MEETING OF THE
ADVISORY COMMITTEE ON THE
MEDICAL USES OF ISOTOPES

April 20-21, 2005

MEETING SUMMARY

PURPOSE: To discuss issues related to the implementation of the Nuclear Regulatory Commission (NRC) regulations in 10 Code of Federal Regulations (CFR) Part 35, "Medical Use of Byproduct Material."

OUTCOME: The staff gained more 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. Staff will consider these views in its continuing effort to make 10 CFR Part 35 more useful, practical, and not overly burdensome on licensees, while maintaining public health and safety.

TUESDAY, APRIL 20, 2005

ACMUI REVIEW OF MEDICAL EVENTS INVOLVING IODINE-131 (I-131)

Douglas F. Eggli, MD, ACMUI, presented this topic to the ACMUI. This presentation was given so that the ACMUI Subcommittee on Review of Medical Events Involving I-131, could forward to the full Committee its recommendation(s) on what licensees can do to help reduce the number of medical events involving I-131.

The Subcommittee reviewed several I-131 medical events, to evaluate the general nature of the events and to recommend actions that licensees, and/or the NRC can take to help reduce the number of events. The Subcommittee found that the number of I-131 medical events was small, compared to the total number of therapeutic administrations of radioactive material. Most of the events were attributable to human error related to: failure to pay attention to detail; failure to follow established policies and procedures; and miscommunication among key personnel.

To help reduce the number of medical events involving I-131, the Subcommittee developed several recommendations to the ACMUI. The Subcommittee clarified that it is not its intent that these recommendations should be implemented via changes to the 10 CFR Part 35 rule.

Following Practices are the Subcommittee Recommendations Submitted to ACMUI for Further Consideration

1. **Patient verification procedures similar to blood administration could be considered.**
2. **Verbal orders should not be permitted in any step of the therapeutic dosage administration process.**
3. **The dosage to be administered must be verified against the written directive prior to administration.**

4. **The therapeutic dosage should be re-verified in a dose calibrator on site prior to administration.**
5. **Communication between the Authorized User and the individual administering the dosage should be strengthened.**

Motion: That the Subcommittee's recommendations be endorsed by the full Committee and forwarded to NRC staff. Motion was seconded and passed.

The ACMUI also recommended that documentation of events in the Nuclear Materials Events Database be revised to include causes and contributing factors to events.

CASE EXPERIENCE USING IODINE -125 (I-125) SEEDS AS MARKERS

Richard J. Vetter, PhD, ACMUI, presented some actual findings, from Mayo Clinic, of the off-label use of I-125 seeds as markers for breast cancer tumors. Mayo Clinic uses I-125 seeds to define the border of breast cancer tumors as an alternate to the traditional method of using wires (called "wire localization.") Dr. Vetter reported that a small study was conducted at Mayo Clinic, in which the use of I-125 seeds as markers was compared to the traditional use of wires as markers. Mayo Clinic found that the use of 1-125 seeds has certain advantages, including: the ability to implant the seeds up to 5 days before surgery, thereby minimizing scheduling conflicts; the ability to bracket lesions; the ability to perform post-localization mammograms without being impeded by wires; and reduced cost. Mayo Clinic's conclusion was that the use of I-125 seeds as markers was easier, more convenient, preferred by physicians, and a more accurate method to mark breast cancer tumors than wire localization.

FOOD AND DRUG ADMINISTRATION (FDA) RADIATION DOSE LIMITS FOR HUMAN RESEARCH SUBJECTS USING CERTAIN RADIOLABELED DRUGS

Orhan Suleiman, PhD, ACMUI, made a presentation on the current FDA thinking regarding radiation dose limits for human research subjects using a certain class of radiolabeled drugs.

Dr. Suleiman explained that the FDA is revisiting the dose limits allowed to persons participating in research involving radiolabeled drugs because dose limits have changed since FDA first promulgated its rules in 1975, regarding human research subjects. The concept of effective dose is now in place; there's more scientific data regarding radiation risk; and there are also new human research regulations for institutional review boards. As a result, FDA is now proposing to update dose limits for human research subjects.

Dr. Suleiman explained that there are challenges in determining appropriate dose limits. Following are some challenges: Are the current dose limits still appropriate for research conducted under 21 CFR Part 361, "Radioactive drugs for certain research uses"? If not, what dose limits are appropriate? Taking into account the risk in differences in radiation exposure risks (higher risk for the very young and the very old), should there be different dose limits for different adult age groups? Regarding pediatric doses, should these considerations be taken into account as well?

The ACMUI commented that it may be appropriate to devise a weight-based or age-based sliding scale of doses, to take into account of different risks of radiation exposure to different age groups

ESTABLISHING GUIDANCE ON EXCEEDING DOSE LIMITS FOR MEMBERS OF THE PUBLIC

Sami Sherbini, PhD, NRC, made a presentation to inform the ACMUI of the NRC staff's approach in developing guidance that would allow members of the public to receive radiation doses in excess of that in the regulatory limits, when caring for sick relatives who are hospitalized. Staff took action to develop this guidance, based upon comments the ACMUI made at the October 13-14, 2004, ACMUI public meeting.

Dr. Sherbini explained that the current dose limit for members of the public is 100 millirem (although, under certain conditions, the 100 millirem limit may be raised to 500 millirem). Dr. Sherbini explained that in drafting the guidance, the staff reviewed several existing guidelines and criteria, seeking a higher limit that would be reasonable, but not inappropriately high. National Council on Radiation Protection and Measurements standards and emergency dose limits were among the criteria reviewed.

The staff found that existing guidelines and criteria did not suggest an ideal dose limit, higher than the current limit of 100 millirem, that would be appropriate to the unique situation of care givers exposed to radiation while caring for sick relatives. Therefore, the staff concluded that the best approach would be to let the licensee determine the appropriate dose limit, based upon each unique situation, then obtain NRC approval, via a license amendment, to allow such a limit for that specific situation. This approach was forwarded to the Commission for approval.

ACMUI expressed a concern that seeking approval via license amendment may not be an expedient approach. In response, Dr. Sherbini explained that the process would be set up in such a way that it is anticipated that an amendment will take no more than a few days. Furthermore, if a licensee demonstrates a need to have this authority on a regular basis, it might be possible to put this provision directly in the license so that no amendment would be necessary.

STATUS OF RULEMAKING, PART 35 - TRAINING AND EXPERIENCE

Roger Broseus, PhD, NRC, gave an update on the status of the 10 CFR Part 35 rulemaking effort. Dr. Broseus stated that the rule was published on March 30, 2005, with an effective date of April 29, 2005. However, licensees have until October 24, 2005, to implement the changes in the rule, and Agreement States have up to three years to implement the rule.

Dr. Broseus explained that the purpose of his presentation was to give an overview of the key changes to the rule. An abbreviated list of these changes include:

- Revision of requirements for specialty board recognition
- Revision of some requirements to obtain recognition via the alternate training pathway
- Revision of the preceptor statement to require preceptors to "attest" to competency rather than to "certify" competency

- Removal of requirement that Authorized Users gain experience with elution of generators

One ACMUI member expressed a concern about the revision to the requirement to obtain recognition via the alternate training pathway. This member believed that the revision was too prescriptive, in this regard. There were also some concerns that certain terms were not well-defined in the rule.

Dr. Broseus acknowledged the hard work that ACMUI undertook, particularly the Subcommittee on Training and Experience, to help the staff complete the complex, multiyear effort to put into place regulations and requirements for the training and experience of radiation safety officers, authorized medical physicists, authorized nuclear pharmacists, and authorized users. Dr. Broseus personally thanked the ACMUI for its efforts in this undertaking, and stated that thousands of licensees, NRC staff, and Agreement State staff will benefit from these changes.

THURSDAY, APRIL 21, 2005

STATUS AND UPDATE: REDEFINING MEDICAL EVENTS

ACMUI Subcommittee on Redefining Medical Events discussed its progress on redefining medical events, and submitted to the full ACMUI its recommendations to redefine medical events within 10 CFR Part 35.[1] The Subcommittee discussed four major areas to be considered for revision:

1. Redefining medical events involving permanent radioactive seed implant therapy (otherwise known as permanent "brachytherapy.")
2. Clarifying the completion of the procedure for the written directive in permanent brachytherapy use.
3. Communicating effectively to the patient, risks associated with medical events.
4. Redefining medical events for modalities other than radioactive brachytherapy.

Regarding the first major area, redefining medical events involving permanent brachytherapy, the ACMUI Subcommittee forwarded the following recommendation to the full ACMUI for further consideration.

Proposed Brachytherapy Medical Event Definition #1:

> **Any permanent implant in which there is no occurrence of seed migration and patient intervention, is a medical event if:**

[1] In SRM MO40302B, the Commission instructed staff to provide the Commission with recommendations concerning the current definition of medical events and how to communicate effectively to the public associated risks, if any. In developing recommendations, the staff should confirm that there was an appropriate basis for applying the 20% reporting threshold for medical events to each modality, in the final Part 35 rule that became effective in October 2002. Furthermore, the staff should involve the ACMUI in the development of these recommendations.

a) The total source strength implanted anywhere in the patient exceeds the written directive by more than 20 percent or;

b) The total source strength implanted in the target volume deviates from the written directive by more than 20 percent.

There was much discussion of the use of the terminology "target volume." One Committee member believed this term should be replaced with the term "treatment site" because there are different definitions for the term "target volume." Thus, the second definition of medical event was proposed.

Proposed Brachytherapy Medical Event Definition #2:

> **Any permanent brachytherapy is a medical event, excluding seed migration and patient intervention, if a total source strength implanted in the treatment site in the patient varies from the written directive by more than 20 percent.**

As the ACMUI continued discussing this definition, it commented on the challenge in proposing a sound medical event definition that is firm enough to capture events where it is evident that radioactive sources were mistakenly implanted outside of the intended the treatment site, yet be flexible enough to not count as medical events, instances where practitioners purposely implant sources in tissues slightly outside of the treatment site, in order to achieve good treatment coverage.

As the ACMUI continued to discuss how to draft such language, it agreed that an advisable next step would be to circulate the draft language among its colleagues, to get other professional opinions about how to make the definition flexible, yet capture egregious errors. Toward this goal, the ACMUI formulated the following action items.

ACTION ITEM: **The ACMUI will circulate the draft language in Proposed Definitions #1 and #2, among other professional colleagues, to get insights on crafting language that will give physicians flexibility to treat slightly outside the perimeter of the treatment site, yet capture egregious errors where tissue clearly outside the intended treatment site was implanted.**

ACTION ITEM: **Dr. Nag will e-mail the other ACMUI members and NRC staff a copy of some slides he created, which gives his opinion on how to best define medical events involving permanent brachytherapy. The ACMUI will consider Dr. Nag's opinions as it moves forward in drafting the language for medical events involving permanent brachytherapy.**

ACTION ITEM: **The NRC liaison to the Medical Event Subcommittee, Dr. Ronald Zelac, will obtain input from NRC staff for ACMUI, regarding whether Proposed Definition #1, or Proposed Definition #2, or some combination of the two, is preferred as a definition that would provide necessary physician flexibility yet capture gross implantation errors.**

Regarding the second major area, clarifying the completion of the permanent brachytherapy use, the ACMUI agreed that this could be done without a rule change in 10 CFR Part 35. To help obtain this objective, the ACMUI suggested that NRC staff develop a generic communication that would define the completion of the permanent brachytherapy use. To assist staff, the ACMUI Subcommittee will provide the ACMUI and the NRC staff, for consideration, its view of when a permanent brachytherapy procedure is completed.

Regarding the third major area considered for revision, communicating risks to patients, the Medical Event Subcommittee agreed that after a medical event has occurred, the appropriate approach would be using the performance-based intent of 10 CFR Part 35. This could be done by creating language that would define a clinical outcome that every practitioner would recognize for reporting events to patients. The ACMUI prefers this approach, because every situation with each patient has enough variables to render impractical the use of a precise, prescriptive definition requiring patient notification. The Subcommittee still needs to develop draft language that will honor this approach to patient notification of medical events. This approach would require revision of the0 patient reporting requirement in 10 CFR 35.3045(e).

Regarding the fourth major area considered for revision, the redefinition of the medical event criteria for modalities other than permanent brachytherapy, the Medical Event Subcommittee did not recommend any change to the current rule criteria. Instead, the Subcommittee affirmed the adequacy of the current criteria, and stated the philosophical approach it believed that the NRC should use so that the current threshold of plus or minus 20% is appropriately applied. The following philosophical approach was endorsed by the ACMUI:

The current threshold of plus or minus 20% of the intended dose is a reasonable action level for reporting medical events involving temporary implants, external beam treatments, and unsealed radiopharmaceutical administrations, as long as any event reporting is not automatically treated as an indicator of potential patient harm.

Thus, the Subcommittee advanced its belief that NRC should view medical events strictly as performance indicators that may warrant further Agency response. However, the occurrence of medical events are not, of themselves, evidence of patient harm.

The ACMUI made the following recommendation:

As long as medical event reporting is not automatically treated as an indicator of potential patient harm, (plus or minus) 20 percent remains a reasonable action level for reporting events of Quality Assurance significance to NRC for the following modalities: temporary implants, external beam treatments and unsealed radiopharmaceutical administrations.

Motion: That the Subcommittee's recommendations be endorsed by the full Committee and forwarded to NRC staff. Motion was seconded and passed.

PATIENT SAFETY ISSUES WITH GAMMA STEREOTACTIC RADIOSURGERY

Douglas Kondziolka, MD, of the International Radiosurgery Association (IRSA), presented IRSA's views and recommendations on physician presence and responsibilities during gamma stereotactic radiosurgery (GSR). Dr. Kondziolka is a professor of neurological surgery, and of radiation oncology. He is also the current president of IRSA and a past president of the American Society for Stereotactic and Functional Neurosurgery.

Dr. Kondziolka stated that his experience with GSR administration includes over 3,000 patient treatments. At the University of Pittsburgh, his current institution, he stated that over 7,000 gamma knife treatments have been performed.

NRC's regulations in 10 CFR Part 35.600 require the presence of a team including the radiation oncologist and the medical physicist. Dr. Kondziolka affirmed NRC's regulatory approach that a team of trained professionals is needed to safely and effectively deliver GSR treatments, and stated that in the team approach, no individual is more important than any other individual, as all bring strengths related to efficacy and safety. However, Dr. Kondziolka believed that neurosurgeons, trained in GSR, are also essential members of the GSR team, and stated that NRC's regulations are remiss in not requiring the presence of the trained neurosurgeon, along with the radiation oncologist and medical physicist. He stated that the neurosurgeon is the physician primarily responsible for the patient's treatment, and therefore, should be required during the GSR administration. Dr. Kondziolka further stated that radiation oncologists are not trained in many components of radiosurgery, as are neurosurgeons. Therefore, there is increased risk to patients when neurosurgeons' presence is not required.

Dr. Kondziolka recommended the following changes to 10 CFR Part 35, which he believes will serve to augment patient safety:

- The term "authorized user" in 10 CFR Part 35 should be replaced with the terms authorized neurosurgeon, and authorized radiation oncologist.
- Clean and concise regulations for GSR are needed; regulations that are distinct from cobalt teletherapy and reflect how this procedure was performed.
- Either the neurosurgeon or the radiation oncologist should be present at the console during dose delivery, taking care of their joint patient.
- Authorized medical physicists should be in the vicinity, but should not be required to be at the console, since they are not medically trained.

THE IMPORTANCE OF RADIATION ONCOLOGIST PRESENCE AND AUTHORIZED USER STATUS FOR GAMMA STEREOTACTIC SURGERY PROCEDURES

David Larson, MD, representing the American Society of Therapeutic Radiology and Oncology (ASTRO) gave a presentation on ASTRO's views regarding radiation oncologists' presence during GSR. Dr. Larson is past president of IRSA, and a professor of radiation oncology. Dr. Larson is also a non paid scientific advisor of the Elektra Scientific Board (Elektra manufactures

a GSR unit). Dr. Larson stated that he holds a PhD in high energy physics in addition to his medical degree.

Dr. Larson stated that ASTRO has long maintained a collegial and clinically cooperative relationship with neurosurgeons, for the administration of GSR since the inception of this procedure. Several organizations, including ASTRO, affirmed that GSR should be performed by both neurosurgeons and radiation oncology participants. However, ASTRO feels compelled, according to Dr. Larson, to address what he characterized as "gross misrepresentations" made by IRSA. Dr. Larson stated that ASTRO "absolutely" supports NRC's current regulations, which requires only the presence of radiation oncologists and medical physicists during GSR, as adequate for patient safety.

Dr. Larson stated that radiation oncologists receive comprehensive training to handle all aspects of treatment planning, delivery, and safety. Furthermore, ASTRO objects to IRSA's position regarding medical physicists' presence, which ASTRO believes is essential during GSR.

Accompanying Dr. Larson was Dr. Paul Wallner, senior vice president of 21st Century Oncology, and the previous chief of the Clinical Radiation Oncology branch of the National Cancer Institute. Dr. Wallner stated that IRSA is a "trade organization" who joined with several individual neurosurgeons to petition a change to 10 CFR Part 35.960, and, in doing so, has demonstrated a "basic lack of understanding of the entire authorized user issue." Dr. Larson stated that ASTRO has never suggested that neurosurgeons should not be part of the GSR team, and that this whole issue is really a credentialing and privileging issue, and not a safety issue. Dr. Wallner stated that he "completely disagreed" with IRSA's remarks regarding the training and qualifications of radiation oncologists, in relation to their ability to safely administer GSR treatments to patients.

The ACMUI questioned the representatives from IRSA and ASTRO, but made no recommendation for a change to the physical presence rule in 10 CFR part 35.600.

ADMINISTRATIVE CLOSING

Angela McIntosh, NRC, lead the discussion on this topic. During this discussion, Ms. McIntosh and the ACMUI reviewed the recommendations and action items arising from this meeting, and discussed proposed meeting dates for the Fall 2005 meeting. The proposed meeting date for the fall meeting is October 25-26, 2005.

The meeting was adjourned at 4:44 p.m.

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