February 6, 2002

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

Dear Ms. Cerone:

This letter is in response to your application dated September 6, 2001, requesting amendment of your registration for the Model TheraSphere device, Registration No. NR-0220-D-113-S. We are in the process of evaluating your request. In order to continue our evaluation, we need additional information regarding the issues listed in the Enclosure.

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.

If you have any questions, please contact me at (301) 415-7904 or Dr. Seung Lee at (301) 415-5787.

Sincerely,

/RA/

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

Enclosure:
as stated

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Enclosure

Please provide the following additional information regarding MDS Nordion's request , dated September 6, 20001, for amendment of the registration for the Model TheraSphere device, Registration No. NR-0220-D-113-S

1. Precise Description of Components

Diagrams 1 and 2 in Appendix 1, and pp. 19-22 in Appendix 2, show the components in the device. However, no information was provided regarding precise, definitive description such as technical drawings, dimensions, specification of materials, re-use or disposability of components. Please provide for each component No. 1 through 31:

- dimensions, and engineering drawings, where applicable. For example, provide a dimensional, engineering drawing for the vial and the vial shield; provide a drawing to show the physical size of the stand; specify the size and length for the lines and catheters; specify needle types and sizes; specify stopcock types and sizes.
- material specifications, addressing compatibility with fluids and radiation,
- use of components: disposable, re-usable (specify how many times), or permanent component
- vendor or supplier (MDS Nordion, physician, commercial supplies, etc.)

2. Interchangeability of components

2.1 Describe whether alternative models or suppliers are acceptable for any of the components.

2.2 Specifically address whether any syringe other than the Model MONARCH 25 can be used.

2.3 Provide the specifications that MDS Nordion prescribes to the users regarding components which are not supplied by MDS Nordion.

2.4 The application repeatedly referred to the use of two Model RAD-60 (RADOS 1) dosimeters in the device to measure full transfer of the microspheres. However, the training material refers to a Model Rados RAD-50 personal dosimeter to verify "successful transfer of the beads to the patient" (p. 28, Appendix 3). Please clarify the discrepancy.

2.4 Please also delineate the calibration requirements for the dosimeter that MDS Nordion as the manufacturer may specify for the user.

3. Needles

The use of the original short blunt bevel on the tip of the 20 Ga needles was identified as a root cause for septa coring. Septa coring can increase TheraSphere® microsphere administration

problems. The application indicated that 20 Ga needles with long tapered bevels performed better and are now required as inlet and outlet needles (Section 6.2, Appendix 1). Please clarify the following:

3.1 Are the 20 Ga needles with long tapered bevels the only needles provided in the TheraSphere® Administration kit. If so, why are they referred to as "replacement" needles (Page 8, Appendix 2)?

3.2 If other needles are included in the kit, identify them and explain why they are in the kit. If the 20 Ga needles with the short blunt bevel are included in the TheraSphere® Administration kit, why are they included when you have demonstrated poor performance? What steps are taken to prevent the wrong needles from being used?

3.3 Provide drawings and specifications for the filter vent assembly, the inlet needle (showing the check-valve) and the outlet needle. Please clarify the discrepancy between page 11 of Package Insert which indicates either replacement needle can be used to replace the inlet needle and page 9 which states the inlet needle is "equipped with" a check-valve.

4. Red Vs Blue Stopcock - Use of tool

Because the red stopcock is on the non-radioactive side of the apparatus, one might not expect to need a tool to reduce radiation exposure while opening or closing the stopcock. However, the application did not describe the ambient radiation level at that point prior to treatment, during routine treatment, or when microspheres go into the waste container.

5. Working Life

Please provide information on the working life and shelf life for the components as applicable. For example, specify the components that are to be permanently used for extended periods of time, the components that are used for a number of cycles, or components which are for single use only.

6. Labels

6.1 Please modify the text of the labels to meet the provisions of 10 CFR 32.74(a)(2)(viii) and 32.74(a)(3).

6.2 Please provide the final configuration for the labels instead of drafts (p.12, Appendix 1). The information should address the text for the labels as well as the physical design and dimensions of the labels.

7. Delivery Parameters

7.1 The proposal presented an extensive set of "recommended infusion pressures" in terms of other delivery parameters such as catheter type and internal diameter, catheter length, or infusion rate (p. 18, Appendix 1). However, the Package Insert (Appendix 2), which presumably will be sent by MDS Nordion to the user, presented different values

and in a different format (p. 8, Appendix 2). In addition, the training material (Appendix 3) does not address either of the two sets of parameters. Please provide one definitive set of delivery parameters.

7.2 The application presented an empirical equation, derived from data fitting in a linear regression model, for "% Delivery" (p. 16, Appendix 1). Please provide the details of the analysis of how the equation was derived and delineate how and when the equation is to be used.

8. Radiation Protection

8.1 Please provide the maximum radiation levels around the device as mounted in the Administration Set when it contains the maximum activity level. If the radiation level is below background, please state so. Regarding the use of the device, please indicate the dose that each of the administering personnel is likely to receive with one application; and provide an estimate of how many procedures the administering personnel are likely to perform a year. Please also calculate the annual dose rate that the personnel is expected to receive from the use.

8.2 The proposal stated that the acrylic box of the Administration Accessory Kit provide beta radiation shielding (Item 1, Table 1, p. 4, Appendix 1). However, the box is constructed with four sides only. What radiation protection measures are provided for the two open sides?

8.3 To reduce high radiation hand dose, the proposal described the use of the stopcock extension tool for the blue stopcock only (Item 4, Table 1, p. 4, Appendix 1). Why is such precaution not addressed for the red stopcock?

9. Prototype Testing

Prototype testing of the vial with the former stopper design and the vial shield had been adequately addressed in the earlier registration. The stopper and needle guides are new, the administration kit is also new. The application presents the results of clinical tests from the medical point of view only (pp. 14-19, Appendix 1). The tests refer to such issues as flow rate variations due to catheter size, or changes made in the elasticity of the septum due previous failures to radiation exposure. These tests are development tests, which are part of the design process. Prototype testing of the final product, regarding the normal use and likely accident conditions for an SSD registration was not presented in the application. Such issues as cycling of nondisposable components, or accidental drops of the device were not addressed. Please provide the results of prototype testing as specified in the provisions of Section 10.5, NRC Report NUREG-1556, Volume 3. For example, provide prototype test information on the illustrating transportation accidents and accidental drops likely to be encountered during storage and use such as dropping the device from a height of 1 m to a typical hospital floor.

10. TheraSphere Training Program

The application described the training program as a requirement for the use of the TheraSpheres (Section 5, Appendix 1, and Appendix 4). Please modify the description of the

training program to address clearly the following: the Nordion TheraSphere® microspheres are brachytherapy sources which must be used in accordance with NRC requirements for brachytherapy sources as well as with the guidance developed to account for the unique properties of the microspheres.

The training for NRC licensees should accurately reflect the NRC regulations and requirements. For example, dose calculations are for individual doses and not dose ranges, TheraSphere® microspheres should be referred to as brachytherapy sources and not radiopharmaceuticals or radioactive drugs, and your radiation safety instruction should address patient release criterial and the potential for an individual to receive in excess of 100 millirem from a patient and need for instructions between 100 and 500 millirem.

11. Finalized Documents

The TheraSphere Package Insert provided in the application (Appendix 2) is in draft form. Please provide the final version.

12. Quality Assurance:

Please indicate if the Quality Assurance program, described in your document No. QAM 00 (9), dated December 27, 2000, has received an ISO-9000 approval. If yes, please provide a copy of the ISO registration certificate with the expiration date.

13. FDA Approval

The FDA approval for humanitarian exemption device (HDE) was addressed to Dr. James Goin, President, DataMedix Corp., Media, Pennsylvania. NRC needs to obtain documentation to show the connection between DataMedix, in Media, PA and MDS Nordion in Canada.

14. Summary Information

We also request that you provide, as a summary, a table listing Components 1-31 (shown on Page 6 of 19, Appendix 1) and the following additional information for each component: (1) whether the component is contained in the Administration Accessory Kit, the Administration Set, or to be obtained from other suppliers, (2) whether the component is permanent, re-usable (please show how many times), or disposable.

15. Typographic Correction

Please provide the correct value for “3.4 mCi (± 3.8)” as shown in Line 3, Paragraph 5, p. 7, Appendix 1.