)	<i>NA</i>	
See "ANSI and Other Standards" list for references for particular source/device designs (e.g. radiography, Brachytherapy, etc.)	✓	

APPENDIX C

**CHECKLIST**

**Registration Certificate Holder:**

**Model:**

DESCRIPTION	OK/DEF	COMMENTS
<b>LABELING</b>		
Copy of label	✓	
Materials, dimensions, colors (note on registration certificate if labeling is exempt from the color requirements of 10 CFR Part 20)		def. question
Permanent attachment and location(s) - visible to users?		def. question
Contents: Model#, Serial#, Isotope, Activity, Manufacturer, Date of Assay, Trefoil, "CAUTION - RADIOACTIVE MATERIAL" (Depleted Uranium information must be included)		def. question re. serial no.
<b>CONDITIONS OF USE</b>		
Expected working life of the source/device (years, operations)	✓	
Actions to be taken when product reaches end of its working life.	✓	
Maximum allowable temperature, vibration, shock, corrosion, etc. (during use, handling, storage, and transport)	✓	
How the device will be used	✓	
Meets dose limits of Part 32 for distribution general licensees or persons exempt from licensing	NA	
<b>PROTOTYPE TESTING/HISTORICAL USE</b>		
Tests methods and conditions (for source and device)	1	def. question
Tests results		def. question
Years of use (incidents, failures, etc.)	1	def. question
Similarities to other sources/devices if they are used as basis.		def. question
<b>RADIATION PROFILES</b>		
Survey instrument used (type, window thickness, sensitivity, etc.)	✓	
Conditions: including environments, scatter (product in beam), and use of guards and shields	NA	
Distance from source/surface (per ANSI 538-1979)		def. question
Shutter Open and Closed/Source Shielded	NA	
Verify radiation surveys for $\gamma$ radiation meet $inv^2$ law.	NA	
Verify radiation surveys for non- $\gamma$ radiation have not been calculated using $inv^2$ law.		def. question

## CHECKLIST

**Registration Certificate Holder:**

**Model:**

DESCRIPTION	OK/DEF	COMMENTS
QUALITY ASSURANCE		
Materials, subassemblies, services	✓	
Assembly methods (screws, welding, etc.)	✓	
Dimensions and tolerances	✓	
Activity, radiation levels, leak tests	✓	
QA Manual and comparison of manual to Regulatory Guide 6.9	✓	
INSTALLATION		
Fixed, portable, movable, fixed installation but portable source housing	✓	
Inherent shielding, inaccessibility	✓	
Beam access: size of air gap/opening to beam and use of interlocks, locks, additional shielding or barriers	NA	
Mounting integrity	NA	
SAFETY INSTRUCTIONS		
Operation, maintenance, calibration, damage/failure, specific warnings, leak test, and radiation surveys	✓	
ACCOMPANYING DOCUMENTATION		
Leak tests results and radiation surveys	NA	
Transportation documents	✓	
Operation, maintenance, calibration, damage/failure, specific warnings, leak test, and radiation survey instructions if applicable	✓	
For Distribution to General Licensees: Verify NRC Regions and Agreement State listing is up-to-date and copies of all pertinent regulations	NA	

APPENDIX C

**CHECKLIST**

**Registration Certificate Holder:**

**Model:**

DESCRIPTION				OK/DEF	COMMENTS
SERVICING					
The following activities may be performed by the persons indicated:					
Activity	by a General Licensee	Only by a Specific Licensee	Will be Offered by the Applicant		
Installation				} NA	
Relocation					
Maintenance					
Repair					
Source Exchange					
Calibration					
Leak Testing					
Radiation Survey					
Training					
FOREIGN VENDORS					
Drop ship				} NA	
Who and where is source installed					
Leak test and radiation surveys					
QA in the U.S.					



UNITED STATES  
NUCLEAR REGULATORY COMMISSION

WASHINGTON, D.C. 20555-0001

November 23, 1999

Ms. Ann Warbick Cerone  
Manager, Regulatory Affairs  
MDS Nordion  
447 March Road  
Kanata, Ontario, Canada  
K2K 1X8

Dear Ms. Cerone:

This letter is in response to your application dated July 2, 1999, and your letter dated August 13, 1999, requesting registration of your Model TheraSphere device under the provisions of 10 CFR 32. We are in the process of evaluating your request. In order to continue our evaluation, we need additional information on the following issues:

1. Provide a drawing, showing the major dimensions, for the "12 mm lucite vial shield" and its closure (as described on page 2 and shown in Figure 1 of the application). The drawing should also illustrate the cavity for the glass vial containing the microspheres.
2. Provide a drawing, showing the major dimensions, for the lead shield in which the lucite vial is stored and transported. The drawing should illustrate the cavity for the lucite container. An assembly drawing for Items 1 and 2 is also acceptable if it displays the information which we request.
3. Regarding labeling, please specify
  - a. the material, thickness and adhesive characteristics of the label which you intend to use on the lead-pot/lucite-shield (page 7 of the application);
  - b. the handling and storing instructions as required by 10 CFR 32.74 (a)(2)(viii);
  - c. how you will designate the activity level as required by 10 CFR 32.74 (a)(3).
4. Specify if you use serial numbers to identify each TheraSphere dose. If yes, please indicate where the serial number is located and how durable the identification is. If no, describe why individual dose identification is not needed.
5. Regarding prototype testing, we understand that testing of individual microspheres has not been performed by MDS Nordion, due to the limitations of their microscopic size. Therefore, please provide historical data on the TheraSphere devices (i.e. microspheres in the lucite container) that have been manufactured over the years and used in other countries. Specify how many years they have been in use and what accident conditions they have survived. State that the products are identical in size and construction, and whether or not problems have been encountered in transportation, handling and in clinical practice.

- 6. Provide prototype test information on the lucite shield and its closure illustrating transportation accidents and accidental drops likely to be encountered during storage and use. For example, you may show how it retains its content if dropped from a height of 1 m to a typical hospital floor.
- 7. Regarding external radiation levels, NRC needs information on the device itself, not on the radiation levels around the patient as addressed in the application. Therefore, please specify:
  - a. External radiation levels around the lucite vial containing the maximum dose of 20 GBq (540 mCi). Provide the data, preferably, at the surface, and at 5, 30 and 100 cm. If there are no meaningful readings at these locations, please state so.
  - b. Provide similar external radiation levels, if any, outside the lead pot with the lucite vial inside containing a maximum dose of microspheres.
  - c. Please specify the instrumentation which you used to perform the radiation profile measurements by listing the instrument manufacturers, model numbers, calibration dates, sensitivity, etc.
  - d. Provide the annual occupational dose rate to personnel administering the microspheres. Base your calculation on how many administrations a person would likely complete in a year, how much the activity level in a kit could be on the average, and on how long each procedure would take. In your response, please describe the assumptions on which you base your calculations.
- 8. Procedure No. 990602.SPE refers to Yttrium-89. Specify that it applies to Yttrium-90 used in the manufacture of the microspheres for the TheraSphere device.

Please submit the requested information within thirty days of the date of this letter. If we have not received complete information within thirty days of the date of this letter, we will consider your application as having been abandoned by you. This is without prejudice to the resubmission of a complete application.

Please also note that NRC cannot issue a registration of your device until FDA has approved it for medical use in this country. Therefore, please send us a copy of Form 510k when you receive it.

If you have any questions, please contact me at (301) 415-7904 or Dr. Seung Lee at (301) 415-5788.

Sincerely,

*JS*  
 John P. Jankovich, Ph.D., Sr. Engineer  
 Materials Safety and Inspection Branch  
 Division of Industrial and  
 Medical Nuclear Safety  
 Office of Nuclear Material Safety  
 and Safeguards

Distribution:

MSIB r/f    SSD-99-44    NE01    SSD File # NR-220-D-113-S

DOCUMENT NAME: H:\SSDFILES\LETTERS\Nr220113.def

To receive a copy of this document, indicate in the box: "C" = Copy without attachment/enclosure "E" = Copy with attachment/enclosure "N" = No copy

OFFICE	MSIB	E	MSIB	E				
NAME	JJankovich/jj		SLee	cl				
DATE	11/24/99		11/24/99					

OFFICIAL RECORD COPY



**UNITED STATES  
NUCLEAR REGULATORY COMMISSION**

WASHINGTON, D.C. 20555-0001

November 23, 1999

Ms. Ann Warbick Cerone  
Manager, Regulatory Affairs  
MDS Nordion  
447 March Road  
Kanata, Ontario, Canada  
K2K 1X8

Dear Ms. Cerone:

This letter is in response to your application dated July 2, 1999, and your letter dated August 13, 1999, requesting registration of your Model TheraSphere device under the provisions of 10 CFR 32. We are in the process of evaluating your request. In order to continue our evaluation, we need additional information on the following issues:

1. Provide a drawing, showing the major dimensions, for the "12 mm lucite vial shield" and its closure (as described on page 2 and shown in Figure 1 of the application). The drawing should also illustrate the cavity for the glass vial containing the microspheres.
2. Provide a drawing, showing the major dimensions, for the lead shield in which the lucite vial is stored and transported. The drawing should illustrate the cavity for the lucite container. An assembly drawing for Items 1 and 2 is also acceptable if it displays the information which we request.
3. Regarding labeling, please specify
  - a. the material, thickness and adhesive characteristics of the label which you intend to use on the lead-pot/lucite-shield (page 7 of the application);
  - b. the handling and storing instructions as required by 10 CFR 32.74 (a)(2)(viii);
  - c. how you will designate the activity level as required by 10 CFR 32.74 (a)(3).
4. Specify if you use serial numbers to identify each TheraSphere dose. If yes, please indicate where the serial number is located and how durable the identification is. If no, describe why individual dose identification is not needed.
5. Regarding prototype testing, we understand that testing of individual microspheres has not been performed by MDS Nordion, due to the limitations of their microscopic size. Therefore, please provide historical data on the TheraSphere devices (i.e. microspheres in the lucite container) that have been manufactured over the years and used in other countries. Specify how many years they have been in use and what accident conditions they have survived. State that the products are identical in size and construction, and whether or not problems have been encountered in transportation, handling and in clinical practice.

- 6. Provide prototype test information on the lucite shield and its closure illustrating transportation accidents and accidental drops likely to be encountered during storage and use. For example, you may show how it retains its content if dropped from a height of 1 m to a typical hospital floor.
- 7. Regarding external radiation levels, NRC needs information on the device itself, not on the radiation levels around the patient as addressed in the application. Therefore, please specify:
  - a. External radiation levels around the lucite vial containing the maximum dose of 20 GBq (540 mCi). Provide the data, preferably, at the surface, and at 5, 30 and 100 cm. If there are no meaningful readings at these locations, please state so.
  - b. Provide similar external radiation levels, if any, outside the lead pot with the lucite vial inside containing a maximum dose of microspheres.
  - c. Please specify the instrumentation which you used to perform the radiation profile measurements by listing the instrument manufacturers, model numbers, calibration dates, sensitivity, etc.
  - d. Provide the annual occupational dose rate to personnel administering the microspheres. Base your calculation on how many administrations a person would likely complete in a year, how much the activity level in a kit could be on the average, and on how long each procedure would take. In your response, please describe the assumptions on which you base your calculations.
- 8. Procedure No. 990602.SPE refers to Yttrium-89. Specify that it applies to Yttrium-90 used in the manufacture of the microspheres for the TheraSphere device.

Please submit the requested information within thirty days of the date of this letter. If we have not received complete information within thirty days of the date of this letter, we will consider your application as having been abandoned by you. This is without prejudice to the resubmission of a complete application.

Please also note that NRC cannot issue a registration of your device until FDA has approved it for medical use in this country. Therefore, please send us a copy of Form 510k when you receive it.

If you have any questions, please contact me at (301) 415-7904 or Dr. Seung Lee at (301) 415-5788.

Sincerely,

*JS*  
 John P. Jankovich, Ph.D., Sr. Engineer  
 Materials Safety and Inspection Branch  
 Division of Industrial and  
 Medical Nuclear Safety  
 Office of Nuclear Material Safety  
 and Safeguards

Distribution:

MSIB r/f      SSD-99-44      NE01      SSD File # NR-220-D-113-S

DOCUMENT NAME: H:\SSDFILES\LETTERS\Nr220113.def

To receive a copy of this document, indicate in the box: "C" = Copy without attachment/enclosure "E" = Copy with attachment/enclosure "N" = No copy

OFFICE	MSIB	<input checked="" type="checkbox"/>	E	MSIB	<input checked="" type="checkbox"/>				
NAME	JJankovich/jj			SLee	<i>cl</i>				
DATE	11/24/99			11/24/99					

OFFICIAL RECORD COPY

Ms. Cerone

2

Withholding from public inspection shall not affect the right, if any, of persons properly and directly concerned to inspect the documents. If the need arises, we may send copies of this information to our consultants working in this area. We will, of course, ensure that the consultants have signed the appropriate agreements for handling proprietary information.

If the basis for withholding this information from public inspection should change in the future such that the information could then be made available for public inspection, you should promptly notify the NRC. You also should understand that the NRC may have cause to review this determination in the future, for example, if the scope of a Freedom of Information Act request includes your information. In all review situations, if the NRC makes a determination adverse to the above, you will be notified in advance of any public disclosure.

Sincerely,

*JS*

John P. Jankovich, Ph.D., Sr. Engineer  
Materials Safety and Inspection Branch  
Division of Industrial and  
Medical Nuclear Safety  
Office of Nuclear Material Safety  
and Safeguards

Distribution:

SSSS r/f                      SSD-99-44  
SSD File # NR-220-D-113-S

NE01 *JK*

DOCUMENT NAME: G:\Jankovich\sphere.prp

To receive a copy of this document, indicate in the box: "C" = Copy without attachment/enclosure "E" = Copy with attachment/enclosure "N" = No copy

OFFICE	IMNS	<input checked="" type="checkbox"/>	OGC	<input checked="" type="checkbox"/>				
NAME	JJankovich/jj		MPSiemien					
DATE	10/19/99		10/21/99					

OFFICIAL RECORD COPY



UNITED STATES  
NUCLEAR REGULATORY COMMISSION

WASHINGTON, D.C. 20555-0001  
October 26, 1999

Ms. Ann Warbick Cerone  
Manager, Regulatory Affairs  
MDS Nordion  
447 March Road  
Kanata, Ontario  
Canada K2K 1X8

SUBJECT: REQUEST FOR WITHHOLDING INFORMATION FROM PUBLIC DISCLOSURE,  
MDS NORDION INC. MODEL THERASPHERE DEVICE

Dear Ms. Cerone:

By MDS Nordion Inc.'s (Nordion's) application dated July 2, 1999, your letter dated September 29, 1999, and an affidavit, executed by E. S. Martell, dated September 30, 1999, Nordion submitted an application for registration of the Model TheraSphere microspheres. Nordion has requested that two test procedures, No. 990601.SPE, entitled "YAS Glass Frit," and No. 990602.SPE, entitled "Yttrium-89 Microspheres," be withheld from public disclosure pursuant to 10 CFR 2.790.

Nordion stated that these test procedures should be considered exempt from mandatory public disclosure for the following reasons:

1. The disclosure of the information contained in the procedures would cause irreparable harm to Nordion. In particular, these procedures contain information, developed by Nordion with Nordion's resources regarding specifications such as acceptance/rejection tolerances for materials used in the production of the microspheres.
2. The information is not available in public sources.

We have reviewed Nordion's application and the test procedures in accordance with the requirements of 10 CFR 2.790 and, on the basis of your statements, have determined that the submitted information sought to be withheld contains proprietary commercial information.

Therefore, Procedure Nos. 990601.SPE and 990602.SPE of the submitted information, listed as proprietary, will be withheld from public disclosure pursuant to 10 CFR 2.790(b)(5) and Section 103(b) of the Atomic Energy Act of 1954, as amended.

947 Marsh Road  
Kanata, Ontario  
Canada K2K 1X8  
Tel. 613 592-2790



*Science Advancing Health*

September 29, 1999

John Jankovich  
Sealed Source Section  
Division of Nuclear Materials Safety and Safeguard  
U.S. Nuclear Regulatory Commission  
Mail Stop: T8F-5 White Flint North  
11545 Rockville Pike  
Rockville, MD  
20555

Dear Mr. Yankovich;

**RE: Request for Withdrawal of Documents from Public Disclosure further to Device Approval Application for TheraSphere**

In accordance with 10 CFR Part 2.79, this is to inform you of a request for withdrawal of documents from public disclosure in support of the application for device approval of TheraSphere. These documents are specifications 990601.SPE and 990602.SPE. An affidavit statement is attached.

The reason for the requests for non-public disclosure of the documents is that they contain information that would be of benefit to competitors if made public.

If you require more information or more detail please do not hesitate to contact me.

Yours sincerely,

A handwritten signature in cursive script, appearing to read "Ann Warbick Cerone".

Ann Warbick Cerone  
Manager, Regulatory Affairs  
Tel: (613) 592-3400 Ext. 2033  
Fax: (613) 591-7481



*Science Advancing Health*

**AFFIDAVIT**

**RE: Attachments to Letter Dated August 13, 1999 – TheraSphere Application for USNRC sealed Source and Device Registration**

I, E.S. Martell, in my capacity as Vice-President, Quality and Regulatory Affairs, having been duly authorized to apply for withholding of disclosure of proprietary information by and on behalf of MDS Nordion Inc., do depose and say:

1. I, E.S. Martell, am the Vice-President, Quality and Regulatory Affairs and Operations Services of MDS Nordion Inc.
2. Information contained in the following specification documents is proprietary to MDS Nordion Inc:  
  
990601.SPE YAS Glass Frit  
990602.SPE Yttrium-89 Microspheres
3. MDS Nordion believes that information contained in specification documents pertaining to TheraSphere is proprietary and would be of benefit to competitors if made public
4. This information is held in confidence by MDS Nordion Inc. and any disclosure thereof for developmental purposes, has been accompanied by a confidentiality agreement protecting the trade secrets contained therein.
5. This information has been transmitted to and received by the Nuclear Regulatory Commission in the United States in confidence.

A handwritten signature in black ink, appearing to read 'E.S. Martell'.

E.S. Martell  
Vice-President, Quality Assurance and Regulatory Affairs

SWORN BEFORE ME THIS 30th  
DAY OF SEPTEMBER, 1999  
IN THE CITY OF KANATA, IN  
THE PROVINCE OF ONTARIO.

A handwritten signature in black ink, appearing to read 'Neil Gotfrit'.

Neil Gotfrit, Notary Public



UNITED STATES  
NUCLEAR REGULATORY COMMISSION

WASHINGTON, D.C. 20555-0001  
October 26, 1999

Ms. Ann Warbick Cerone  
Manager, Regulatory Affairs  
MDS Nordion  
447 March Road  
Kanata, Ontario  
Canada K2K 1X8

SUBJECT: REQUEST FOR WITHHOLDING INFORMATION FROM PUBLIC DISCLOSURE,  
MDS NORDION INC. MODEL THERASPHERE DEVICE

Dear Ms. Cerone:

By MDS Nordion Inc.'s (Nordion's) application dated July 2, 1999, your letter dated September 29, 1999, and an affidavit, executed by E. S. Martell, dated September 30, 1999, Nordion submitted an application for registration of the Model TheraSphere microspheres. Nordion has requested that two test procedures, No. 990601.SPE, entitled "YAS Glass Frit," and No. 990602.SPE, entitled "Yttrium-89 Microspheres," be withheld from public disclosure pursuant to 10 CFR 2.790.

Nordion stated that these test procedures should be considered exempt from mandatory public disclosure for the following reasons:

1. The disclosure of the information contained in the procedures would cause irreparable harm to Nordion. In particular, these procedures contain information, developed by Nordion with Nordion's resources regarding specifications such as acceptance/rejection tolerances for materials used in the production of the microspheres.
2. The information is not available in public sources.

We have reviewed Nordion's application and the test procedures in accordance with the requirements of 10 CFR 2.790 and, on the basis of your statements, have determined that the submitted information sought to be withheld contains proprietary commercial information.

Therefore, Procedure Nos. 990601.SPE and 990602.SPE of the submitted information, listed as proprietary, will be withheld from public disclosure pursuant to 10 CFR 2.790(b)(5) and Section 103(b) of the Atomic Energy Act of 1954, as amended.

Ms. Cerone

2

Withholding from public inspection shall not affect the right, if any, of persons properly and directly concerned to inspect the documents. If the need arises, we may send copies of this information to our consultants working in this area. We will, of course, ensure that the consultants have signed the appropriate agreements for handling proprietary information.

If the basis for withholding this information from public inspection should change in the future such that the information could then be made available for public inspection, you should promptly notify the NRC. You also should understand that the NRC may have cause to review this determination in the future, for example, if the scope of a Freedom of Information Act request includes your information. In all review situations, if the NRC makes a determination adverse to the above, you will be notified in advance of any public disclosure.

Sincerely,



John P. Jankovich, Ph.D., Sr. Engineer  
Materials Safety and Inspection Branch  
Division of Industrial and  
Medical Nuclear Safety  
Office of Nuclear Material Safety  
and Safeguards

Distribution:

SSSS r/f                      SSD-99-44  
SSD File # NR-220-D-113-S

NE01 *JK*

DOCUMENT NAME: G:\Jankovich\sphere.prp

To receive a copy of this document, indicate in the box: "C" = Copy without attachment/enclosure "E" = Copy with attachment/enclosure "N" = No copy

OFFICE	IMNS	<input checked="" type="checkbox"/>	OGC	<input checked="" type="checkbox"/>				
NAME	JJankovich/jj		MPSierlien					
DATE	10/19/99		10/21/99					

OFFICIAL RECORD COPY



**UNITED STATES  
NUCLEAR REGULATORY COMMISSION**

WASHINGTON, D.C. 20555-0001  
October 26, 1999

Ms. Ann Warbick Cerone  
Manager, Regulatory Affairs  
MDS Nordion  
447 March Road  
Kanata, Ontario  
Canada K2K 1X8

**SUBJECT: REQUEST FOR WITHHOLDING INFORMATION FROM PUBLIC DISCLOSURE,  
MDS NORDION INC. MODEL THERASPHERE DEVICE**

Dear Ms. Cerone:

By MDS Nordion Inc.'s (Nordion's) application dated July 2, 1999, your letter dated September 29, 1999, and an affidavit, executed by E. S. Martell, dated September 30, 1999, Nordion submitted an application for registration of the Model TheraSphere microspheres. Nordion has requested that two test procedures, No. 990601.SPE, entitled "YAS Glass Frit," and No. 990602.SPE, entitled "Yttrium-89 Microspheres," be withheld from public disclosure pursuant to 10 CFR 2.790.

Nordion stated that these test procedures should be considered exempt from mandatory public disclosure for the following reasons:

1. The disclosure of the information contained in the procedures would cause irreparable harm to Nordion. In particular, these procedures contain information, developed by Nordion with Nordion's resources regarding specifications such as acceptance/rejection tolerances for materials used in the production of the microspheres.
2. The information is not available in public sources.

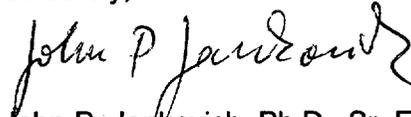
We have reviewed Nordion's application and the test procedures in accordance with the requirements of 10 CFR 2.790 and, on the basis of your statements, have determined that the submitted information sought to be withheld contains proprietary commercial information.

Therefore, Procedure Nos. 990601.SPE and 990602.SPE of the submitted information, listed as proprietary, will be withheld from public disclosure pursuant to 10 CFR 2.790(b)(5) and Section 103(b) of the Atomic Energy Act of 1954, as amended.

Withholding from public inspection shall not affect the right, if any, of persons properly and directly concerned to inspect the documents. If the need arises, we may send copies of this information to our consultants working in this area. We will, of course, ensure that the consultants have signed the appropriate agreements for handling proprietary information.

If the basis for withholding this information from public inspection should change in the future such that the information could then be made available for public inspection, you should promptly notify the NRC. You also should understand that the NRC may have cause to review this determination in the future, for example, if the scope of a Freedom of Information Act request includes your information. In all review situations, if the NRC makes a determination adverse to the above, you will be notified in advance of any public disclosure.

Sincerely,

A handwritten signature in black ink, appearing to read "John P. Jankovich". The signature is fluid and cursive, with a large, sweeping flourish at the end.

John P. Jankovich, Ph.D., Sr. Engineer  
Materials Safety and Inspection Branch  
Division of Industrial and  
Medical Nuclear Safety  
Office of Nuclear Material Safety  
and Safeguards

437 March Road  
Kawata, Ontario  
Canada K2K 1X8  
Tel: (613) 592-2790



*Science Advancing Health*

September 29, 1999

John Jankovich  
Sealed Source Section  
Division of Nuclear Materials Safety and Safeguard  
U.S. Nuclear Regulatory Commission  
Mail Stop: T8F-5 White Flint North  
11545 Rockville Pike  
Rockville, MD  
20555

Dear Mr. Yankovich;

**RE: Request for Withdrawal of Documents from Public Disclosure further to Device Approval Application for TheraSphere**

In accordance with 10 CFR Part 2.79, this is to inform you of a request for withdrawal of documents from public disclosure in support of the application for device approval of TheraSphere. These documents are specifications 990601.SPE and 990602.SPE. An affidavit statement is attached.

The reason for the requests for non-public disclosure of the documents is that they contain information that would be of benefit to competitors if made public.

If you require more information or more detail please do not hesitate to contact me.

Yours sincerely,

A handwritten signature in cursive script, appearing to read 'Ann Warbick Cerone'.

Ann Warbick Cerone  
Manager, Regulatory Affairs  
Tel: (613) 592-3400 Ext. 2033  
Fax: (613) 591-7481



**AFFIDAVIT**

**RE: Attachments to Letter Dated August 13, 1999 – TheraSphere Application for  
USNRC sealed Source and Device Registration**

I, E.S. Martell, in my capacity as Vice-President, Quality and Regulatory Affairs, having been duly authorized to apply for withholding of disclosure of proprietary information by and on behalf of MDS Nordion Inc., do depose and say:

1. I, E.S. Martell, am the Vice-President, Quality and Regulatory Affairs and Operations Services of MDS Nordion Inc.
2. Information contained in the following specification documents is proprietary to MDS Nordion Inc:  
  
990601.SPE YAS Glass Frit  
990602.SPE Yttrium-89 Microspheres
3. MDS Nordion believes that information contained in specification documents pertaining to TheraSphere is proprietary and would be of benefit to competitors if made public
4. This information is held in confidence by MDS Nordion Inc. and any disclosure thereof for developmental purposes, has been accompanied by a confidentiality agreement protecting the trade secrets contained therein.
5. This information has been transmitted to and received by the Nuclear Regulatory Commission in the United States in confidence.

E.S. Martell  
Vice-President, Quality Assurance and Regulatory Affairs

SWORN BEFORE ME THIS 30th  
DAY OF SEPTEMBER, 1999  
IN THE CITY OF KANATA, IN  
THE PROVINCE OF ONTARIO.

  
Neil Gotfrit, Notary Public