# MEETING AGENDA
# ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES
# September 10–11, 2019
### Two White Flint North Building (T-2D30), Rockville, Maryland

NOTE: Sessions of the meeting may be closed pursuant to 5 U.S.C. 552(b) to discuss organizational and personnel matters that relate solely to internal personnel rules and practices of the ACMUI; information the release of which would constitute a clearly unwarranted invasion of personal privacy; information the premature disclosure of which would be likely to significantly frustrate implementation of a proposed agency action; and disclosure of information which would risk circumvention of an agency regulation or statute.

## Tuesday, September 10, 2019
## CLOSED SESSION

| | | |
|---|---|---|
| 7:30 – 8:30 | **1. Badging and Enrollment** | **ACMUI** |

## OPEN SESSION

| | | |
|---|---|---|
| | **2. Opening Remarks**<br>Mr. Einberg will formally open the meeting and Ms. Kock will provide opening remarks. | **C. Einberg, NRC**<br>**A. Kock, NRC** |
| | **3. Old Business**<br>Ms. Jamerson will review past ACMUI recommendations and provide NRC responses. | **K. Jamerson, NRC** |
| 8:30 – 10:30 | **4. Open Forum**<br>The ACMUI will identify medical topics of interest for further discussion. | **ACMUI** |
| | **5. Training and Experience Evaluation**<br>Ms. Lopas and Ms. Ayoade will provide an update on the staff's evaluation of the training and experience requirements for radiopharmaceuticals requiring a written directive. | **M. Ayoade, NRC**<br>**S. Lopas, NRC** |
| | **6. Medical Events Subcommittee Report**<br>Dr. Ennis will provide an analysis of FY18 medical events. | **R. Ennis, ACMUI** |
| 10:30 – 10:45 | **BREAK** | |
| 10:45 – 12:15 | **7. Appropriateness of Medical Event Reporting Subcommittee Report**<br>Dr. Ennis will discuss the subcommittee's recommendations on the appropriateness of the required medical event reporting in accordance with 10 CFR 35.3045. | **R. Ennis, ACMUI** |
| | **8. Evaluation of Infiltrations Subcommittee Report**<br>Ms. Martin will discuss the subcommittee's recommendations on the evaluation of the NRC's 1980 infiltration decision. | **M. Martin, ACMUI** |
| 12:15 – 1:30 | **LUNCH** | |

| | | |
|---|---|---|
| | **9. Special Presentation to Dr. Palestro**<br>Chairman Svinicki will make a special presentation to Dr. Palestro. | **K. Svinicki, NRC** |
| 1:30 – 2:45 | **10. Dr. Palestro's Thoughts on Leaving the ACMUI**<br>Dr. Palestro will share his thoughts on leaving the ACMUI, after serving eight years, two of which he served as ACMUI Chairman. | **C. Palestro, ACMUI** |
| | **11. Xcision GammaPod Licensing Guidance Subcommittee Report**<br>Dr. Wolkov will discuss the subcommittee's recommendations on the NRC's draft Xcision® GammaPod Licensing Guidance. | **H. Wolkov, ACMUI** |
| 2:45 – 3:00 | **BREAK** | |

**Tuesday, September 10, 2019**
**CLOSED SESSION**

| | | |
|---|---|---|
| | **12. INFOSEC Training** | **R. Norman, NRC** |
| 3:00 – 5:00 | **13. Ethics Training** | **C. Safford, NRC** |
| | **14. Allegations Training** | **S. Hawkins, NRC** |

**Wednesday, September 11, 2019**
**OPEN SESSION**

| | | |
|---|---|---|
| | **15. Reducing Radioactive Materials**<br>Ms. Taalbi will provide an overview of the NNSA's initiative to reduce radioactive materials using alternative technologies. | **M. Taalbi, NNSA** |
| 8:30 – 10:30 | **16. ACMUI's Institutional Memory Subcommittee Report**<br>Dr. Schleipman will discuss the subcommittee's recommendations for improving the ACMUI's institutional memory. | **A. Schleipman, ACMUI** |
| | **17. Open Forum**<br>The ACMUI will discuss medical topics of interest previously identified. | **ACMUI** |
| | **18. ACMUI External Communications**<br>Dr. Palestro will discuss the 2019 Society of Nuclear Medicine and Molecular Imaging Annual Meeting. | **C. Palestro, ACMUI** |
| 10:30 – 10:45 | **BREAK** | |
| 10:45 – 11:15 | **19. NRC Regulatory Process and Other Tools**<br>NRC staff will provide an overview of NRC's regulatory process, to include the lifecycle of ACMUI recommendations and open items from initiation to disposition. | **I. Irvin, NRC** |
| | **20. Status of Emerging Technologies Licensed under 10 CFR 35.1000**<br>Mr. Sheetz will provide a presentation on the status of emerging technologies licensed under 10 CFR 35.1000. | **M. Sheetz, ACMUI** |

| | | |
|---|---|---|
| | **21. U.S. Pharmacopeia (USP) General Chapter <825>**<br>Mr. Green will provide a presentation on the new USP General Chapter <825> for Radiopharmaceuticals. | **R. Green, ACMUI** |
| 11:45 – 1:00 | **22. ACMUI Membership Composition and Balance**<br>Ms. Dimmick will provide a discussion of the ACMUI membership and balance. | **L. Dimmick, NRC** |
| | **23. Administrative Closing**<br>Ms. Jamerson will provide a meeting summary and propose dates for the spring 2020 meeting. | **K. Jamerson, NRC** |
| 1:00 | **ADJOURN** | |

# Opening Remarks

NO HANDOUT

| | ITEM | DATE | STATUS | |
|---|---|---|---|---|
| 33 | NRC staff should modify 10 CFR 35.491(b)(2) to specify 'superficial' ophthalmic treatments. Additionally, NRC staff should change the title of 10 CFR 35.491 to specify 'superficial' ophthalmic treatments. | 10/22/07 | *Not Accepted* | *Closed* |
| 34 | NRC staff should not revise 10 CFR 35.491 (intended for ophthalmologists) to include training and experience for the new intraocular device. Instead, NRC staff should regulate the new intraocular device under 10 CFR 35.490. | 10/22/07 | *Not Accepted* | *Closed* |
| | See Memorandum in ADAMS Accession No. ML19232A141 | | | |
| | | | | |

2008 ACMUI RECOMMENDATIONS AND ACTION ITEMS

| | ITEM | DATE | STATUS | |
|---|---|---|---|---|
| 19 | NRC staff should accept the six recommendations of the Permanent Implant Brachytherapy Subcommittee report with one modification. Recommendation six should be modified to read, "When a Written Directive (WD) is required, administrations without a prior WD are to be reported as regulatory violations and may or may not constitute an ME." | 10/27/08 | *Partially accepted* | Closed |
| 26 | NRC staff should revise 10 CFR 35.40 to clarify that the AU should sign and date both the pre-implantation and post-implantation portions of the WD for all modalities with two part WDs | 10/28/08 | *Not Accepted* | Closed |
| 27 | NRC staff should revise 10 CFR 35.40 to clarify that <u>an</u> AU, not <u>the</u> AU, should sign and date both the pre-implantation and post-implantation portions of the WD for all modalities with two part WDs. [Note this allows for one AU to sign the pre-implantation portion of the WD and another AU to sign the post-implantation portion of the WD] | 10/28/08 | *Not Accepted* | Closed |
| | See Memorandum in ADAMS Accession No. ML19232A141 | | | |

| | ITEM | DATE | STATUS | |
|---|---|---|---|---|
| 6 | ACMUI created an action item to reevaluate its satisfaction with the reporting structure annually. | 1/12/11 | *Accepted* | Closed |
| | See Memorandum in ADAMS Accession No. ML19232A141 | | | |

| | ITEM | DATE | STATUS | | Target Completion Date for NRC Action |
|---|---|---|---|---|---|
| 16 | Dr. Alderson formed a subcommittee to review and evaluate the training and experience requirements for all modalities in 10 CFR Part 35. Subcommittee members include: Dr. Langhorst, Dr. Metter, Dr. Palestro (chair), Dr. Suh and Ms. Weil. NRC staff resource: Maryann Abogunde. | 2/25/2016 | *Accepted* | Closed | |
| 24 | The ACMUI will contact their respective professional organizations to request and encourage interactions between the NRC and ACMUI with their organization. | 3/18/2016 | *Accepted* | Closed | Jan. 2020 |
| 39 | The Committee recommended that staff issue a generic communication (information notice) regarding tubing issues (kinking, connection, hub etc.) during the administration of Y-90 microspheres brachytherapy. | 10/6/16 | *Accepted* | Closed | Dec. 2019 |
| 42 | The Committee recommended that the Pathway 2 remain for the Y-90 Microsphere Brachytherapy Licensing Guidance. The NRC/OAS working group should determine what the requirements should be for the proctoring of cases by the manufacturer(s). | 10/7/16 | *Accepted* | Closed | Dec. 2019 |
| 43 | The Committee recommended to support the update to the waste disposal section and the review of the Y-90 radiation safety issues in autopsy and cremation in the draft revision of the Y-90 Microsphere Brachytherapy Licensing Guidance. | 10/7/16 | *Accepted* | Closed | Dec. 2019 |
| 44 | For the NorthStar Guidance Subcommittee: The Committee recommended that NorthStar provide a video clip of how the system operates in the training module. | 10/7/16 | *Not Accepted* | Closed | |
| 45 | For the NorthStar Guidance Subcommittee: Given the unique design and operation of the NorthStar system, the Committee agreed that NorthStar should have sole responsibility for the content of the training course and certification. | 10/7/16 | *Accepted* | Closed | |
| 46 | For the NorthStar Guidance Subcommittee: The Committee stated that it is important to clarify that a System Administrator can be any individual assigned by the AU without a specifically defined educational or training background. Given the unique role of the System Administrator, perhaps that individual should be named on the license. | 10/7/16 | *Not Accepted* | Closed | |
| 47 | For the NorthStar Guidance Subcommittee:The Committee recommended an explicit statement regarding the System Administrator Designee, although it may not have been intended, one could infer from the description of the system administrator designee that there can be only one designee. Presumably, there can, and should, be multiple System Administrator designees. | 10/7/16 | *Not Accepted* | Closed | |

| | ITEM | DATE | STATUS | | Target Completion Date for NRC Action |
|---|---|---|---|---|---|
| 48 | For the NorthStar Guidance Subcommittee:The Committee recommended that the appropriate time period allotted for training on the “changes” and the responsibility of the vendor/manufacturer to inform and train the applicants on changes in a timely manner be specified. | 10/7/16 | *Not Accepted* | Closed | |
| 49 | For the NorthStar Guidance Subcommittee: The Committee recommended that the guidance clarify whether the generator will be “non-operational” until ALL individuals handling the generator are trained in the changes, including the AU, RSO, system administrator, etc. or does it require only the AU to be trained on the “changes.” If the latter, once the AU is trained on the “changes”, is the AU then solely responsible for training all others on these changes? This should be stated. | 10/7/16 | *Accepted* | Closed | |
| 50 | For the NorthStar Guidance Subcommittee: The Committee recommended using the term, “individual tasks” throughout the document for consistency and to clarify that there is only one protocol and software program with this system. | 10/7/16 | *Partially Accepted* | Closed | |
| 51 | For the NorthStar Guidance Subcommittee: The Committee recommended that the manufacturer’s procedures be reviewed and incorporated into the Licensing Guidance itself. | 10/7/16 | *Not Accepted* | Closed | |
| 52 | For the NorthStar Guidance Subcommittee: The Committee recommended that the term “higher than expected” be defined in terms of a maximum specific exposure or exposure-rate limit which a survey meter should be capable of measuring. | 10/7/16 | *Not Accepted* | Closed | |
| 53 | The Committee endorsed the NorthStar Mo-99/Tc-99m Generator (RadioGenix) Subcommittee Report. | 10/7/16 | *Accepted* | Closed | |
| | For Items #44-52, see Memorandum at ADAMS Accession No. ML19158A292 | | | | |

| | ITEM | DATE | STATUS | | Target Completion Date for NRC |
|---|---|---|---|---|---|
| 13 | The ACMUI recommended that the NRC establish a program allowing a medical use licensee to evaluate MEs as described in 10 CFR 35.3045, in NRC 10 CFR 35.1000 licensing guidance, and in 10 CFR 35.3047 with an approved patient safety program. | 9/11/2017 | *Not Accepted* | Closed | |
| 14 | The ACMUI recommended that NRC licensees with an NRC-approved patient safety program will continue to report medical events as required with the following conditions: (1) The NRC will not include this event notification in the Event Notification Report posted on its website. If this is not possible, the ME notification posted on the website will leave the licensee information and location anonymous. (2) The NRC will not conduct a reactive inspection of the ME unless the event results or will result in death, unintended permanent harm, or unintended significant temporary harm for which medical intervention was or will be required to alleviate the harm or reduce radiation effects. (3) The medical use licensee will write a report available for the next NRC inspection describing the event cause and corrective action taken. (4) NRC will develop, with ACMUI advice, new temporary inspection procedures for NRC review of licensee patient safety event reports, and will evaluate, with ACMUI advice, need to change enforcement manual procedures regarding MEs to support a test of this program. | 9/11/2017 | *Partially Accepted* | Closed | Dec. 2019 |
| 15 | The ACMUI recommended that NRC should test out this program with two large medical centers, two community hospitals, two rural hospitals, and two patient clinics for a year, evaluating the ME reports with the ACMUI. During this test period, the NRC, with advice from the ACMUI, should do the following: (1) Develop the minimum criteria for patient safety program reviews; (2) Assess how this change in ME reporting impacts the NRC's ability to protect patient health and to minimize danger to the patient's life; and (3) Evaluate the different types of patient safety programs in how lessons learned from their patient safety incident reviews are shared with the medical community. | 9/11/2017 | *Not Accepted* | Closed | |
| 16 | The ACMUI recommended that after completion of the test year, the NRC should consider opening the program to all NRC medical use licensees who request approval of their patient safety program, and to Agreement States who request to implement the program with their medical licensees. | 9/11/2017 | *Not Accepted* | Closed | |

| | | | | | |
|---|---|---|---|---|---|
| 17 | The ACMUI recommended that the NRC redefine its perspective of patient safety to be different from occupational safety and from public safety. | 9/11/2017 | *Not Accepted* | Closed | |
| 18 | The ACMUI recommended that NRC partner with the Department of Health and Human Services (HHS), specially the Agency for Healthcare and Research and Quality (AHRQ) , and ACMUI to develop a national database taxonomy specific for reporting patient events involving medical use of byproduct material. | 9/11/2017 | *Not Accepted* | Closed | |
| 19 | The ACMUI recommended that the NRC Update its Medical Use Policy Statement and 10 CFR 35 event reporting regulations for patient safety programs to verify the active involvement of the licensee's patient safety program review of medical errors and reporting of reviews to the national patient safety database. | 9/11/2017 | *Not Accepted* | Closed | |
| 20 | The ACMUI endorsed the Medical Event Reporting and Impact on Medical Licensee Patient Safety Culture Draft Report, as amended to support the concept of the pilot program with the total number of sites and duration to be determined at a later date and to include the Patient Intervention Subcommittee recommendations as an addendum . | 9/11/2017 | *Pending* | Open | |
| | See Memorandum at ADAMS Accession No. ML19232A141 | | | | |

| | ITEM | DATE | STATUS | | Target Completion Date for NRC |
|---|---|---|---|---|---|
| 1 | The ACMUI recommended that there be no breast feeding cessation for $^{11}C$, $^{13}N$, $^{15}O$, and $^{82}Rb$; a 12-hours cessation for $^{18}F$-labeled and 68Ga-labeled; a 24-hours cessation for $^{99m}Tc$-labeled; 7-days cessation for $^{123}I$-NaI and $^{111}In$-leukocytes; 14 days cessation for $^{201}$-Tl-chloride; 28 days cessation for $^{67}Ga$ and $^{89}Zr$; 35 days for $^{177}Lu$, diagnostic; and total stop of breastfeeding for $^{131}I$-NaI, $^{177}Lu$, therapeutic, $^{223}Ra$ and all alpha emitters. | 2/15/2018 | *Accepted* | Closed | Apr. 2020 |
| 2 | The ACMUI endorsed the Nursing Mother Guidelines for the Medical Administration of Radioactive Materials Subcommittee Report, as amended to: (1) include recommended cessation periods for both 100 and 500 mrem limits; (2) acknowledge benefits of breastfeeding; (3) incorporate corrections as needed for gamma ray constants; (4) convert the units from conventional to SI units; and (5) correct references. | 2/15/2018 | *Accepted* | Closed | |
| 6 | The NRC staff will create an ACMUI Recommendations Web page and post the full ACMUI Recommendations and Actions charts on the ACMUI Web page from 2007 – present | 3/7/2018 | *Accepted* | Closed | Dec. 2019 |
| 7 | The NRC staff will send out a medical list server announcement to inform subscribers of the availability of ACMUI and NRC ME slides each time that they are posted on the Medical Toolkit. | 3/7/2018 | *Accepted* | Closed | Dec. 2019 |

| | | | | | |
|---|---|---|---|---|---|
| 11 | The ACMUI endorsed the report of the Subcommittee on the Nursing Mother Guidelines for the Medical Administration of Radioactive Materials with added language that this document reflects the FDA approved radiopharmaceuticals on the market at this time and that licensees are obligated to carefully evaluate radiopharmaceuticals that are not encompassed in this report to keep exposures ALARA to patients, staff, and members of the public. The recommendation passed unanimously. | 9/20/2018 | *Accepted* | Closed | |
| 14 | Dr. Palestro amended the membership of the Training and Experience for All Modalities Subcommittee. Subcommittee membership now includes Dr. Metter (chair), Dr. Ennis, Dr. Schleipman, Ms. Weil, Ms. Shober, and Mr. Sheetz. The NRC staff resource continues to be Ms. Maryann Ayoade. | 9/20/2018 | *Accepted* | Closed | |
| 15 | Dr. Palestro formed a subcommittee to review the Germanium-68/Gallium-68 Pharmacy Grade Generator Licensing Guidance. Subcommittee membership includes Ms. Shober (chair), Dr. Metter, Mr. Sheetz, and Ms. Martin. The NRC staff resource is Dr. Said Daibes. | 9/21/2018 | *Accepted* | Closed | |
| 16 | Dr. Palestro formed a subcommittee to review the revisions to Regulatory Guide 8.39, “Release of Patients Administered Radioactive Material.” Subcommittee membership includes Mr. Sheetz (chair), Ms. Shober, Dr. Dilsizian, Dr. Schleipman, Ms. Martin, and Ms. Weil. The NRC staff resource is Dr. Said Daibes. | 9/21/2018 | *Accepted* | Closed | |

| | | | | | |
|---|---|---|---|---|---|
| 17 | Dr. Palestro formed a subcommittee to review the Yttrium-90 Microspheres Brachytherapy Sources and Devices TheraSphere® and SIR_Spheres® Licensing Guidance. Subcommittee membership includes Dr. O'Hara (chair), Dr. Dilsizian, Mr. Ouhib, Ms. Marin, Dr. Metter, and Dr. Schleipman. The NRC staff resource is Dr. Katie Tapp. | 9/21/2018 | *Accepted* | Closed | |
| 18 | Dr. Palestro formed a subcommittee to review and update the ACMUI Bylaws as needed, including a review of the role of the ACMUI Chair and his or her participation on subcommittees. Subcommittee membership includes Ms. Weil (chair), Dr. Schleipman, Ms. Shober, and Mr. Sheetz. The NRC staff resource is Ms. Sophie Holiday. | 9/21/2018 | *Accepted* | Closed | |
| 19 | Dr. Palestro formed a subcommittee to review the appropriateness of the required elements of medical event reporting, the adherence to these requirements, and recommend actions to improve reporting. Subcommittee membership includes Dr. Ennis (chair), Ms. Weil, Ms. Martin, Mr. Ouhib, Dr. Dilsizian, and Ms. Shober. The NRC staff resource is Ms. Lisa Dimmick | 9/20/2018 | *Accepted* | Closed | |
| 20 | The Committee recommended for the NRC to draft an Information Notice on the best practices that could help prevent medical events. | 9/21/2018 | *Accepted* | Closed | Oct. 2019 |
| | See Memorandum at ADAMS Accession No. ML19232A141 | | | | |

2019 ACMUI RECOMMENDATIONS AND ACTION ITEMS

| | ITEM | DATE | STATUS | | Target Completion Date for NRC Action |
|---|---|---|---|---|---|
| 1 | The ACMUI recommended adding language into the draft *Training and Experience Requirements for All Modalities Subcommittee report* regarding the Committee's desire to work with the NRC staff to develop a curriculum for limited-scope authorized user pathway. | 2/26/2019 | *Accepted* | Open | Dec. 2019 |
| 2 | The ACMUI endorsed the *Training and Experience Requirements for All Modalities Subcommittee Report,* and the recommendations included therein. | 2/26/2019 | *Accepted* | Closed | Dec. 2019 |
| 3 | The ACMUI endorsed the Yttrium-90 Microspheres Brachytherapy Licensing Guidance, Rev. 10 Subcommittee Report, and the recommendations therein, with the caveat that the term "drug" be changed to "device." | 4/3/2019 | *Accepted* | Closed | Dec. 2019 |
| 4 | Dr. Palestro formed a subcommittee to re-evaluate the 1980 infiltration decision and report to the Committee at the fall 2019 meeting with any recommendations. Subcommittee members include: Dr. Vasken Dilsizian, Mr. Richard Green, Ms. Melissa Martin (Chair), Mr. Michael Sheetz, Ms. Megan Shober, and Ms. Laura Weil. The NRC staff resource is Maryann Ayoade. | 4/3/2019 | *Accepted* | Closed | |
| 5 | The ACMUI endorsed the Germanium-68/Gallium-68 Generator Licensing Guidance, Rev. 1 Subcommittee Report and the recommendations therein. | 4/3/2019 | *Accepted* | Closed | |

| | | | | | |
|---|---|---|---|---|---|
| 6 | The ACMUI endorsed the ACMUI Bylaws Subcommittee Report, with the following amendments: 1) amend the subcommittee's recommendation regarding the Chair's role on subcommittees in Section 1.3.6 to remove the phrase in the "in these instances"; 2) add language in Section 1.3.6 regarding the ACMUI Chairman serving on a subcommittee at the subcommittee's discretion; 3) amend the subcommittee's recommendation regarding explicit language defining Conflict of Interest in Section 4.1 to instead reference the appropriate OGE reference | 4/4/2019 | *Accepted* | Closed | |
| 7 | The ACMUI recommended that the NRC staff request a presentation from NNSA to review their plans for isotope utilization in the United States. The presentation will be given at the Fall 2019 ACMUI Meeting . | 4/4/2019 | *Accepted* | Closed | |
| 8 | The NRC staff will amend its Opening Remarks such that a statement regarding Conflict of Interest willl be included at every ACMUI Meeting. | 4/4/2019 | *Accepted* | Closed | |
| 9 | The ACMUI recommended that the NRC add a column to the Recommendation and Action Charts to include the date anticipated completion date for NRC staff action. | 4/4/2019 | *Accepted* | Closed | |
| 10 | Dr. Palestro formed a subcommittee to improve the ACMUI's institutional memory. Subcommittee members include: Dr. Ronald Ennis, Dr. Michael O'Hara, Dr. A. Robert Schleipman (chair), Ms. Megan Shober, and Ms. Laura Weil. The NRC staff resource is Ms. Kellee Jamerson. | 4/4/2019 | *Accepted* | Closed | |
| 11 | The ACMUI tentatively scheduled its fall 2019 Meeting for September 11-12, 2019. The alternate date is September 10-11, 2019. | 4/4/2019 | *Accepted* | Closed | |

| | | | | | |
|---|---|---|---|---|---|
| 12 | The Committee approved the proposed amendments to the ACMUI Bylaws, with specific changes to Sections 1.3.6 and 4.1, regarding the ACMUI Chairman's involvement in subcommittees and conflicts of interest, respectively. | 6/10/2019 | ACMUI Action | Open | |
| 13 | The ACMUI endorsed the Regulatory Guide 8.39, "Release of Patients Administered Radioactive Material" Subcommittee Report and the recommendations provided therein. | 6/10/2019 | ACMUI Action | Open | |
| 14 | The Committee recommended that the NRC's medical event Abnormal Occurrence criteria need to be reviewed and revised. | 7/24/2019 | ACMUI Action | Open | |

# Open Forum

NO HANDOUT

**Update on the NRC Staff's Evaluation of Training & Experience Requirements for Radiopharmaceuticals**

Maryann Ayoade
Medical Radiation Safety Team, NMSS
September 10, 2019

## Purpose

- Provide a status update on the staff's evaluation of training and experience (T&E) requirements for radiopharmaceuticals under 10 CFR 35.300, "Use of unsealed byproduct material for which a written directive is required."
- Discuss the options in the staff's draft T&E Commission paper.
- Outline the next steps of the evaluation.

2

## Status

- Since the ACMUI's September 2018 meeting, the NRC staff has:
  - Implemented the stakeholder outreach plan
  - Received input from the medical community and the Agreement States via two public comment periods
  - Developed a draft Commission paper that provides options regarding the NRC's T&E requirements

3

## Medical Community Feedback

- Nuclear medicine and radiation oncology communities strongly support maintaining the status quo, and oppose tailoring T&E to create new limited authorized user (AU) pathways.
- Non-traditional physicians wishing to treat patients with "patient-ready" radiopharmaceuticals support tailored T&E; suggest 80 hours of T&E.

4

## Agreement State Feedback

- The Organization of Agreement States (OAS) and some States oppose tailoring T&E.
- Some States support the status quo.
- The OAS and some other States suggest that the NRC and States should no longer review and approve T&E for physicians, and instead rely on other entities to "credential" AUs.
  - They commented that the current T&E requirements are not aligned with the NRC's Medical Policy Statement.

5

## T&E Options

- Options in the draft Commission paper fall under two general approaches:
  - **Approach 1.** Revise the T&E regulatory framework to remove prescriptive requirements, and the NRC and Agreement States would no longer review and approve T&E for AUs.
  - **Approach 2.** Maintain or enhance the existing T&E regulatory framework.

6

## Approach 1

- **Option 1a, Specialty Board Credentialing** – Physicians must be certified by any medical specialty board.
- **Option 1b, Licensee Credentialing** – Licensees develop their own policies and procedures for credentialing their physicians.
- **Option 1c, NRC-Recognized Specialty Board Credentialing** – Physicians must be certified by a medical specialty board that has been recognized by the NRC as meeting *high-level* board certification criteria.

7

## Approach 2

- **Option 2a, Status Quo** – No changes.
- **Option 2b, Tailored Requirements** – T&E would be tailored and reduced for use of individual or categories of radiopharmaceuticals.
- **Option 2c, Emerging Radiopharmaceuticals** – Individual reviews of each emerging radiopharmaceutical to determine drug-specific T&E and other requirements.
- **Option 2d, Team-Based Requirements** – T&E would be reduced based on pairing AUs with other individuals with radiation safety training.

8

## Next Steps

- ACMUI T&E Subcommittee and Agreement State review of draft Commission paper options: August – October
- ACMUI T&E Subcommittee comments due: October 7
- ACMUI Public Teleconference on T&E Subcommittee comments: October 2019
- Agreement State comments due: October 18, 2019
- Staff finalizes Commission paper: November – December
- Deliver paper to Commission: December 20, 2019

9

## Acronyms

ACMUI – Advisory Committee on the Medical Uses of Isotopes

AU – Authorized User

NRC – U.S. Nuclear Regulatory Commission

OAS – Organization of Agreement States

T&E – training and experience

10

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

# Medical Events Subcommittee Report (FY 2018)
## *Reported 10/01/17 – 9/30/18*

Ronald D. Ennis, M.D.
Advisory Committee for the Medical Uses of Isotopes
September 10, 2019

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

## Subcommittee Members

- Ronald D. Ennis, M.D. (Chair)
- Richard Green
- Darlene Metter, M.D.
- Michael Sheetz
- Harvey Wolkov, M.D.

- NRC Staff Resource: Donna-Beth Howe, Ph.D.



U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

| | FY 2013 | FY 2014 | FY 2015 | FY 2016 | FY2017 | FY2018 |
|---|---|---|---|---|---|---|
| 35.200 | 2 | 6 | 4 | 8 | 6 | 0 |
| 35.300 | 2 | 4 | 7 | 5 | 4 | 2 |
| Manual brachy | 16 | 5 | 8 | 7 | 5 | 13 |
| HDR | 8 | 9 | 13 | 5 | 14 | 10 |
| GK | 2 | 1 | 8 | 3 | 0 | 1 |
| Microspheres | 13 | 24 | 18 | 26 | 23 | 19 |
| RSL/intravascular brachy | 1/0 | 1/0 | 1/0 | 0/0 | 2/0 | 1/1 |



U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

## Conclusions

- No concerning trends or emerging new issues have been reported.

- One potential new issue is emerging – There is an increasing use of radiopharmaceuticals of high activity and high volume. This increases the risk of MEs and of their potential for serious medical consequences.

- Full trend analysis of MEs over a several year period will be performed in 2020.

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

## Acronyms

- FY - Fiscal Year
- HDR - High Dose-Rate
- GK - Gamma Knife
- IVB - Intravascular Brachytherapy
- ME - Medical Event
- Micro-Sph - Micro-Spheres
- RSL - Radioactive Seed Localization

5

# Nuclear Regulatory Commission (NRC)

# Advisory Committee on the Medical Uses of Isotopes (ACMUI)

# Subcommittee on Medical Events

Subcommittee Final Report

Submitted On: August 21, 2019

Subcommittee Members: Mr. Richard Green, Dr. Ronald D. Ennis (Chair), M.D., Dr. Darlene F. Metter, Mr. Michael Sheetz, Dr. Harvey Wolkov

**Charge**

The specific charge of this subcommittee is to annually review the medical events (MEs) with an eye to advising the ACMUI and NRC about emerging trends needing regulatory attention.

**Background**

At the Fall 2018 ACMUI meeting this subcommittee presented an in-depth trend analysis of MEs over a four-year period and made specific recommendations. Because there are relatively few MEs each year and trends in MEs tend to emerge slowly, it was decided that the subcommittee would perform an in depth tend analysis every two years. In the intervening year, the subcommittee would perform a review of MEs of the previous fiscal year looking for urgent issues that need to be addressed immediately and cannot wait for the in-depth review of the following year. The subcommittee herein provides such a report.

**Findings**

The Subcommittee on Medical Events reviewed the Medical Events from FY 2018. Events from each section were reviewed in detail by a subcommittee member with expertise in the area. There were no new notable event types. There were no apparent marked increases in any of the event categories or types compared to prior years.
One area identified by the subcommittee that could emerge in coming years involves new radiopharmaceuticals which have a high activity and are given in a relatively large volume of fluid (i.e. more than a few milliliters). These characterisitics increase the risk of MEs and of their potential for serious medical consequences. There are two newer agents that have these features: lutetium-177 dotatate (Lutethra) and iobenguane Iodine-131 (Azedra). The subcommittee will pay particular attention to these agents when it does its next review. The Subcommittee does not recommend any action regarding these agents at this time.

**Concluding Remarks**

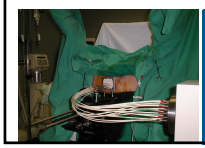
The subcommittee looks forward to performing an in depth trend analysis in 2020.
The subcommittee welcomes any comments and/or suggestions.

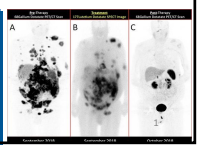
Respectfully Submitted,
*The Medical Event Subcommittee*

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

# Appropriateness of Medical Event Reporting Subcommittee Report

Ronald D. Ennis, M.D.
Advisory Committee on the Medical Uses of Isotopes
September 10, 2019






## Subcommittee Members

- Dr. Dilsizian
- Dr. Ennis (Chair)
- Ms. Martin
- Mr. Ouhib
- Ms. Shober
- Ms. Weil (has rotated off ACMUI)

- NRC Staff Resource: Lisa Dimmick

2

## Subcommittee Charge

- To review the appropriateness of the required elements of medical event reporting; the adherence to these requirements; and recommend actions to improve reporting.

3

- The subcommittee presented preliminary findings at the April 3, 2019 ACMUI meeting.

- Herein is the final report of the Subcommittee.

4

## Purpose of Reporting

- An ME is reported to an Agreement State or NRC per 10 CFR 35.3045 as summarized in "Event Reporting Schedule for Agreement States 7/29/12" and SA-300 "Reporting Material Events" – "The information collected on … medical events … is invaluable in *assessing trends or patterns,* identifying generic issues or generic concerns, and *recognizing any inadequacies or unreliability of specific equipment or procedures.* The reported information is critical for initiating a timely and effective response to security-related events and *will significantly aid in understanding why the event occurred and identifying any actions necessary to improve the effectiveness of NRC and Agreement State regulatory programs."*

5

## NMED Issues

- Frequently, narrative is inadequate for an ACMUI reviewer to understand an event, its cause and contributing factors, and the adequacy of the corrective action.
- At times, there appears to be a disconnect between the narrative and the chosen cause from the "cause pick list."
- At times, there appears to be a disconnect between the narrative and the chosen corrective action from the "corrective action pick list."

6

## NMED Issues

- NMED lacks information from some inspections that has been conducted by the NRC Region or Agreement State.
- In 23% of MEs from FY 2017-18, either no cause or no corrective action was indicated in NMED report.
- Of all 2017 MEs, 11% are incomplete and an additional 11% are pending additional information.
- Public, including AUs and RSOs, only have access to an NMED annual report.

7

## Time course of reporting – 10 CFR 35.3045

- Must make initial report of the discovery of the event within 24 hours.
- A written report with the elements detailed within 15 days.

8

## 10 CFR 35.3045 - Required elements of an ME report due within 15 days

- (i)The licensee's name;
- (ii) The name of the prescribing physician;
- (iii) A brief description of the event;
- (iv) Why the event occurred;
- (v) The effect, if any, on the individual(s) who received the administration;
- (vi) What actions, if any, have been taken or are planned to prevent recurrence; and
- (vii) Certification that the licensee notified the individual (or the individual's responsible relative or guardian), and if not, why not.

9

## SA-300

- An ME is reported to an Agreement State or NRC per 10 CFR 35.3045, as summarized in SA-300 "Reporting Material Events" and "Handbook on Nuclear Material Event Reporting in the Agreement States Final Report March 2013"

10

## SA-300

- Follow-up information for nuclear material event reports (e.g., providing additional information regarding initial event reports) *should* provide the results of investigations as to what, where, when and how the event or conditions occurred. Agreement States should provide the items below when reporting follow-up information:
- *On a monthly basis,* follow-up reports through the closeout of the event *should* be provided in writing to the RMSB Branch Chief … or electronically to the NMED
- No actual requirements, no actual deadlines

11

## SA-300 - Minimum elements for complete report

- Narrative event description including source, radionuclide, activity, manufacturer, model, serial number, equipment problems, type of procedure, dose intended, actual dose, target organ
- Was patient and referring notified
- Report number, event date, notification date, licensee, location of event, whether it is reportable and the applicable reporting requirement
- Cause and corrective action
- Notifications to police, FBI, etc.
- Indicate Generic implications

12

## Regulatory Gaps

- Minimal requirements re: data elements in medical event report as given by 35.3045 are vague and limited
- No requirement that a NMED report be completed
- If incomplete, a Request for Additional Information (RAI, as per NMED Coding Manual Appendix D) as an automatic email goes out to the responsible agency 57 days after a report was first created.
- No further outreach is done thereafter
- Only regulatory action related to this is the Integrated Material Performance Evaluation Program (IMPEP) in which NRC and Agreement States are reviewed every 4 years

13

## Recommendations of the Subcommittee

- In NMED, for both root cause and corrective action sections, in addition to the pick lists, a narrative, searchable free text section should be created
- A two-stage approach is recommended
  - Develop materials to be shared with the regulator and user communities regarding what constitutes an optimal NMED report along with a rationale for why this is important
  - If the above is unsuccessful them, implement requirements to improve NMED reporting

14

## Components of Educational Effort Regarding Key Elements of a Useful NMED report

- The elements that make a useful root cause analysis narrative
  - What happened – with enough detail that an uninvolved AU would have full understanding of the ME.
    - When in the process of radiation delivery did the event occur?
    - Who was present at the time of the ME?
    - What preceded the ME?
    - How did the ME occur?
    - What helped catch the ME?
    - Who/what detected the ME?

15

## Components of Educational Effort Regarding Key Elements of a Useful NMED report (cont'd.)

- The elements that make a useful corrective action narrative
  - Short-term and long-term corrective actions undertaken
  - Specify how the corrective action is linked to the events of the ME
- Importance of adding information provided by manufacturer (when applicable)
- Importance of including medical as well as technical information about the event
- Importance of including the 15 day report in the submission (stored in ADAMS).
- Importance of completing the report within 12 months

16

## Methods of Promulgation of these Recommendations

- Informational Notice from NRC should be issued
- Presentations at OAS, CRCPD, and medical professional society meetings should be conducted

17

## Conclusion

- Significant opportunities exist to enhance the utility of medical event reporting, the NMED database, and the promulgation of the information to the user community.
- If these efforts prove ineffective at improving the quality of NMED reporting, then regulatory approaches should be considered.

18

## Acronyms

- ACMUI – Advisory Committee on the Medical Use of Isotopes
- ADAMS - Agencywide Documents Access and Management System
- AU – Authorized user
- CFR – Code of Federal Register
- CRCPD - Conference of Radiation Control Program Directors
- FBI – Federal Bureau of Investigations
- FY - Fiscal Year
- ME – medical event
- NMED – Nuclear Materials Event Database
- NRC – Nuclear Regulatory Agency
- OAS – Organization of Agreement States
- RMSB - Radioactive Materials Safety Branch
- RSO – Radiation Safety Officer

19

# Nuclear Regulatory Commission (NRC)

# Advisory Committee on the Medical Uses of Isotopes (ACMUI)

# Subcommittee on the Appropriateness of Medical Event Reporting

Subcommittee Final Report

Submitted On: August 28, 2019

Subcommittee Members: Dr. Vasken Dilsizian, Dr. Ronald D. Ennis (Chair), Ms. Melissa Martin, Mr. Zoubir Ouhib, Ms. Megan Shober

## Charge

The charge of this subcommittee is review the appropriateness of the required elements of medical event (ME) reporting; the adherence to these requirements; and recommend actions to improve reporting.

## Background

An ME is reported to an Agreement State or NRC in accordance with Title 10 *Code of Federal Regulations* (10 CFR) 35.3045, "Report and Notification of a Medical Event". The purpose of medical event reporting[1] was initially published May 14, 1980. Back then, a medical event was known as a "misadministration". In the Federal Register, dated May 14, 1980, the following statement is made **"The Commission's purpose in requiring misadministration reports to NRC was to identify their causes in order to correct them and prevent their recurrence. The Commission was able to notify other licensees if there was a possibility that they could make the same errors" (45 FR 31701, May 14, 1980).**

Similarly, as summarized in "Event Reporting Schedule for Agreement States 7/29/12" and SA-300, "Reporting Material Events" – "The information collected on … medical events … is invaluable in *assessing trends or patterns,* identifying generic issues or generic concerns, and *recognizing any inadequacies or unreliability of specific equipment or procedures.* The reported information is critical for initiating a timely and effective response to security-related events and *will significantly aid in understanding why the event occurred and identifying any actions necessary to improve the effectiveness of NRC and Agreement State regulatory programs."*

Each year, an NRC staff member and an ACMUI subcommittee conduct a review of the Nuclear Materials Events Database (NMED) of the MEs reported within the immediate past Fiscal Year

[1] https://www.nrc.gov/materials/miau/med-use-toolkit.html#report

(FY). The ACMUI members have come to find the information in NMED lacking in a way that impedes the ability of NMED to be a source of information to prevent future MEs.

Specifically, at the spring, 2019 meeting the Subcommittee identified the following issues with NMED.

- Frequently, the narrative is inadequate for an ACMUI reviewer to understand an ME, its root cause and contributing factors, and the adequacy of the corrective action.
- At times, there appears to be a disconnect between the narrative and the chosen root cause from the "cause pick list."
- At times, there appears to be a disconnect between the narrative and the chosen corrective action from the "corrective action pick list."
- NMED lacks information from some follow-up inspections that have been conducted by the respective NRC region or Agreement State.
- In 23% of MEs from FY 2017-18, there was either no cause or no corrective action indicated in the NMED report.
- Of all 2017 MEs, 11% are incomplete and an additional 11% are pending additional information.
- Members of the public, including authorized users and radiation safety officers, only have access to an NMED annual report.

At the spring 2019 meeting, the subcommittee made some preliminary recommendations and was tasked with making final recommendations at the fall 2019 meeting.

**<u>Subcommittee Findings</u>**

The Subcommittee has determined that the regulatory requirements for reporting an ME (as per 10 CFR 35.3045) are:

- An initial report must be made within 24 hours of discovery of the event
- A written report must be submitted by 15 days
    - The elements required for the 15-day report are:
        - (i) The licensee's name
        - (ii) The name of the prescribing physician;
        - (iii) A brief description of the event;
        - (iv) Why the event occurred;
        - (v) The effect, if any, on the individual(s) who received the administration;
        - (vi) What actions, if any, have been taken or are planned to prevent recurrence; and
        - (vii) Certification that the licensee notified the individual (or the individual's responsible relative or guardian), and if not, why not.

Guidance regarding the expectations of reporting into NMED is provided in SA-300 Reporting Material Events" and the "Handbook on Nuclear Material Event Reporting in the Agreement States Final Report March 2013". This guidance is:

- Follow-up information for nuclear material event reports (e.g., providing additional information regarding initial event reports) *should* (italics added by this report) provide the results of investigations as to what, where, when and how the event or conditions occurred. Agreement States should provide the items below when reporting follow-up information:
- *On a monthly basis,* (italics added) follow-up reports through the closeout of the event *should* (italics added) be provided in writing to the RMSB Branch Chief … or electronically to the NMED
- The minimum elements for a complete NMED report are:
    - Narrative event description including source, radionuclide, activity, manufacturer, model, serial number, equipment problems, type of procedure, dose intended, actual dose, target organ
    - Was patient and referring notified
    - Report number, event date, notification date, licensee, location of event, whether it is reportable and the applicable reporting requirement
    - Cause and corrective action
    - Notifications to police, FBI, etc.
    - Indicate Generic implications

The subcommittee's conclusions regarding the reporting requirements are:

- The minimal requirements re: data elements in the medical event reports as given by 35.3045 are vague and limited
- There is no actual requirement that NMED reports be completed
- If incomplete, a Request of Additional Information (RAI), per NMED Coding Manual Appendix D) as an automatic email goes out to the responsible agency 57 days after a report was first created, but no further outreach is done
- The only oversight related to this is the Integrated Material Performance Evaluation Program (IMPEP) in which the NRC and Agreement States are reviewed every 4 years

**<u>Subcommittee Recommendations</u>**

The Subcommittee recommends two enhancements to NMED to increase the value of information in the database.

1. The NMED programmers should add a narrative field to the root cause and corrective action sections, in addition to the existing pick lists. This new narrative field should be a searchable free text section. (At a subcommittee meeting, an NMED representative has assured the subcommittee that this can be done.)

2. NRC, in coordination with the ACMUI, should provide additional information to NMED users on best practices for writing NMED reports for medical events.

For the second recommendation, a two stage approach should be implemented:

First, develop educational materials to be shared with the regulator and user communities regarding what constitutes an optimal NMED report along with the rationale for why this is important.

Specifics elements of this educational program are:

- The elements that make a useful root cause analysis narrative include:
  - What happened – with enough detail that an uninvolved AU and uninvolved radiation safety personnel would have full understanding of the ME.
    - When in the process of radiation delivery did the event occur?
    - Who was present at the time of the ME?
    - What preceded the ME?
    - How did the ME occur?
    - What helped catch the ME?
    - Who/what detected the ME?
    - Was the manufacturer notified?
- The elements that make a useful corrective action narrative include:
  - Short term and long term corrective actions undertaken
  - Specify how the corrective action is linked to the events of the ME
- Importance of adding information provided by manufacturer (when applicable)
- Importance of including medical as well as technical information about the event
- Importance of including the 15 day report in the submission (stored in ADAMS).
- Importance of completing the report within 12 months

The subcommittee recommends this information be promulgated via:

An Informational Notice from the NRC

Presentations at OAS, CRCPD and medical professional society meetings.

Second, if the educational approach is not successful at improving the quality of NMED reporting, then the subcommittee recommends implementation of specific *requirements* to improve the reporting

**Concluding Remarks**

Significant opportunities exist to enhance the utility of ME reporting, the NMED database, and the promulgation of the information to the user community as detailed above.

If these efforts prove ineffective at improving the quality of NMED reporting, then regulatory approaches should be considered.

The Subcommittee welcomes any comments and/or suggestions.

Respectfully Submitted,
*The Appropriateness of Medical Event Reporting Subcommittee*

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

## Evaluation of Extravasations Subcommittee

**Presented by: Richard Green**
**Melissa C. Martin, Subcommittee Chair**
**Advisory Committee on the Medical Uses of Isotopes**
**September 10, 2019**

1

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

## Financial Disclosures

- None

2

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

## Subcommittee Members

- Vasken Dilsizian, M.D.
- Richard Green
- Melissa Martin (Chair)
- Michael Sheetz
- Megan Shober
- Laura Weil

- NRC Staff Resource: Said Daibes, Ph.D. (formerly Maryann Ayoade)

3

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

## Subcommittee Charge

Re-evaluate and provide recommendations on the NRC decision on infiltrations and extravasations published in the *Federal Register*, Volume 45, No. 95, on May 14, 1980.

4

## Purpose of the Subcommittee

Subcommittee and its Chair were appointed by ACMUI Chairman, Dr. Christopher Palestro, at the ACMUI meeting on April 3, 2019, to review the NRC current decision on infiltrations and extravasations when radionuclides are injected into patients.



## Criteria for Misadministration from May 14, 1980 *Federal Register* (45 FR 95)

- Misadministration means the administration of:
  - wrong source
  - wrong patient
  - wrong route of administration
  - diagnostic dose differing by more than 50% from prescription
  - therapeutic dose differing by more than 10% from prescription



## Exclusion of Extravasation from Misadministration Definition

- Specific request for the NRC to review this exclusion as stated in the May 14, 1980 FR:
  - "Extravasation is the infiltration of injected fluid into the tissue surrounding a vein or artery.
  - Extravasation frequently occurs in otherwise normal intravenous or intra-arterial injections.
  - It is virtually impossible to avoid.
  - Therefore, the Commission does not consider extravasation to be a misadministration."



## Medical Event Definition: 10 CFR 35.3045

- 10 CFR 35.3045 "Report and Notification of a Medical Event" (published in 2002) changed "misadministration" to "medical event."
- Medical event is defined as a discrepancy of a total dosage of +/- 20% delivered dose.

## Prior Discussions of Extravasation of Radiopharmaceuticals

- Clinical aspects of extravasation of radiopharmaceuticals has been discussed previously by the ACMUI at the December 18, 2008 and May 8, 2009 meetings.
- Decisions at both of these meetings was that extravasation of radiopharmaceuticals not be considered to be a medical event at that time.

9

## Technology Presentation at April 3, 2019 ACMUI Meeting

At the April 3, 2019 ACMUI meeting, a technology was presented that identifies:

- Extravasations of PET radiopharmaceutical injection sites early in the process.
- The effect on the Standardized Uptake Value (SUV) of tumors or organs when extravasation occurs.

10

## Clinical Aspects of Extravasation

- Main point of discussion of extravasation of radiopharmaceuticals is that the denominator for this problem is several million injections per year of **ALL** radiopharmaceuticals injected.
- Extravasation problem is **NOT LIMITED to PET** isotopes only.
- Prevention of extravasation is a medical training issue for the Authorized User (AU) physician and the technologist under the supervision of the AU which is considered medical practice.

11

## SUV of F-18 PET Isotopes

- Currently 48 radiopharmaceuticals approved by the FDA, including five IV therapeutic drugs.
- Extravasation of the 6 fluorinated compounds including the F-18 PET drugs can bring about discrepancies in the SUV.
- SUV value is **NOT** relied on solely.

12

## Isotopes Other than F-18

- For isotopes other than FDG isotopes used for PET, it is difficult to quantify non-F-18 drugs left at the injection site and difficult to assign the radiation dose attributable to it.
- When extravasation of radiopharmaceuticals occurs, there is a variable delay in the biodistribution of the isotope after injection.
- **NONE** of the total doses in these extravasations meet the NRC's medical event criteria.

13

## Extravasation Occurrences

- This subcommittee does not consider extravasation a de facto medical event.
- Extravasation frequently occurs in otherwise normal intravenous or intra-arterial injections and is virtually impossible to avoid.
- Not all nuclear medicine cameras in use today (PET and SPECT) can quantify the amount of radiopharmaceutical localized in the extravasation site.
- Subcommittee members are unaware of any cases of documented patient harm due to extravasation as of today.

14

## Subcommittee Recommendations

- Extravasation is a practice of medicine issue and not an item that needs to be regulated by the NRC.

15

## Subcommittee Recommendations

- There is no evidence at this time for this subcommittee to recommend a reclassification of extravasation at the injection site for radiopharmaceuticals to be considered a medical event.
- The subcommittee recommends that extravasations that lead to "unintended permanent function damage" be reportable as a Medical Event under 10 CFR 35.3045(b).

16

## Subcommittee Recommendations

The subcommittee recommends that extravasations be considered a type of passive "patient intervention", similar to the recommendations from the ACMUI Subcommittee (Presented during the ACMUI public meeting in October 2015 and referenced in the Patient Intervention Subcommittee report dated April 27, 2017) and should be captured in the NRC's current definition of patient intervention under 10 CFR 35.2.



## Minority Opinion

- One member of the subcommittee had a different perspective on potential medical event reporting due to extravasation.
  - This member wants extravasation occurrences that trigger ME criteria of >50 rem tissue dose or <80% of the prescribed dose delivered to the patient, to be reported as a Medical Event. This would be consistent with all other MEs that cause no patient harm and are currently required to be reported. The exclusion of extravasation is inconsistent with other regulation and is unwarranted.



## Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- AU – authorized user
- FDA – U.S. Food and Drug Administration
- FDG – fluorodeoxyglucose
- FR – *Federal Register*
- IV – intravenous therapy
- ME – medical event
- NRC – U.S. Nuclear Regulatory Commission
- PET – positron emission tomography
- SPECT – single-photon emission computed tomography
- SUV – Standardized Uptake Value

**Nuclear Regulatory Commission (NRC)**
**Advisory Committee on the Medical Use of Isotopes (ACMUI)**
**Subcommittee on Extravasation**

**Draft Report Submitted on: August 15, 2019**

**Subcommittee Members:** Vasken Dilsizian, M.D., Richard Green, Melissa Martin (Chair), Michael Sheetz, Megan Shober, Laura Weil
**NRC Staff Resource:** Said Daibes, PhD (formerly Maryann Ayoade)

DRAFT

**Subcommittee Charge:**

Re-evaluate and provide recommendations on the NRC decision on infiltrations and extravasations published in the Federal Register, Volume 45, No. 95, on May 14, 1980.

**Background:**

The subcommittee and its Chair were appointed by ACMUI Chairman, Dr. Christopher Palestro, at the ACMUI meeting on April 3, 2019. The purpose of the subcommittee was to review the NRC current decision on infiltrations and extravasations when radionuclides are injected into patients which was published in the Federal Register, Volume 45, No. 95, Page 31701-31704 on May 14, 1980. The following specific requirements are pertinent to this request for review.

"Extravasation is the infiltration of injected fluid into the tissue surrounding a vein or artery. Extravasation frequently occurs in otherwise normal intravenous or intra-arterial injections. It is virtually impossible to avoid. Therefore, the Commission does not consider extravasation to be a misadministration."

The criteriafor a misadministration as outlined in this publication is:
§ 35.41 Definition of a misadministration.
For this part, misadministration means the administration **of:**
(a) A radiopharmaceutical or radiation from a sealed source other than the one intended;
**(b)** A radiopharmaceutical or radiation, to the wrong patient;
**(c)** A radiopharmaceutical or radiation by a route of administration other than that intended by the prescribing physician;
**(d)** A diagnostic dose of a radiopharmaceutical differing from the prescribed dose by more than 50 percent;
(e) A therapeutic dose of a radiopharmaceutical differing from the prescribed dose by-more than 10 percent; or
**(f)** A therapeutic radiation dose from a sealed source such that errors in the source calibration, time of exposure and treatment geometry result in calculated total treatment dose differing from the final prescribed total treatment dose by more than 10 percent.
(Ref: Section 35.41as published in the Federal Register, Volume 45, No. 95 on May 14, 1980)

In 2002, current medical event definition was changed from misadministration as published in the Federal Register at the following reference: 10 CFR 35.3045 "Report and Notification of a Medical Event."

At the April 3, 2019 meeting of the ACMUI, a presentation was made regarding a technology, which may help identify extravasations. The goal for the use of this product is to reduce the frequency extravasations. Data was presented relative to this product's use for PET isotope injections and the effect on Standardized Uptake Value (SUV) of tumors or organs when extravasation occurs. There was a request for the NRC to review 1980 policy exemption due to extravasation.

**Discussion**:

The subcommittee again discussed the topic of extravasation of radiopharmaceuticals at the injection site. This topic has been discussed at two previous ACMUI meetings (December 18, 2008 and May 8, 2009) with the decisions made that this not be reported as a medical event at the current time.

- **Clinical aspects of the occurrence of extravasation of radiopharmaceuticals**:
  The main point of this discussion is that the denominator for this problem is several million injections per year of all radiopharmaceuticals used. The problem is not limited to PET isotopes only. If an extravasation occurs to the extent that the image quality is compromised, the procedure is repeated the following day or shortly thereafter at the discretion of the authorized physician. The prevention of extravasation is a medical training issue for the authorized user (AU) physician and the technologist under the supervision of the AU, which is considered medical practice and not something that needs NRC regulation.

- There are currently 48 radiopharmaceuticals approved by the FDA (including five IV therapeutic drugs). Extravasation of the six fluorinated compounds including the F-18 PET drugs can bring about discrepancies in the SUV. However, the SUV value is not relied on solely. It is one way to give a quantified value to the images. It is common to have some remaining isotope at the injection site. For isotopes other than FDG isotopes used for PET, it is difficult to quantify non F-18 drugs left at the injection site and difficult to assign the radiation dose attributable to it. When extravasation of radiopharmaceuticals occurs, there will be a variable delay in the biodistribution after injection. None of the total doses in these extravasations meet the NRC's medical event criteria of a discrepancy of a total dosage of +/- 20% delivered dose criteria. This subcommittee does not consider extravasation a defacto medical event.

- Extravasation frequently occurs in otherwise normal intravenous or intraarterial injections and is virtually impossible to avoid. While there are devices in the market today that can identify extravasation, not all cameras (PET and SPECT) can quantify for all radiopharmaceuticals. These methods do not quantify the amount of activity that is infiltrated but it does alert personnel to the occurrence of an infiltrate. Members of this subcommittee are unaware of any cases where there has been patient harm due to extravasation as of today.

DRAFT

**<u>Subcommittee Recommendations</u>:**

- Extravasation is a practice of medicine issue and not an item that needs to be regulated by the NRC.

- The subcommittee recommends that extravasations be considered a type of passive "patient intervention", similar to the recommendations from the ACMUI subcommittee (presented during the ACMUI public meeting on October 2015 and referenced in the Patient Intervention subcommittee report dated April 27, 2017), and should be captured in the NRC's current definition of patient intervention under 10 CFR 35.2.

- There is no evidence at this time for this subcommittee to recommend a reclassification of extravasation at the injection site for radiopharmaceuticals to be considered a medical event. The subcommittee recommends that extravasations that lead to "unintended permanent function damage" be reportable as a Medical Event under 10 CFR 35.3045(b).

One member of the subcommittee had a different perspective on potential medical event reporting due to extravasation. Her minority opinion is included here, in its entirety.

*One member of the Subcommittee expressed concern with the existing 1980 exclusion of extravasation events from ME status. This member acknowledges the Subcommittee consensus that there would be only rare incidence of extravasation triggering ME criteria of >50 rem tissue dose or <80% of prescribed dose delivered to the patient, and believes the extravasation exemption in the 1980 language is unnecessary. Only rare gross discrepancies in delivered dose or tissue exposure would be reportable, and this member believes that those rare instances should be reported just as any other misadministration of such magnitude would be reported as MEs. The fact that they may result in no patient harm should have no bearing on the requirement to report. This would be consistent with the fact that all other ME's that cause no patient harm are currently required to be reported. When/if NRC decides to redefine ME criteria to exclude events that do not cause patient harm, then extravasation incidents would be included in such exclusion. But this member believes that the current specific exclusion of extravasation is inconsistent with other regulation and unwarranted.*
*Respectfully submitted,*
*Laura Weil*

**Respectfully submitted, August 15, 2019,**
**Subcommittee on Extravasation**
**Submitted to:**
**Advisory Committee on the Medical Use of Isotopes (ACMUI),**
**Nuclear Regulatory Commission (NRC)**

DRAFT

Special Presentation

to

Dr. Christopher Palestro

NO HANDOUT

# Thoughts on Leaving the ACMUI

NO HANDOUT

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

# Xcision® GammaPod™ Licensing Guidance Subcommittee

**Harvey B. Wolkov, M.D.**
**Advisory Committee on the Medical Uses of Isotopes**
**September 10, 2019**

## Xcision® GammaPod™ Licensing Guidance Subcommittee

**Subcommittee Charge:** To review and comment on the draft Xcision® GammaPod™ Licensing Guidance

**Subcommittee Members:**
Zoubir Ouhib, M.S.
Michael Sheetz, M.S.
Megan Shober, M.S.
Harvey Wolkov, MD (Chair)

**NRC Staff resource**: Katie Tapp, Ph.D.

2

## Background

- A non-invasive stereotactic radiotherapy system utilizing Co-60 sources to treat breast cancer
- System is different from Gamma Knife STR
  - uses vacuum-assisted breast cup immobilization and stereotactic localization system
  - rotating source and collimator carrier
  - table moves during treatment

3

## Background

- Currently, there are 2 units operational in the U.S. (University of Maryland and University of Texas SW), with plans to begin treatment at Alleghany General Hospital in Pittsburgh and at the University of Ottawa in Canada.
- The NRC/Agreement States Working Group determined the device should be licensed under 10 CFR 35.1000

4

## Adjuvant Radiation Therapy

- Whole breast radiation therapy (delivers treatment to the entire breast and the low axilla)
- Multiple regimens
  - 42.56 Gy in 16 fractions (most common in US)
- Accelerated partial breast irradiation (APBI)

5

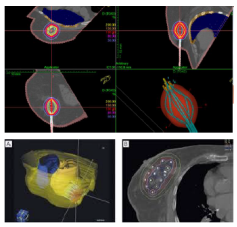
## Rationale for Accelerated Partial Breast Irradiation

- Current treatment regimen of whole breast irradiation likely over treats many patient's breast cancers
- Surgical series show rare cancer cells >1 cm away from the tumor bed
- Majority of in-breast recurrences occur at the lumpectomy site compared to elsewhere in the breast, despite administration of whole breast irradiation or omission of whole breast irradiation
- Convenience

6

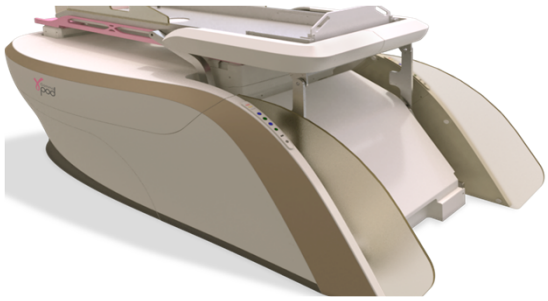
## Current techniques of APBI

- Multi-catheter interstitial brachytherapy
- Balloon based brachytherapy
- Intraoperative radiation therapy
- Stereotactic body radiation therapy
  - Cyberknife
  - GammaPod



7

## GammaPod



8

## GammaPod

- 2006 – Patented by Dr. William Regine and Cedric Yu at University of Maryland (UMM)
- 2007- $3.5M NIH grant for the development of the GammaPod system
- 2015- First clinical trial launch at UMM
- December 2017 - FDA clearance

9

## GammaPod Treatment Delivery System

- The GammaPod irradiation unit sits beneath the treatment couch, so patients are positioned above the sources for treatment delivery.
- Multisource Cobalt-60 stereotactic radiotherapy system
  - Continuously rotates during treatment, creating thousands of beam angles.
  - Individual beams converge to create an intense focal spot, delivering the full dose to the target while sparing surrounding healthy tissue
- 25mm and 15mm collimators dynamically change during treatment
- Table motion during treatment enables dynamic dose painting as the target moves across the focal spot in three dimensions.

10

## Breast Immobilization and Localization Stereotactic Breast Cup System

- Stereotactic radiotherapy requires a high degree of precision to ensure accurate dose delivery.
- The GammaPod uses a vacuum-assisted, dual-cup system that adheres noninvasively to the breast.
- The GammaPod breast cup system provides breast tissue immobilization, serves as a stereotactic frame, and enables reproducible setup between imaging and treatment.

11

## Stereotactic Breast Cup System

*How it works*

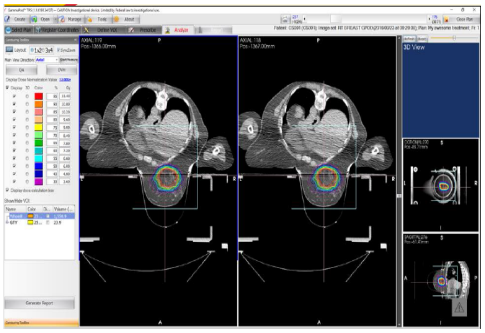
- Patients are custom fit with the appropriately sized inner cup
- Inner cup is joined via a silicone flange to a rigid outer cup containing an embedded stereotactic fiducial wire
- Adhesive on the flange helps the device adhere to the patient
- Attached suction pump evacuates the air from between the cups to provide a stable immobilization

12

## Breast Cups

13

## GammaPod Treatment Plan



14

## GammaPod Patient Loader

- Clinical trials have found that prone positioning for breast cancer radiotherapy offers benefit.
- The affected breast naturally falls away from the chest wall and treatments can be designed to limit dose to the heart and lungs.
- The GammaPod uses prone patient loaders in the imaging and treatment rooms.

15

## GammaPod Loader

16

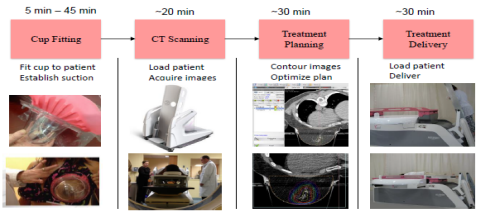
## GammaPod Treatment Loader

*How it works*

- Patients step onto the loader wearing the breast cup, which fits through an aperture in the couch and is securely docked in place
- Smooth rotation of the couch moves patients from the standing to prone position
- For the *Imager Loader*, the CT table receives the couch and patient, which is then positioned for scanning
- For the *Treatment Loader*, the GammaPod receives the couch and patient, which is then positioned for treatment.

17

## *GammaPod™ workflow for each treatment fraction*




**Total treatment time: ~1 hr**

18

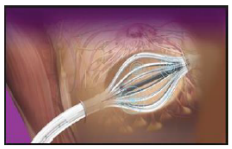
## *How is the GammaPod Currently Used?*

- APBI
  - 5 fraction regimen delivered every other day
  - 14 patients complete
  - Minimal fatigue
  - Minimal skin reaction – no 'burns' or 'peeling'
- Boost
  - Shorten treatment time by 3-4 days by delivering the 'boost' portion of treatment in one fraction
  - 14 patients completed

19

## *Opportunities for the GammaPod*

- Replace invasive methods of partial breast irradiation
- Comparisons show improved dosimetry with the GammaPod
- Logistically easier: 5 fractions, once a day as opposed to 10 fractions twice daily
- Improved ability to optimize dose off of the skin and chest wall.



20

## Subcommittee Recommendations: Training and Experience

GammaPod is very different from the Elekta Gamma Knife (GK) devices. The Subcommittee determined that experience with Elekta GK does not assure competence with GammaPod.

1) The draft guidance currently does not require attestation for AU's, AMP's, and RSOs who are qualified to use GK

- Subcommittee recommends attestation for non-board certified AU's, AMP's, and RSO even if they are already authorized users of other stereotactic radiosurgery units.
- Subcommittee recommends the inclusion of a 2-year delay for the written attestation requirement for the RSO's to conform with the proposed 2 year delay for the AU's and AMP's.

21

## Subcommittee Recommendations: Training and Experience

2) The draft guidance currently recommends training on the differences between GK and GammaPod for those who are qualified for GK

- Subcommittee recommends removing the requirement for GK-trained individuals (AUs, AMPs, and RSOs) to be trained on the differences in the device operation, safety procedures, and clinical use of the GammaPod compared to the Elekta GK.
- Subcommittee does not feel training on the differences between Elekta GK and GammaPod provides increased safety with respect to how these devices operate.

22

## Subcommittee Recommendations: Training and Experience

3) The draft guidance currently allows residency program directors to provide written attestation similar to 10 CFR 35.600

- Subcommittee recommends removing the ability of a residency program director to provide a written attestation since it is not likely the programs will include GammaPod experience at this time and it is unlikely GammaPod will be a standard treatment modality included in most residency programs. The attestation should be restricted to the AU for GammaPod.

23

## Subcommittee Recommendations: Training and Experience

4) The draft guidance currently allows a physician, under the supervision of an AU, who has been trained in the operation and emergency response for the unit, to be physically present instead of the AU during continuation of patient treatments.

- Subcommittee recommends explicit specification of who provides training in operation and emergency response for the physical presence requirement.

24

## Subcommittee Recommendations: Associate RSO

The draft guidance currently provides guidance for an Associate RSO

- Subcommittee recommends not including the ARSO in Part 35.1000 licensing guidance documents because their roles are outlined in the new Part 35 rule and addressed in NUREG -1556, Volume 9. The RSO cannot be replaced by an ARSO. The ARSO involvement confounds the RSO responsibility.

25

## Subcommittee Recommendations: Calibration and Spot Checks

- Subcommittee recommends splitting Full Calibration and Periodic Spot checks into two separate sections.
- Subcommittee recommends the clear specification of the geometric accuracy and source exposure indicator light spot checks be performed on a daily basis.
- Subcommittee recommends deleting the phrase " in addition to daily QA" in the monthly spot check statement.

26

## Subcommittee Recommendations: Calibration and Spot Checks

The draft guidance states the frequency for speed of the table motion and collimator and source rotation and location of the radiation isocenter should be done approximately every 6 months while the sealed source and device (SSD) registration sheet states that these tests should be performed annually.

- Subcommittee recommends resolving the discrepancy between the frequency for speed of the table motion and collimator and source rotation and location of the radiation isocenter.

27

## Subcommittee Recommendations: Written Directive and Source Description

- Subcommittee recommends adding frequency of fractions to the written directive.
- In Section 3.3, the Subcommittee recommends replacing the "GammaPod Model A" in the chemical/physical form line with the source models as listed in the SSD registration sheet (e.g., Model "INIF-SF-1.0-03-AE" for the 25-source configuration).

28

## Acknowledgements

The Subcommittee wishes to acknowledge Dr. Elizabeth Nichols and Dr. Stewart Becker of the University of Maryland for providing slide presentation material.

29

## Acronyms

- AMP – Authorized Medical Physicist
- APBI – accelerated partial breast irradiation
- ARSO – Associate Radiation Safety Officer
- AU – Authorized User
- RSO – Radiation Safety Officer

30

**U.S. Nuclear Regulatory Commission (NRC)**

**Advisory Committee on the Medical Use of Isotopes ACMUI)**

**Subcommittee on Xcision® GammaPod™ Licensing Guidance**

**Draft Report**

**Submitted on August 19, 2019**

## Subcommittee Members

Zoubir Ouhib, M.S.
Michael Sheetz, M.S.
Megan Shober, M.S.
Harvey Wolkov, M.D. (Chair)

NRC Staff Resource: Katie Tapp, Ph.D.

## Background

The Subcommittee and its Chair were appointed by ACMUI Chairman, Christopher Palestro, on May 16, 2019. The subcommittee charge was to review and comment on the NRC staff's draft Xcision® GammaPod™ Licensing Guidance.

## Introduction

The Xcision® GammaPod™ (hereafter the GammaPod™) is a non-invasive gamma stereotactic radiosurgery unit which delivers a therapeutic dose to a partial volume of the breast as a component of Breast Conserving Therapy for breast cancer. Although GammaPod™ is a gamma stereotactic radiosurgery device, its design and operation significantly differ from traditional gamma stereotactic radiosurgery units, and a joint NRC/Agreement State working group determined that the GammaPod™ will be licensed under 10 CFR 35.1000. GammaPod™ has several new engineering features that are not addressed in 10 CFR 35, Subpart H, including its vacuum-assisted breast cup immobilization and stereotactic localization system, rotating source and collimator carriers, and table motion during treatment.

The Subcommittee endorses the draft licensing guidance, subject to the specific changes outlined below.

## Training and Experience

Because the GammaPod is very different from the Elekta Gamma Knife (GK) devices, the Subcommittee determined that experience with the GK does not assure competence with GammaPod.

1. The draft guidance does not require attestation for AU's, AMP's, and RSO's who are qualified to use GK.

The Subcommittee recommends attestation for non-board certified AU's, AMP's and RSO's, even if they are already authorized users of other gamma stereotactic radiosurgery units.

The Subcommittee recommends the inclusion of a 2 year delay for the written attestation requirement for the RSO's to conform with the proposed 2 year delay for AUs and AMPs.

2. The draft guidance recommends training on the differences between GK and GammaPod for those who are qualified for GK.

The Subcommittee recommends removing the requirement for GK-trained individuals (AUs, AMPs, RSOs) to be trained on the differences in the device operation, safety procedures, and clinical use of the GammaPod compared to the Elekta GK.

The Subcommittee does not feel training on the differences between Elekta GK and GammaPod provides increased safety with respect to how these devices operate.

3. The draft guidance allows residency program directors to provide written attestation similar to 10 CFR 35.600

The Subcommittee recommends removing the ability of a residency program director to provide a written attestation since it is not likely the programs will include GammaPod experience at this time and it is unlikely GammaPod will be a standard treatment modality included in most residency programs. The attestation should be restricted to the AU for GammaPod.

4. The draft guidance allows a physician, under the supervision of an AU, who has been trained in the operation and emergency response for the unit, to be physically present instead of the AU during continuation of patient treatments.

The Subcommittee recommends explicit specification of who provides training in operation and emergency response for the physical presence requirement.

**Associate RSO**

Draft guidance provides guidance for an Associate RSO.

The subcommittee recommends not including the ARSO in Part 35.1000 licensing guidance documents because their roles are outlined in the new Part 35 rule and

addressed in NUREG-1556, Volume 9. The RSO cannot be replaced by an ARSO. The ARSO involvement confounds the RSO responsibility.

## Calibration and Spot Checks

The Subcommittee recommends splitting Full calibration and Periodic Spot checks into two separate sections.

The Subcommittee recommends clearly specifying that the geometric accuracy and source exposure indicator light spot checks be performed on a daily basis.

The Subcommittee recommends deleting the phrase "in addition to daily QA" in the monthly spot check statement.

The draft guidance states the frequency for speed of the table motion and collimator and source rotation and location of the radiation isocenter should be done approximately every 6 months while the sealed source and device (SSD) registration sheet states that these tests should be performed annually.

The Subcommittee recommends resolving the discrepancy between the frequency for speed of the table motion and collimator and source rotation and location of the radiation isocenter.

## Written Directive and Source Description

The subcommittee recommends adding frequency of fractions to the written directive.

In Section 3.3, the Subcommittee recommends replacing "GammaPod Model A" in the chemical/physical form line with the source models as listed in the SSD registration sheet (e.g., Model INIS-SF-1.0-03-AE for the 25-source configuration).

**Respectfully submitted, August 19, 2019**
**Subcommittee on Xcision® GammaPod™ Licensing Guidance**
**Advisory Committee on the Medical Uses of Isotopes (ACMUI),**
**Nuclear Regulatory Commission (NRC)**

ACMUI Training

[CLOSED MEETING PORTION]

NO HANDOUT

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

# ACMUI Institutional Memory Subcommittee

Dr. A. Robert Schleipman
Advisory Committee on the Medical Uses of Isotopes
September 11, 2019

## ACMUI Institutional Memory Subcommittee

- ***Charge:*** *"to improve the ACMUI's institutional memory and provide possible recommendations for methods of tracking and/or retrieving ACMUI documents."*
- ***Subcommittee membership:***
  Dr. Ronald Ennis, Dr. Michael O'Hara, Dr. A. Robert Schleipman (chair), Ms. Megan Shober, and Ms. Laura Weil
- The NRC staff resource is Ms. Kellee Jamerson.

2

## Introduction

- April 2019 meeting - ACMUI members discussed difficulties in readily recalling or accessing past ACMUI deliberations and discussions.
- Office of Nuclear Materials Safety and Safeguards (NMSS) staff members often "fill in the gaps"
- Rotating NMSS staff assignments and ACMUI turnover may contribute to a loss of continuity and institutional memory.

3

## Background

- As a Federal Advisory Committee, ACMUI's open sessions are transcribed and documented for member and public review. While these transcripts clearly reflect the comments and proposals of the open session; they do not capture all decision-making comments and rationales discussed by ACMUI members and NRC staff.
- For example, the ACMUI RECOMMENDATIONS AND ACTION ITEMS list discussed at the April 2019 meeting presents pending and open action items extending back to 2007, without clear documentation of why certain items remain open. Present NMSS staff members were able to clarify many of these standing or unresolved items.

4

## ACMUI – Online Tools

- NMSS staff have recently enhanced the ACMUI webpage https://www.nrc.gov/about-nrc/regulatory/advisory/acmui.html
- Additionally, the NRC website provides links to regulatory processes, sections on rulemaking and procedures, authorizing and governing legislation, the NMSS section, and an NRC Ethics section with links to the Office of Government Ethics. https://www.nrc.gov

5

## ACMUI Webpage

***ACMUI webpage* (reviewed on July 18, 2019)**:

- ACMUI Charter (as of March 10, 2016)
- ACMUI Bylaws (as of July 10, 2019)
- ACMUI History page with historical membership list (1988- 2017; acknowledged as incomprehensive)

6

## ACMUI Webpage

***ACMUI webpage* (reviewed on July 18, 2019)**:

- ACMUI current membership page
- ACMUI Meetings and Related Documents – includes agendas, meeting handouts, slides, summary reports, open meeting transcripts
- ACMUI Recommendations and Actions (items, dates, status, in .pdf format), 2007-2018

7

## ACMUI Webpage

***ACMUI webpage***:

- ACMUI Subcommittee reports page* (2002-2019) *Reviewed/Updated May 28, 2019*
- ACMUI Subcommittees file* (name, charge, members including NRC staff resource, status; spanning Jan. 30, 2014 - March 25, 2019)

*provides a record of varied subcommittees' make-up, dates of formation and deactivation, and their actual output, whether as draft or final reports

8

## ACMUI Webpage

***Webpage updates*** (per NMSS staff consult)

- Webpage updates commenced before 2010
- Updates are posted by the ACMUI Coordinator
- The posting frequency varies, and is generally subject to availability of resources and documents received from the ACMUI
- Final Subcommittee Reports are posted after a report is finalized and received

9

## ACMUI Webpage

***Webpage functionality***

- Depends on the quality of the search engine and database
- Varied options available to add this type of functionality to existing, static websites.
- Current NRC website main page does provide a Search box (designated as *"Google Custom Search"*) directly linked to, and available from, the ACMUI webpage.

10

## ACMUI Webpage

***Website functionality***

- Search box entry does not easily discriminate all acronyms, e.g., "AO" yields "*annotated outline*" and "*abnormal occurrence*" documents
- Retrieved documents are Commission-wide, *i.e.*, not specific to ACMUI or medical related

- NB: Adding *" , ACMUI"* to search categories, *e.g.*, *"90Y, ACMUI"*, appears to delimit the search to ACMUI documents related to 90-Yttrium.

11

## ACMUI Webpage Functionality

*Website search:* ***90Y***

Request for Additional Information For Review of the Model No. JRF ...
https://www.nrc.gov/docs/ML0932/ML093210566.pdf
Nov 5, 2009 **...** This refers to your request dated July 20, 2009, for a recommendation concerning the revalidation of the Model No. JRF-**90Y**-950K package, ...

JRF-**90Y**-950K Response to 2nd RAI Schedule Change.
www.nrc.gov/docs/ML1020/ML102040501.pdf
May 19, 2010 **...** Subject: FW: 2nd Request for Information on JRF-**90Y**-950K. Attachments: TNI letter JRF CEX-10-00016265.pdf.

*Website search:* ***90Y/ACMUI***

ACMUI Subcommittee Reports - NRC
https://www.nrc.gov/reading-rm/doc-collections/**acmui**/reports/
The following table presents a chronological list of **ACMUI** subcommittee reports. ... Amendments to the **ACMUI** Bylaws Report · Yttrium-**90** (**Y**-90) Microsphere ...

**ACMUI**
https://www.nrc.gov/docs/ML1610/ML16109A042.pdf
Jan 15, 2016 **...** DOUGLAS BOLLOCK, **ACMUI** Designated Federal. Officer ..... (Quadramet), 131I - tositumomab (Bexxar) and **90Y**-ibritumomab tiuxetan.

12

## ACMUI New Member Orientation

- NRC website "New Employees" portal does not apply to ACMUI members; though does include "*Major Ethics Rules Affecting NRC Special Government Employees"*
- NUREG/BR-0309, "*Serving on the Advisory Committee on the Medical Uses of Isotopes (ACMUI): A Member's Guide*
  - provides an overview of ACMUI functions, purpose, and interactions with the Commission.
  - last updated in 2004

13

## ACMUI New Member Orientation

- Subcommittee members suggested a less formal, ACMUI-specific onboarding guide.
  - Provide a glossary for perennial topics and perhaps a "current events" backgrounder.
- If deemed helpful, subcommittee members are willing to draft this with staff assistance.

14

## ***Practice-based Changes*** *(Suggested)*

- Each new Subcommittee tasked to review available materials regarding previous ACMUI deliberations relating to the subcommittee's charge
- Summarized in a few paragraphs with deliberate references to past, related ACMUI/NRC documents
- Members could more easily trace relevant historical documents
- Provides continuity and a reference point for new deliberations

15

## ***Other Data Sources*** *(Tangential Item)*

- Are ACMUI/NRC documents from sources other than the GPO, ADAMS, or the Commission's website, e.g., SharePoint, enterprise Dropbox, LAN (local area network), or other shared file applications used by NRC?

- ACMUI access to LAN requires additional training and NRC security monitoring of ACMUI members' computers; thus not previously endorsed by ACMUI members.

16

## *Summary*

- ACMUI institutional memory is, in part, diminished by the necessary turnover of ACMUI members, and the transfers and occasional reassignments of NMSS staff.
- A review of current resources identifies ACMUI-focused searches of the NRC website as a robust and accessible source of ACMUI documents.
- The ACMUI webpage provides archived reports in systematic fashion.

17

## *Subcommittee Recommendations*

1. Enhance onboarding process for new ACMUI members with an updated new member guide (NUREG/BR-0309), and possibly an ACMUI-generated background/perennial topics sheet.
2. With NMSS staff assistance, augment ACMUI Subcommittee reports with a brief summary of previous ACMUI deliberations on the topic, specifically referencing related ACMUI/NRC documents.

18

## Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- ADAMS – Agencywide Documents Access and Management System
- GPO – Government Publishing Office
- LAN – local area network
- NMSS – Office of Nuclear Material Safety and Safeguards
- NRC – Nuclear Regulatory Commission

19

# U.S. Nuclear Regulatory Commission
# Advisory Committee on the Medical Use of Isotopes (ACMUI)

## ACMUI Institutional Memory Subcommittee

Draft Report
Submitted on: August 8, 2019

***Subcommittee membership:***
Dr. Ronald Ennis, Dr. Michael O'Hara, Dr. A. Robert Schleipman (chair), Ms. Megan Shober, and Ms. Laura Weil

The NRC staff resource is Ms. Kellee Jamerson.

***Introduction:***
At the April 3-4, 2019 meeting, ACMUI members discussed difficulties in readily recalling or accessing past ACMUI deliberations and discussions. While the Office of Nuclear Materials Safety and Safeguards (NMSS) staff members often "fill in the gaps"; their rotating assignments, and ACMUI turnover, may further contribute to a loss of continuity and institutional memory. This subcommittee was formed at that meeting.

The verbatim charge is: "*to improve the ACMUI's institutional memory and provide possible recommendations for methods of tracking and/or retrieving ACMUI documents*".

***Background:***
Open public meetings are held by the Nuclear Regulatory Commission (NRC) as required by the Government in the Sunshine Act.[1] Furthermore, as a Federal Advisory Committee, the ACMUI holds a number of open sessions which are transcribed and documented for member and public review.[2] While these transcripts clearly reflect the comments and proposals of the open session; they do not capture all decision-making comments and rationales discussed by ACMUI members and NRC staff. For example, the ACMUI RECOMMENDATIONS AND ACTION ITEMS list discussed at the April 2019 meeting presents pending and open action items extending back to 2007, without clear documentation of why certain items remain open. Present NMSS staff members were able to clarify many of these standing or unresolved items.

Of note, NMSS staff have recently enhanced the ACMUI website, which provides a considerable amount of pertinent information.[3] In addition to the ACMUI site, the agency (NRC) website

---

[1] Pub. L. No. 94-409, 90 Stat. 1241 (1976) (5 U.S.C. §552b)
[2] 41 C.F.R. § 102–3.
[3] U.S. Nuclear Regulatory Commission. *Advisory Committee on the Medical Uses of Isotopes.* April 2, 2019. Retrieved from: https://www.nrc.gov/about-nrc/regulatory/advisory/acmui.html

provides links to regulatory processes, sections on rulemaking and procedures, authorizing and governing legislation, the NMSS section, and an NRC Ethics section with links to the Office of Government Ethics. [4]

***Current resources***

ACMUI/NRC website

The afore mentioned ACMUI website, last reviewed on 18 July 2019 provides the following:

- ACMUI Charter (as of 10 March 2016)
- ACMUI Bylaws (as of 10 July 2019)
- A brief ACMUI History page with historical membership list (1988-2017; acknowledged as incomprehensive)
- ACMUI current membership page
- ACMUI Meetings and Related Documents page includes agendas, meeting handouts, slides, summary reports, open meeting transcripts
- ACMUI Recommendations and Actions (items, dates, status, in pdf format), 2007-2018
- ACMUI Subcommittee reports page (2002-2019) Last Reviewed/Updated 28 May 2019
- ACMUI Subcommittees file (name, charge, members – including NRC staff resource, status) spanning 30 Jan 2014 – 25 March 2019

These last two items provide considerable documentation, and a record of varied subcommittees' make-up, dates of formation and deactivation, and their actual output, whether as draft or final reports. This provides much of the institutional memory in an accessible format for members, as well as, in keeping with Open Government ideals, the public.

***Website update frequency***

Ms. Jamerson and Ms. Holiday noted that the website updates commenced before 2010 and are posted by the ACMUI Coordinator. Posting frequency varies and is generally subject to availability of resources and documents received from the ACMUI. For example, documents from the April 2019 meeting were posted around 2 weeks prior to the meeting – as that was the timeframe in which they were submitted by presenters. Final Subcommittee Reports are posted after a report is received.

***Website functionality***

Subcommittee members pointed out that a search function would greatly facilitate navigating to the desired documents. As an example, entering "AU" could link to reports featuring Authorized User content. Of course, this would depend on the quality of the search engine and database. There are varied options available to add this type of functionality to existing, static websites.

The current NRC website does provide a Search box (designated as *"Google Custom Search*") directly linked to, and available from, the ACMUI website page. However, the search box entry does not easily discriminate all acronyms. For example, an entry of "AO" yields "annotated

[4] U.S. Nuclear Regulatory Commission. Retrieved from: https://www.nrc.gov

outline" documents, as well as "abnormal occurrence" documents for reactor issues in addition to medical use reports. Furthermore, the search box function generates a search of all retrievable NRC documents, so that "AO" also yields Commission reports to Congress. Empiric testing with more granular entries, *e.g*., "Abnormal Occurrence, ACMUI" yielded specific and relevant documents (draft and final ACMUI reports, corresponding SECY papers, etc.). Adding *"_ , ACMUI"* to search categories, e.g., *"90Y, ACMUI"*, appears to delimit the search to ACMUI documents related to 90-Yttrium.

***New Member Orientation***

The NRC website includes a New Employees portal that does not quite apply to ACMUI members; though it does include "*Major Ethics Rules Affecting NRC Special Government Employees*" document, which does apply. The ACMUI website Membership page provides a link to NUREG/BR-0309, "*Serving on the Advisory Committee on the Medical Uses of Isotopes (ACMUI): A Member's Guide*.[5] The guide provides an overview of ACMUI functions, purpose, and interactions with the Commission. It was last updated in 2004.

Subcommittee members suggested a less formal, ACMUI-specific onboarding guide. This might contain a glossary for perennial topics and perhaps a "current events" backgrounder. If deemed helpful, subcommittee members are willing to draft this with staff assistance.

**Alternative Options**

*Practice-based changes*

Subcommittee members suggested and endorsed a practice-based addition to current ACMUI subcommittee reporting. Essentially, each new subcommittee would be tasked to review available materials regarding previous ACMUI deliberations relating to the subcommittee's charge. This could be succinctly summarized in a few paragraphs with deliberate references to past ACMUI/NRC documents so that members could more easily trace relevant historical documents.

*Miscellany*

A tangentially related issue is the availability of ACMUI/NRC documents from sources other than the GPO, ADAMS, or the Commission's website. NMSS staff were asked if a SharePoint, enterprise Dropbox, LAN (local area network,) or other shared files application were used by NRC; and perhaps available to ACMUI members for tracking subcommittee reports as they evolve. The response was that ACMUI members do not have access to the LAN (local area network). The rationale for this is that having access to the LAN would subject the ACMUI to much more annual training requirements, as well as the NRC's ability to monitor members' computers. This has been the biggest point of contention and basis for why the ACMUI has

---

[5] U.S. Nuclear Regulatory Commission, Office of Nuclear Material Safety and Safeguards *NUREG/BR-0309. Serving on the Advisory Committee on the Medical Uses of Isotopes (ACMUI ): A Member's Guide* March 2004. Washington, DC.

been content to not push for this access and its related security requirements. Ms. Holiday noted that in the future there may be additional options (and related training) for ACMUI members to copy files to a shared digital space, enhancing FACA recordkeeping.

**Summary**

ACMUI institutional memory is, in part, diminished by the necessary turnover of ACMUI members, and the transfers and occasional reassignments of NMSS staff. A review of current resources identifies ACMUI-focused searches of the NRC website as a robust and accessible source of ACMUI documents. The ACMUI webpage also provides archived reports in systematic fashion.

**Recommendations**

The Subcommittee identified two recommendations that would potentially enhance ACMUI institutional memory:

1. The Subcommittee recommends enhancing the onboarding process for new ACMUI members with an updated new member guide (NUREG/BR-0309), and possibly an ACMUI generated background/perennial topics sheet.
2. The Subcommittee recommends enhancing ACMUI Subcommittee reports by augmenting each report with a brief summary of previous ACMUI deliberations on the topic, and specifically referencing related ACMUI/NRC documents so that members can more easily trace relevant historical discussions. This will provide continuity and a reference point for new deliberations, preserving some aspects of institutional memory.

Respectfully submitted,
ACMUI Institutional Memory Subcommittee
A. Robert Schleipman, Chair
August 8, 2019

# Open Forum

NO HANDOUT

# ACMUI External Communications

NO HANDOUT

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

# NRC Regulatory Tools

Ian Irvin, Attorney
Office of the General Counsel
September 11, 2019

## Objectives

- Know which regulatory tools the NRC may use to accomplish its regulatory objectives
- Identify when a change to the NRC's regulations is required or may be the best means to accomplish an objective
- Understand the primary steps of the rulemaking process
- Understand the other regulatory tools available to accomplish the NRC's objectives



## Two Fundamental Types of Regulatory Tools

Rules

A rule is a statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy.

Orders

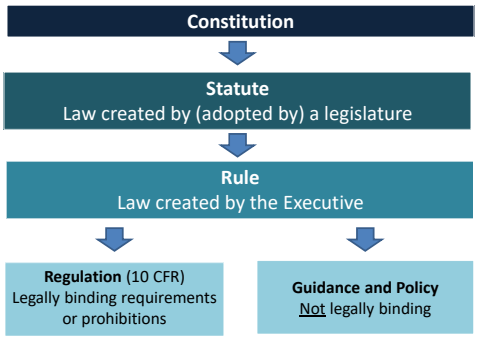
An order is a final disposition of an agency matter other than rulemaking. Licensing is a kind of order – defined as giving permission or approval.



## Regulatory Tools

- Regulation
- Guidance
- Statement of policy
- License
- Civil penalty
- No action
  - Rely on other Federal agency action
  - Rely on State or local governmental action
  - Rely on private entities (corporations, NGOs, individuals)

## Forms of U.S. Law: Statutes and Rules




U.S.NRC

5

## Why Choose a Regulation (Rulemaking)?

- A statute may require rulemaking
- Rulemaking is required to change 10 CFR
- Avoid the possibility of a significant adverse consequence or adverse public reaction that may be inherent in a reactionary approach to regulatory oversight
- Case-by-case review and regulatory action (i.e., licensing, penalties) is too time and resource intensive; fails to provide regulatory certainty and transparency in decisionmaking

U.S.NRC

6

## Rulemaking Pathways

- Advanced Notice of Proposed Rulemaking followed by the Proposed Rule and Final Rule
- Proposed Rule followed by the Final Rule
- Direct Final Rule
- Interim Final Rule

U.S.NRC

7

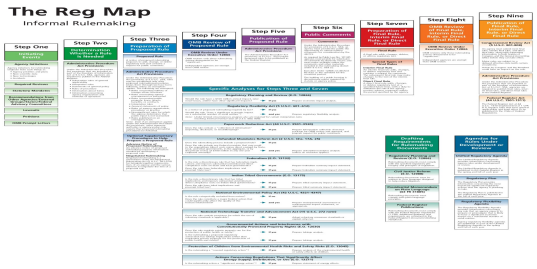
## Some Statutes That Govern Federal Agency Rulemaking Procedure

- Administrative Procedure Act of 1946
- Federal Register Act
- Paperwork Reduction Act
- Congressional Review Act
- National Environmental Policy Act
- Government in the Sunshine Act

U.S.NRC

8

## OMB Rulemaking Map




http://www.reginfo.gov/public/reginfo/Regmap/index.jsp



## Some NRC Regulations and Guidance on Rulemaking Procedure

- 10 C.F.R. Part 2, Subpart H—Rulemaking
- Management Directive 6.3—The Rulemaking Process
- Early Commission involvement in rulemakings: requirement to submit a rulemaking plan for Commission approval to initiate rulemakings



## Overview of NRC's Typical Part 35 Rulemaking Process

- Early public and ACMUI input
- Rulemaking plan for Commission review and approval
- Staff drafts regulatory basis, proposed rule, and guidance
- ACMUI, Agreement States, OAS review draft proposed rule
- Commission reviews and votes on proposed rule
- NRC publishes proposed rule for comment
- Staff summarizes and responds to public comments
- ACMUI, Agreement States, OAS review draft final rule
- Commission reviews and votes on final rule
- NRC publishes final rule



## Overview of NRC's Typical Part 35 Rulemaking Process (continued)

- **Total Time:** Varies greatly depending on several factors
  - the scope and complexity of the rule
  - priority of the rulemaking
  - degree of controversy
  - public input
  - ACMUI recommendations
  - Commission direction, policy
  - agency resources
  - Congressional action, inquiries
- Could be about one year for minor or routine rules or a few to several years for complex and controversial rules

## Some Non-Legally Binding Rules

- Guidance—usually issued by the NRC staff
  - NUREG Series
  - Regulatory Guides
  - Generic Communications
    - Regulatory Issue Summaries
    - Information Notices
- Policy Statements—issued by the Commission
- **Total time:** Varies depending on the scope and complexity of the guidance or policy statement; could be a few months to a few years

U.S.NRC

13

## Some Other Tools

- Specific exemptions from NRC regulations
  - Standard at 35.19: "authorized by law and will not endanger life or property or the common defense and security and are otherwise in the public interest"
  - Used to address unique circumstances
- 35.1000 licensing
  - Used when modality is "not specifically addressed" in Part 35
  - Codifies the process by which the NRC may license new and emerging technologies without having to first develop generic regulatory requirements
  - **Total time**: usually approximately one year

U.S.NRC

14

## ACMUI Recommendations

- Review of draft documents to include: SECY paper, rule text, NUREG-1556 licensing guidance, 35.1000 licensing guidance, and regulatory guides.

→Based on evaluation of recommendations, could result in changes to said document.

**Example**: Part 35 Rulemaking Subcommittee, Reg Guide 8.39 Subcommittee, Yttrium-90 Microspheres Brachytherapy Licensing Guidance Subcommittee.

U.S.NRC

15

## ACMUI Recommendations

- In other cases, the ACMUI are given a topic to provide recommendations on, without having a draft staff-generated document to review.

→ Based on evaluation of recommendations, staff must determine the more appropriate regulatory tool and path forward.

**Example**: Extravasations Subcommittee, Nursing Mothers' Guidelines Subcommittee

U.S.NRC

16

## ACMUI Recommendations

**Scenario 1**: Abnormal Occurrence Criteria Subcommittee

The staff reviewed the report and agreed with some of the ACMUI's recommendations. This was considered and discussed in the staff's SECY paper. If the proposed changes had been accepted (by the Commission), this would have resulted in changes to the Agency's Abnormal Occurrence Criteria Policy.

U.S.NRC

17

## ACMUI Recommendations

**Scenario 2**: Nursing Mothers' Guidelines Report

Amongst many things, this report included breast feeding interruption values. While the ACMUI did not specifically suggest that such values be included into Regulatory Guide 8.39, the NRC staff suggested this approach. As such, the draft Reg Guide 8.39, Revision 1, included many of the values from the report, and was issued for public comment on July 26, 2019.

U.S.NRC

18

## Summary

- NRC uses two fundamental regulatory tools: rules and orders
- Rules may be legally binding (regulations) or non-legally binding (guidance, policy)
- Which tool is appropriate to accomplish a regulatory objective depends on many factors, including timing, scope of the regulatory objective, and available resources
- ACMUI should continue to make all recommendations that it deems appropriate
- NRC will continue to act on ACMUI recommendations, as appropriate, using the regulatory tool it deems best suited to accomplish regulatory objectives

U.S.NRC

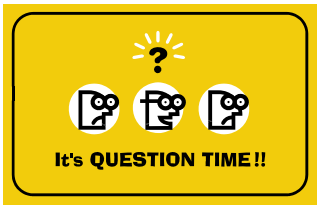
19

## Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- CFR – Code of Federal Regulations
- NGO – non-governmental organization
- NRC – U.S. Nuclear Regulatory Commission
- OAS – Organization of Agreement States

U.S.NRC

20




U.S.NRC
Protecting People and the Environment

21

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

# Status of Emerging Technologies Licensed under 10 CFR 35.1000

Michael Sheetz
Advisory Committee on the Medical Use of Isotopes
September 11, 2019

## Outline

- Types of Medical Use Licensed Under 35.1000
- Status of Existing Technologies
- Emerging Technologies that may be licensed under 35.1000
- Other Emerging Technologies
- Q&As

2

## Regulation of Emerging Medical Technologies

- 10 CFR Part 35, Subpart K – Other Medical Uses of Byproduct Material or Radiation from Byproduct Material (10 CFR 35.1000)
  - New medical use of byproduct material which is not addressed in other parts of 10 CFR 35
  - Licensing guidance to address specific radiation safety aspects, and set training and experience requirements

3

## Beta-Cath Intravascular Brachytherapy (IVB) System

- Device uses beta radiation from Sr-90 sources for treatment of coronary in-stent restenosis
- Widely used in early 2000s, but was replaced with drug eluting stents
- Guidance issued 2006
- Still used at approximately 35 centers for recurrent in-stent restenosis

4

## I-125 Iotrex Liquid Brachytherapy Source in GliaSite Radiation Therapy System

- Device used for treatment of recurrent brain tumors
- Guidance issued 2006
- Inflatable balloon catheter placed in resection cavity with infusion of aqueous solution of iodine-125
- Studies showed only a modest survival benefit
- Device no longer available

5

## Low Activity Radioactive Seeds used for Localization of Non-Palpable Lesions (RSL)

- I-125 seed implanted near tumor to guide surgical excision
- Initial licensing guidance developed in 2006
- Revised licensing guidance issued in 2016 more aligned to how procedure is performed
- Procedure widely performed by many licensees

6

## NeoVista Epi-Rad90 (Sr-90) Ophthalmic System

- Hand-held device using Sr-90 source for intraocular treatment of AMD
- Guidance issued 2009
- Results of clinical trials insufficient to justify extending routine use
- Manufacturer no longer in business

7

## TheraSphere and SIR-Spheres Yttrium-90 Microspheres

- Y-90 labeled microspheres for selective intra-arterial radiotherapy for treatment of liver cancer
- Initial guidance issued 2002, revised 9 times, draft revision under review
- Over 15,000 patient treatments in US (2018)
- Currently approximately 300-400 licensees

8

## Leksell Gamma Knife Perfexion and Icon

- Gamma stereotactic radiosurgery device for treatment of brain lesions using 192 Co-60 sources (30 Ci each)
- Initial guidance issued 2007 to cover Perfexion
  - Revised 2016 to include Icon
  - Revised 2019 to change physical presence requirements
- Currently, total of 107 Icon and Perfexion units, and 13 C/4C units in US
- Over 18,000 patient treatments in US (2018)

9

## ViewRay System for Radiation Therapy

- Magnetic resonance image-guided radiation therapy using three 15,000 Ci Co-60 sources
- Guidance issued 2013
- Linac based device developed 2017
- Only 2 sites currently using Co-60 system in US

10

## Recent Generator Devices

- Germanium-68/Gallium-68 Pharmaceutical Grade Generators
  - Ga-68 used for new imaging tracers
  - Initial guidance issued 2017, revised 2019
- NorthStar RadioGenix Molybdenum-99/ Technetium-99m Generator System
  - Device designed to isolate Tc-99m from non-uranium based Mo-99
  - Initial guidance issued 2018

11

## Xcision GammaPod

- Gamma stereotactic radiotherapy system for breast cancer treatment
- Contains 25 Co-60 sources (180 Ci each)
- Source body and collimator system rotate during treatment to deliver focused beam
- Currently at 2 sites in US

12

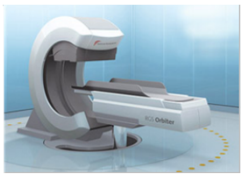
## RGS Vertex 360 Radiosurgery Device

- Rotating gamma stereotactic system for treatment of brain tumors
- Contains 30 Co-60 sources (200 Ci each) located in a 60 degree hemispherical sector
- Beam shaping by synchronous rotation of the source and collimator hemispheres
- Only one device in US

13

## Rotating Gamma System RGS Orbiter

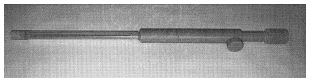
- Rotating gamma stereotactic radiotherapy system for treatment of both head and body
- Contains 42 Co-60 sources (230 Ci each) in 50 degree circular line
- Source body and collimator rotate within a gantry
- Pending FDA approval



14

## Alpha DaRT (Diffuse Alpha Radiation Therapy)

- Ra-224 brachytherapy seeds decay and diffuse Rn-220 for interstitial treatment of cancer
- Radon (and radon daughters) deliver high radiation throughout the tumor
- Source SSD by MA, Source/Applicator IDE by FDA
- Licensing issues:
  - Manual brachytherapy (35.400)?
  - Sealed sources (no leak test required)?
  - WD and ME criteria?



15

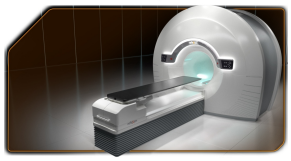
## New Targeted Radiopharmaceutical Therapy (Theranostics)

- Currently Approved
  - Lu-177 Dotatate (Lutathera) for NET
  - I-131 Iobenguane (Azedra) for adrenal gland tumors
- In Clinical Trials
  - Y-90 Dotatoc for NET
  - Lu-177 PSMA-617 for prostate cancer
  - I-131 Iomab-B for AML

16

## RefleXion BgRT

- Device combines PET/CT with linac for biologically guided radiation therapy
- Uses real-time tumor tracking from PET to focus external beam therapy
- Pending FDA approval
- Who will be AU for PET imaging component?



17

## Conclusion

- 10 CFR 35.1000 (Other Medical Uses) provides a process for licensing emergent technologies
- Part 1000 licensing guidance can be revised to meet new uses or applications
- New targeted radiopharmaceutical therapies may present unique radiation safety challenges

18

## Acronyms

- AMD - Age-related Macular Degeneration
- AML - Acute Myeloid Leukemia
- AU – Authorized User
- CT – computed tomography
- FDA – Food and Drug Administration
- IDE – Investigational Device Exemption
- IVB- Intravascular Brachytherapy
- MA – Massachusetts
- ME – Medical Event

19

## Acronyms (cont'd.)

- PET – positron emission tomography
- PSMA – Prostate Specific Membrane Antigen
- NET – Neuroendocrine Tumor
- RSL – Radioactive Seed Localization
- SSD – Sealed Source Device Registry
- US – United States
- WD – Written Directive

20

# U.S. Pharmacopeia (USP) General Chapter <825>

**Richard Green, Nuclear Pharmacist**
**Advisory Committee on the Medical Uses of Isotopes**
**September 11, 2019**

## Disclosure

- Volunteer Member of the USP Expert Panel that wrote Chapter <825> on Radiopharmaceutical Compounding
- This presentation is not endorsed by the USP, nor does it represent the views or opinions of USP

2

## United States Pharmacopeia

- The U.S. Pharmacopeial Convention (USP) is an independent, nonprofit organization that safeguards the public's health by developing quality standards for medicines, dietary supplements and food ingredients.
- The 1906 Pure Food and Drug Act, deemed the United States Pharmacopeia and the National Formulary official compendia under federal law
- These standards are enforceable when recognized and incorporated into laws and regulations

3

## Enforcement of USP Standards

- FDA could enforce, but seldom visits pharmacies, hospitals, or clinics without cause
- Boards of Pharmacy do enforce, and some have promulgated regulations in parallel
- CMS & Deemed Accreditation Bodies are inspecting for compliance during accreditation visits
  - American Osteopathic Association/Healthcare Facilities Accreditation Program (HFAP) HFAP
  - Center for Improvement in Healthcare Quality (CIHQ) CIHQ
  - DNV GL - Healthcare (DNV GL) DNV·GL
  - The Joint Commission (TJC) The Joint Commission

4

## USP <825> was made public June 1, 2019

- Free download available at: https://www.usp.org/chemical-medicines/general-chapter-825
- Date it becomes enforceable:
  - December 1, 2019
- Will your licensees be ready?
- Will your licensees need amendments to prepare for compliance?

5

## 1. Introduction

*[describes intent and applicability]*

- "…intended to provide uniform minimum standards for the preparation, compounding, dispensing, and repackaging of sterile and nonsterile radiopharmaceuticals for humans and animals that occur as part of state-licensed activities (e.g., the practice of pharmacy and the practice of medicine.)"
- "... apply to … radionuclides that emit a single photon, a positron, or a therapeutic particle."
- "… apply to sterile intravascular radioactive devices (e.g., radioactive microspheres for intravascular brachytherapy.)"

6

## 1. Introduction (cont'd.)

*[does not apply to:]*

- "Administration of radiopharmaceuticals to patients"
- "Preparation of non-radioactive drugs, including those used as pharmacologic adjuncts for certain nuclear medicine procedures. These drugs must be prepared following standards described in
  - Pharmaceutical Compounding – Nonsterile Preparations <795>
  - Pharmaceutical Compounding – Sterile Preparations <797>"

7

## 1. Introduction (cont'd.)

*[applies to all practice settings that perform these activities, including:]*

- "state-licensed nuclear pharmacies
- federal nuclear pharmacy facilities, and
- other healthcare facilities, including, but not limited to, nuclear medicine departments in hospitals and clinics, nuclear cardiology clinics (fixed site or mobile), and other specialty clinics."

8

## 1. Introduction (cont'd.)

*[applies to all individuals who perform these activities:]*

- "authorized nuclear pharmacists (ANPs) and authorized user (AU) physicians"
- "individuals working under their supervision … includes, but is not limited to
  - student pharmacists
  - nuclear pharmacy technicians
  - nuclear medicine technologists and students
  - physician residents and trainees"

9

## 2. Sterile Radiopharmaceutical Handling Environments

<825> describes 3 environments where sterile radiopharmaceuticals (RPs) are handled:

Each has their own required attributes and requirements

- Hot Lab
  - Ambient air suitable for Immediate Use
- Segregated Radiopharmaceutical Processing Area (SRPA)
  - PEC located in designated space
- Clean Room Suite
  - PEC located in ISO Classified air
  - Ante room, pressure gradients, ACPH, etc.

10

## Table 7. Preparation Conditions for Sterile Radiopharmaceuticals

| Manipulation | PEC | SEC | BUD (h) |
|---|---|---|---|
| Immediate Use | - | - | 1 |
| Radionuclide generator storage, elution (e.g., non-direct infusion system; $^{99m}$Tc or $^{68}$Ga) | - | SRPA w/ ISO Class 8 total airborne particle count | 12 |
| Dispensing, repackaging, preparation, and preparation w/ minor deviation | ISO Class 5 | SRPA | 12 |
| Dispensing, repackaging, preparation, and preparation w/ minor deviation | ISO Class 5 | ISO Class 8 or better buffer area w/ ISO Class 8 or better ante-room | 24 |

11

## 3. Immediate Use of Sterile RPs

- *Appropriate for a "hot lab" in a hospital or clinic, which does not have an ISO 5 PEC (hood) and does not have $^{99m}$Tc or $^{68}$Ga generators*
- "Appropriate for preparation (including minor deviations) and/or dispensing limited to use for a single patient.
- Preparation (including preparations with minor deviations) components must be sterile, conventionally manufactured drug products (e.g., NDA/ANDA).

12

## 3. Immediate Use of Sterile RPs (cont'd)

- Dispensing of drug products produced under an approved IND or RDRC protocol is allowed.
- Manipulations for any unit doses (e.g., decreasing the dosage, needle changes) or dispensing for one patient (e.g., withdrawing a dose) is allowed."
- "Must be administered within 1 hour of the first container puncture or exposure of any critical site involved (e.g., syringe tip, needle hub or needle) to ambient air, whichever is first.

13

## 3. Immediate Use of Sterile RPs (cont'd)

- All components involved (e.g., $^{99m}$Tc sodium pertechnetate syringe or vial, final prepared radiopharmaceutical kit vial, diluent vial) must be discarded within hour of being punctured or after use for a single patient administration, whichever is first.
- Dose pooling (combining doses from two or more syringes to meet one patient's need) may be performed as immediate use. Any residual activity that remains must be immediately discarded and not utilized for any other patient.
- Follow hand hygiene and garbing in Section 4.4 "*Hand Hygiene and Garbing for Immediate Use Preparations.*"

14

## Additional Sections

- Preparation of Radiolabeled Blood Components (10.3)
- Red Blood Cell radiolabeling (10.4)
- Compounding Nonsterile radiopharmaceuticals (11.1)
- Direct Infusion Systems (12.3)

15

## RAM Licensees should perform internal assessments of activities performed

- Based on the scope of activities performed by the licensee, different portions of <825> are either applicable or not applicable
- Any activity beyond Immediate Use requires an ISO Class 5 PEC and a dedicated space/room.
- A licensee that merely receives patient ready Unit Doses (UD) has only a few of USP <825>'s standards applicable to them

16

## Status of RAM Licensee Compliance

- USP <797> became effective in 2004. USP <825> builds upon the "legacy" of <797>.
- A Licensee's level of preparedness for <825> is largely related to their compliance with <797> in effect now
- Most centralized Nuclear Pharmacies are compliant
- Many hospitals and clinic licensees will need to perform internal assessments, modify activities performed or seek RAM license amendments to remodel facilities

17

## Heads Up for NRC, Agreement States, and ACMUI

- Chapter <825> became official June 1, 2019
- Chapter <825> will become enforceable Dec. 1, 2019
- RAM licensees will likely be evaluating their practices, infrastructure, equipment, training etc. for compliance with the standards in <825>
- In some cases this may necessitate a RAM license amendment to modify facilities, equipment, practices, etc.

18

## Acronyms

| | |
|---|---|
| ACMUI | Advisory Committee on the Medical Uses of Isotopes |
| ANDA | Abbreviated New Drug Application |
| ANP | Authorized Nuclear Pharmacist |
| AU | Authorized User |
| BCNP | Board Certified Nuclear Pharmacist |
| BUD | Beyond Use Date |
| CHM4 | Chemical Medicines Monographs 4 Expert Committee |
| CIHQ | Center for Improvement in Healthcare Quality |
| CMS | Centers for Medicare & Medicaid Services |
| CSP | Compounded Sterile Preparation |
| DNV | GL – Healthcare |
| FDA | Food and Drug Administration |
| HFPA | American Osteopathic Association/Healthcare Facilities Accreditation Program |

19

## Acronyms (Cont'd.)

| | |
|---|---|
| NDA | New Drug Application |
| PEC | Primary Engineering Control |
| RAM | Radioactive Material |
| SNMMI | Society of Nuclear Medicine and Molecular Imaging |
| SRPA | Segregated Radiopharmaceutical Processing Area |
| TJC | The Joint Commission |
| UD | Unit Dose |
| USP | United States Pharmacopeia |
| <797> | USP General Chapter, Pharmaceutical Compounding – Sterile Preparations |
| <825> | Draft USP General Chapter, Radiopharmaceuticals – Preparation, Compounding, Dispensing and Repackaging |

20

U.S.NRC
United States Nuclear Regulatory Commission
*Protecting People and the Environment*

# Advisory Committee on the Medical Uses of Isotopes: Membership Plan

Lisa Dimmick, Team Leader
Medical Radiation Safety Team
September 11, 2019

## ACMUI Membership

- 13 Committee members appointed as Special Government Employees (SGE)
  - Terms are set at 4-years, with a limit of two terms
- Membership Balance Plan
  - Includes health care professionals of diverse specialties who represent diagnostic and therapeutic applications of medicine, medical administration, and patient care advocacy

2

## ACMUI Membership

- Nuclear medicine physician
- Nuclear cardiologist
- Diagnostic radiologist
- Nuclear pharmacist
- 2 Radiation oncologists
- 2 Medical physicists
- Radiation safety officer
- Healthcare administrator
- Patients' rights advocate
- FDA representative
- Agreement states representative

## ACMUI Membership

- Membership composition change
  - The Commission approved the expansion of the ACMUI by one position to include a Diagnostic Radiologist in December 2009
- Should the ACMUI reconsider its membership to include an Interventional Radiologist?
- ACMUI Charter renews every two years
  - Current charter expires March 1, 2020

4

## Interventional Radiologist

- Emerging medical technologies that require skills of an interventional radiologist
- Medical events concerning the administration of Y-90 microspheres
  - 71 medical events from January 1, 2016 through December 31, 2018

5

## Acronyms

- ACMUI - Advisory Committee on Medical Uses of Isotopes
- FDA - Food and Drug Administration
- SGE – Special Government Employee
- Y-90 - yttrium 90

6

# March 2020

| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|
| 1<br>X | 2 | 3 | 4 | 5 | 6 | 7<br>X |
| 8<br>X | 9 | 10<br>X | 11<br>X | 12<br>X | 13 | 14<br>X |
| 15<br>X | 16 | 17 | 18 | 19 | 20 | 21<br>X |
| 22<br>X | 23 | 24 | 25 | 26 | 27 | 28<br>X |
| 29<br>X | 30 | 31 | 1 | 2 | 3 | 4 |
| 5 | 6 | Notes<br>NRC's RIC is March 10-12. (no hotel availability or Commission Meeting possible) | | | | |

# April 2020

| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|
| 29 | 30 | 31 | 1 | 2 | 3 | 4<br>X |
| 5<br>X | 6 | 7 | 8 | 9<br>PESACH | 10<br>PESACH | 11<br>X |
| 12<br>X | 13 | 14 | 15<br>PESACH | 16<br>PESACH | 17 | 18<br>X |
| 19<br>X | 20 | 21 | 22 | 23 | 24 | 25<br>X |
| 26<br>X | 27 | 28 | 29 | 30 | 1 | 2 |
| 3 | 4 | Notes<br>Pesach is April 9-16. April 9-10 and April 15-16 are *yom tov* (work is forbidden) | | | | |