TELECONFERENCE MEETING OF THE
ADVISORY COMMITTEE ON THE
MEDICAL USES OF ISOTOPES

DECEMBER 18, 2008

MEETING SUMMARY

PURPOSE: To discuss issues related to infiltrations of fluorine-18 (F-18) and therapeutic radiopharmaceuticals as medical events (MEs) and training and experience requirements for the medical use of NeoVista, Inc.'s Epi-Rad$_{90}$ strontium-90 (Sr-90) ophthalmic system.

OUTCOME: The Nuclear Regulatory Commission (NRC) staff gained a better understanding of the views and opinions of the Advisory Committee on the Medical Uses of Isotopes (ACMUI), as well as other stakeholders' views and opinions. The staff will add the therapeutic infiltrations issue to the spring 2009 ACMUI meeting agenda for further discussion, and based on ACMUI's recommendation, the staff intends to revise the guidance for the medical use of NeoVista, Inc.'s Epi-Rad$_{90}$ strontium-90 ophthalmic system.

OPENING COMMENTS

Mr. Robert Lewis, NRC, provided a brief overview of the goals for the meeting and discussed current NRC projects of interest to the ACMUI. These projects included: the status of the recently implemented National Source Tracking System (NSTS); NRC's efforts in regards to safety culture; and ACMUI's successful completion of the required information security training.

INFILTRATIONS OF FLUORINE-18 AND THERAPEUTIC RADIOPHARMACEUTICALS AS MEDICAL EVENTS

NRC staff sought input on whether NRC should pursue a change to its current policy which does not require infiltrations of dosages to be reported as MEs even when the resultant dose may exceed the dose threshold in the ME reporting criteria (i.e. 50 rem to an organ or tissue). Ms. Cindy Flannery, NRC, described a recent event reported to the NRC in which 3.6 millicuries of F-18-fluorodeoxyglucose (FDG) was infiltrated into an area near the elbow. The dose to the tissue was estimated to range between 200 millirem and 96 rem. The event was later retracted because NRC staff determined that infiltrations do not require reporting as an ME based on the Supplementary Information that supported the previous equivalent regulation (§35.33), which states "Extravasation is the infiltration of injected fluid into the tissue surrounding a vein or artery. Extravasation frequently occurs in otherwise normal intravenous or intraarterial injections. It is virtually impossible to avoid. Therefore, the Commission does not consider extravasation to be a misadministration." NRC staff also requested input on the applicability of the ME reporting criteria for infiltrations of therapeutic radiopharmaceuticals.

Dr. Richard Vetter, ACMUI, provided information from a 1994 publication by Castronovo that considered infiltrations using a radiopharmaceutical such as thallium, which resulted in skin doses ranging from 40 to 600 rads. Dr. Vetter stated that doses from these types of infiltrations are potentially significant and would be higher than the particular case NRC provided using F-18. Dr. Vetter added that NRC should retain its current policy, which does not require infiltrations to be reported as MEs; however, with increased use of therapeutic

radiopharmaceuticals, staff should pursue the issue further. Dr. Subir Nag, ACMUI, agreed that infiltrations should not be viewed as MEs at this time.

ITEM (1): At this time, NRC should continue its policy of not requiring infiltrations of diagnostic dosages to be reported as MEs.

The motion passed unanimously.

Dr. Darrell Fisher, ACMUI, inquired specifically about infiltrations of therapeutic radiopharmaceuticals rather than the diagnostic agents. Drs. Leon Malmud and Douglas Eggli, ACMUI, responded and explained that they had not experienced therapeutic infiltrations, which were uncommon. Dr. Vetter explained that diagnostic radiopharmaceuticals are injected, while therapeutic radiopharmaceuticals are infused. Dr. Eggli reiterated that the likelihood of an infiltration during a therapeutic infusion was very small; however, he was not opposed to making a therapeutic infiltration an ME. The ACMUI decided this issue required more discussion and requested that the topic be added to the May 7-8, 2009 ACMUI meeting agenda.

TRAINING AND EXPERIENCE REQUIREMEHNTS FOR THE MEDICAL USE OF NEOVISTA, INC.'S EPI-RAD$_{90}$ STRONTIUM-90 OPHTHALMIC SYSTEM

Ms. Cindy Flannery, NRC, described the current licensing guidance for NeoVista Inc.'s Epi-Rad$_{90}$ Sr-90 ophthalmic device, which requires an Authorized User (AU) to meet the Training and Experience (T&E) requirements in either 10 CFR 35.490 or 10 CFR 35.690, which limits the AU to be a radiation oncologist. Ms. Flannery added that at the October 2008 ACMUI meeting, the ACMUI recommended that NRC staff revise the guidance to allow AUs to meet the requirements in 10 CFR 35.491, if accompanied by appropriate device-specific training. NRC staff agreed that T&E under 10 CFR 35.491 would be adequate for the standard treatment of24 Gray of a single lesions for the treatment of age-related macular degeneration as used under the current protocol in the clinical trials; however, Ms. Flannery also informed the ACMUI that the Food and Drug Administration (FDA) recently granted a waiver for use of the device on a patient who did not meet the criteria for inclusion into the current investigational treatment protocol. NRC staff expressed concerns that once the device is approved by the FDA, it may be used under protocols other than the protocol followed under the clinical trials (i.e., off-label use) and staff sought input from ACMUI on whether the T&E under 10 CFR 35.491 is adequate for off-label use.

Dr. Douglas Eggli, ACMUI, clarified that it was his intent at the previous ACMUI meeting to specify T&E only for those ophthalmologists using the Epi-Rad$_{90}$ ophthalmic device under the standard protocols approved for the clinical trials and not for any more extended therapy where dosimetric considerations may become very important. Dr. Subir Nag, ACMUI, expressed concerns that once the device is FDA-approved, it can be used off-label for any other use. Dr. Nag believed this off-label use should involve radiation oncologists; however, Dr. Nag clarified that the radiation oncologist need not be physically present during the procedure. Drs. Bruce Thomadsen and Orhan Suleiman, ACMUI, supported Dr. Nag's concerns. Dr. Nag also mentioned that the other radiation oncologist representative on the ACMUI, Dr. James Welsh, was not present for the entirety of the discussion on October 28, 2008, nor for this discussion. Dr. Welsh's email to the ACMUI expressing his concerns was added as an enclosure to the transcript posted on the NRC's website.

Dr. Jeffrey Heier, a consultant for NeoVista, Inc., explained that it is NeoVista Inc.'s intent for all treatments to be done in accordance with the standard protocol used in the clinical trials, which

is a single dose that was determined in collaboration with radiation oncology and with the radiation physicists.

After a detailed discussion, Dr. Nag made the following motion.

ITEM (2): As recommended at the October ACMUI meeting, NRC staff should revise the guidance, to allow individuals qualified under 10 CFR 35.491 with device-specific training to be AUs for the NeoVista EpiRad device. This authorization only applies for use of the device under the current standard protocol used in the clinical trials. Furthermore, any off-label use of the device should require the AU to meet the current guidance, which states AUs must meet the T&E requirements of 10 CFR 35.490 or 35.690. ACMUI added that there should be no physical presence requirement for individuals qualified under 10 CFR 35.490 or 35.690.

The motion passed with one opposing vote from Ms. Debbie Gilley.