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Mr. John W. Hickey  
Chief, Material Safety & Inspection Branch  
Division of Industrial & Medical Nuclear Safety  
Office of Nuclear Materials Safety and Safeguards  
U.S. Nuclear Regulatory Commission  
Washington, DC

Dear Mr. Hickey:

The purpose of this letter is to supplement our February 12, 2001 letter to you regarding NRC licensing of Novoste's Beta-Cath System by providing information you requested yesterday about maximum activity levels.

In our February 12 letter we objected to a license condition that would limit single sources in a train to 3.5 millicuries, pointing out that the corresponding limit in the Georgia SSDR certificate was 5 millicuries, that a 3.5 millicurie limit would prevent many from using the device to treat patients, that the 3.5 millicurie figure related to a NIST analysis of a single seed that Novoste had used originally as a nominal activity level, that NIST had later provided numbers that enabled Novoste to calculate individual source train dose rates and activities, and that based on this the actual sources varied somewhat (less than 5 millicuries).

As you know, the Novoste Beta-Cath System has been approved by the FDA, based on clinical trial data submitted by Novoste. As would be expected, The Beta-Cath devices actually used in these trials produced dose rates that varied somewhat, ranging upward to 0.107 Grays/second for a particular train (which included a standard twelve sources or seeds). Using a NIST traceable factor that relates dose rate to activity, the activities of the source trains used in these trials ranged upward to a little over 46 millicuries. Since there were 12 sources in each train, this means that the mean source activity in the highest activity train used in the trials was a little over 3.8 millicuries. The range of the mean source activities for the trains used in these trials was 2.7-3.8 millicuries. For discussion purposes, we have rounded up the 3.8 number to 4.0.

These activity numbers reflect actual dose rates (and corresponding calculated activities) for the trains used in the trials; the range of the mean was not intended to accommodate uncertainty around some single activity number (say 3.5 millicuries). There is, of course, some uncertainty in these measurements, as there is in all such measurements.

The 3.5 millicurie maximum activity per source specified in the August 4, 2000 Georgia SSDR certificate (superseded by the November 20, 2000 SSDR) was based simply on a NIST analysis of a single source. The 5.0 millicurie number referenced in the newer SSDR certificate (GA-1115-D-101-S) was intended to reflect the full range of the mean source activities for the trains used in the trials, with some allowance for measurement uncertainty. Since dose rates will only be measured for the full train (and in the trials were measured for the full trains), a license condition which specifies maximum source activity should either refer to the full train (twelve sources) or to the mean activity for the sources in a train.

Novoste's February 12 letter (and Novoste's written testimony before ACMUI) questioned whether NRC should or could enforce FDA requirements<sup>1</sup>. However, if NRC wants to adopt a license condition that imposes an activity limit based on the FDA approval, then Novoste suggests that the appropriate limit would be either 48 millicuries per 12 source train, or 4 millicuries mean activity for the 12 sources in a train.<sup>2</sup> We also believe that there should be some allowance for uncertainty when the licensee verifies the dose rate (and activity) after receiving the device. Also, consistent with NRC policy, we would expect that similar devices from other manufacturers would also be subject to maximum activity license conditions that are based on the dose rates and activities used in their clinical trial data submitted to FDA.

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<sup>1</sup>No NRC safety review is required under 10 C.F.R. § 35.57 for an individual Part 35 licensee to use a sealed source of up to 15 millicuries, that has been manufactured and distributed in accordance with NRC or Agreement State requirements, for check, calibration, and reference use. (The new Part 35 would increase this limit). Thus an NRC limit for a properly manufactured and distributed source of less than 15 millicuries would need to be based on safety concerns associated with some other use of the sealed source. Here that use would be for treatment of patients. However, under the August 3, 2000 Policy Statement, the focus of NRC regulation of patient safety is on assuring that properly trained and qualified user physician instructions are followed. It is not clear to us how a limit on source activity can be justified on this basis. If NRC were to impose a 5 millicurie limit based on the Georgia SSDR, Novoste's ability to distribute devices up to this limit would still be constrained by its need to comply with FDA requirements. See 10 C.F.R. § 35.7.

<sup>2</sup> In our February 12 letter, we said we believed that the use of sources up to 5.0 millicuries was fully consistent with the FDA approval. Based on information Novoste recently received from FDA, Novoste believes that FDA does not currently approve of a shipments of a Beta-Cath device if the activity for the source train is measured to exceed 48 millicuries.

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I hope this information satisfies NRC's needs. I want to express Novoste's appreciation for the consideration you and others at the NRC have given to our licensing concerns. As we said in our February 12 letter, Novoste wants to do all that is necessary to support sound licensing guidance on the use of the Beta-Cath system. Please do not hesitate to call me if you have any further questions.

Very truly yours,

A handwritten signature in black ink, consisting of a large, stylized 'M' followed by a long, horizontal, slightly wavy line extending to the right.

Martin G. Malsch  
Attorney for Novoste