SCHEDULING NOTE

Title: **MEETING WITH THE ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES (Public Meeting)**

Purpose: Provide an opportunity to hear views from the Advisory Committee on the Medical Uses of Isotopes (ACMUI) on medical-related topics of regulatory interest.

Scheduled: **March 8, 2018**
10:00 am

Duration: Approx. 2 hours

Location: Commissioners' Conference Room, 1st fl OWFN

Participants: **Presentation**

ACMUI Panel **50 mins.***

Philip Alderson, M.D., ACMUI Chair
Topic:
- Overview of ACMUI Activities

Christopher Palestro, M.D., ACMUI Nuclear Medicine Physician
Topic:
- ACMUI's Comments on the Training and Experience Requirements for All Modalities (35.300 Uses)

Pat Zanzonico, Ph.D., ACMUI Vice Chair
Topic:
- ACMUI's Comments on the Staff's Recommendations for Revisions to the Patient Release Program

Vasken Dilsizian, M.D., ACMUI Nuclear Cardiologist
Topic:
- ACMUI's Comments on Medical Event Reporting and Impact on Medical Licensee Patient Safety Culture

Laura Weil, ACMUI Patients' Rights Advocate
Topic:
- Patients' Rights Advocate's Perspective on:
  - The Training and Experience Requirements (35.300 Uses)
  - The Staff's Recommendations for Revisions to the Patient Release Program
  - The Medical Event Reporting and Impact on Medical Licensee Patient Safety Culture

Commissioners' Q & A	**20 mins.**
Discussion – Wrap-up	**5 mins.**

*For presentation only and does not include time for Commission Q & A's

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Protecting People and the Environment

Overview of ACMUI Activities

Philip O. Alderson, M.D., ACMUI Chairman

ACMUI Commission Meeting

March 8, 2018

Agenda

- Overview of ACMUI Activities
  - ACMUI Purpose
  - Membership
  - ACMUI Topics
  - Present and Future

ACMUI Purpose

- The ACMUI exists to advise the NRC staff, and thus you, the Commission, on policy on medical uses of radionuclides.
- Also, to provide technical assistance and serve as consultants.

Membership Positions

- Health Care Administrator
- Nuclear Medicine Physician
- 2 Radiation Oncologists
- Nuclear Cardiologist
- Diagnostic Radiologist
- 2 Medical Physicists*
- Nuclear Pharmacist*
- Radiation Safety Officer
- Patients' Right Advocate
- Agreement State Representative*
- U.S. FDA Representative

* Pending security clearance

ACMUI Topics Addressed in Last Year

- T & E requirements for 35.100 uses (unsealed byproduct material for uptake, dilution, and excretion studies for which a written directive is not required)
- ME reporting for all modalities excluding permanent implant brachytherapy

ACMUI Topics (Continued)

- Clarification of patient intervention
- ME reporting and its impact on patient safety culture
- Guidelines for nursing mothers administered diagnostic and therapeutic radiopharmaceuticals

ACMUI Topics (Continued)

- Potential changes to the NRC's Patient Release Program
- Physical presence requirements for the Leksell Gamma Knife Icon
- Progress in improving ACMUI internal and external communications.

Current ACMUI Topics

- Continuing discussions:
  - T&E for AUs of all modalities (current focus on 35.300 uses)
  - Review of MEs
  - Impacts of ME reporting on patient safety culture

Current ACMUI Topics (Continued)

- Potential revisions to Regulatory Guide 8.39, "Release of patients administered radioactive materials"
- Ways to enhance communications between the NRC staff, the ACMUI, and the medical community.

Present and Future

The ACMUI currently has a number of issues under discussion. As new issues arise, including emerging technologies, we will address and provide advice on aspects relevant to safe handling of radioactive sources.

Acronyms

- **ACMUI** – The Advisory Committee on Medical Uses of Isotopes
- **AUs** – Authorized Users
- **FDA** – U.S. Food and Drug Administration
- **ME** – Medical Event
- **NRC** – U.S. Nuclear Regulatory Commission
- **T&E** – Training and Experience

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Comments on Training and Experience Requirements for All Modalities

Christopher J. Palestro, M.D.

ACMUI Nuclear Medicine Physician

ACMUI Commission Meeting

March 8, 2018

ACMUI Subcommittee on T & E

Established in 2016

Charge

- Periodically review T&E requirements currently in effect for all modalities
- Make recommendations for changes as needed

ACMUI Subcommittee on T & E

Review T&E requirements currently in effect for uses of

- Unsealed byproduct materials (10 CFR 35.100, 35.200, 35.300, & 35.1000)
- Sealed byproduct materials (10 CFR 35.400, 35.500, 35.600, & 35.1000)

Review Template

Comprehensive review template developed to ensure

- Standardized review process
- Meaningful comparisons of reviews over time
- Decisions about changes in T&E requirements based on data

Subcommittee Review Plan

Begin with 10 CFR 35.100, followed by 35.200, 35.300, etc.

However, because of ongoing patient access concerns subcommittee directed to prioritize review of T & E requirements for use of unsealed byproduct material for which a written directive is required (10CFR 35.390)

Significant Developments

January 26, 2018: FDA approved ^{177}Lu dotatate for treatment of somatostatin receptor-positive GEP-NET's, including foregut, midgut and hindgut

- Broad indication
- 2nd most common GI tumor

Potentially high demand for ^{177}Lu-dotatate

Significant Developments

Waning number of nuclear medicine physicians in the US.

- Fewer than 50 first time candidates sat for 2016 ABNM CE (80-100 candidates in previous years)
- ACGME database
  - 2007-2008: 61 Nuclear Medicine Residency Programs with 157 residents
  - 2017-2018: 41 Nuclear Medicine Residency Programs with 75 residents

Significant Developments

Number of Nuclear Radiologists appears to be trending downward.

ABR Nuclear Radiology CAQ examination candidates

2008: 3	2013: 13
2009: 2	2014: 11
2010: 5	2015: 10
2011: 7	2016: 2
2012: 7	2017: 5

Emerging Concerns

Previous discussions/presentations focused on sufficient versus insufficient number of AU's at the present time for administration of an infrequently used therapeutic radiopharmaceutical (Zevalin®).

FDA approval of new CFR Part 35.390 drug, ^{177}Lu-dotatate, with potential for high volume suggests reevaluation is in order.

Emerging Concerns

In considering development of alternate pathway

– Future needs should be addressed

– No data to suggest surplus of AUs

– Could a decrease in number of AUs & an increase in procedures affect patient access as new agents in this class of radiopharmaceuticals become available?

Conclusion

Time to reconsider developing an alternate AU pathway for10 CFR 35.390

Acronyms

- ACGME – Accreditation Council for Graduate Medical Education
- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- ABNM – American Board of Nuclear Medicine
- ABR – American Board of Radiology
- AU – Authorized User
- CE – Certification Examination
- CAQ – Certificate of Added Qualifications
- FDA – Food & Drug Administration
- GEP-NETS – Gastroenteropancreatic neuroendocrine tumors
- ^{177}Lu – lutetium-177
- T&E – Training and Experience

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ACMUI Comments on the Staff's Recommendations for Revisions to the Patient Release Program

Pat Zanzonico, PhD

ACMUI Vice Chairman

March 8, 2018

Subcommittee Members

Susan Langhorst, PhD
Christopher Palestro, MD
Laura Weil
Pat Zanzonico, PhD (Chair)

Subcommittee Charge

To review and provide recommendations on the draft SECY paper, "Staff Recommendations for Revisions to the Patient Release Program."

Background

- The current "dose-based" Patient Release Rule (10 CFR 35.75) replaced the "activity-based" rule (the "30 mCi rule") in 1997.
- The current dose-based Rule allows a licensee to release a patient if the TEDE to any other individual, from exposure to the patient, is not likely to exceed 5 mSv (0.5 rem).

Background *cont.*

- COMGBJ-11-0003 (June 23, 2011): Evaluate whether there are gaps in the available data regarding doses received by members of the public from released patients and, if gaps were found, to provide a recommendation on whether and how such data could be accrued.

Background *cont.*

- SECY-12-0011, "Data Collection Regarding Patient Release" (Jan 25, 2012): Gaps identified related to (1) internal doses to members of the public and (2) internal and external doses to members of the public from patients released to locations other than their primary residences (hotels and nursing homes).

Documents Reviewed

- Draft SECY paper
- Licensee survey: "Assessment of Where Patients Reside Immediately Following Their Release Report"
- Literature review + Model calculations: "Patient Release Following Radioiodine Therapy: A Review of the Technical Literature, Dose Calculations, and Recommendations"

Subcommittee Comments and Recommendations 1

- The literature review was thorough and the model calculations sound.
- The current dose-based approach to assessing patient releasability validated as more protective of public safety than the activity-based approach.
- The current 5-mSv (500-mrem) projected dose limit should remain a per-event limit and is appropriate for all potentially exposed cohorts, including pregnant women and children.

Subcommittee Comments and Recommendations 2

- The assumption in regulatory guidance that the internal dose contribution is negligible has been validated.
- Other assumptions and methods in regulatory guidance are excessively conservative → NCRP Report No 155.
- A patient staying at a hotel following radionuclide therapy is not a widespread practice and is unlikely to result in doses to workers and others > 1 mSv (100 mrem).

Subcommittee Comments and Recommendations 3

- Instructions should be provided to the patient well in advance of a planned therapy, but specification of a regulatory time interval for pre-therapy instructions is not recommended → NCRP Report No 155.
- The NRC should consider updating Appendix U (NUREG-1556, Volume 9) to reference Regulatory Guide 8.39 rather than eliminating 8.39 or maintaining two separate guidance documents.

Concluding Remarks

- The findings and recommendations in the draft SECY paper and support documents validate those in the ACMUI's "Patient Release Report" (Dec 13, 2010) and the current Patient Release program.
- The Patient Release Program should be applicable to all radionuclides, flexible, and not overly conservative, so as to not encumber the development of new medical procedures.

Acronyms

ACMUI:	Advisory Committee on Medical Uses of Isotopes
NCRP:	National Council on radiation Protection and Measurement
TEDE:	Total effective dose equivalent

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Medical Event Reporting and Impact on Medical Licensee Patient Safety Culture

Vasken Dilsizian, MD

ACMUI Nuclear Cardiologist

March 8, 2018

ME Reporting

- ME reporting has not changed significantly for many years.
- The annual number of reports is extremely low considering the estimated 15,000,000 diagnostic and 150,000 therapeutic procedures performed annually.

ME Rates Are Extremely Low

- Does it accurately reflect the true number of cases?
- Given the perception of a ME being punitive, are centers reluctant to report MEs?

Medical Event vs Medical Error

- An ME is not necessarily a violation. However, failure to report a ME is a violation.
- Reporting such MEs by a physician may be perceived negatively in most medical centers as they may be interpreted as medical "errors."

What is the Problem That We are Trying to Solve?

- Identify potential ways to improve effectiveness of ME self-reporting in support of a culture of safety.
- Suggest ways to share ME reports and lessons-learned with the medical community to promote safety.

Reporting MEs

Educational rather than Punitive

- Tracking
- Trending
- Identifying the problem
- Reporting to the medical community
- Corrective action
- Feedback loop
- Constructive improvement
- Learn from the Mistakes

Guiding Principles

- Ideally, NRC should enhance patient safety culture while maintaining its regulatory authority to protect patients during medical use of byproduct materials.

- The focus of ME reporting should be on learning and how to avoid/reduce the likelihood of such an event in the future rather than punitive action.

Notification of ME and NRC Inspection

- For example, MEs rarely cause patient harm, but why is notification required so quickly (no later than the next calendar day after discovery of the ME)? Soon after this notification, an NRC inspection generally takes place looking for violations as cause of the ME.

Safety Culture

I. "Nuclear" Safety Culture

- NRC

II. "Patient" Safety Culture in Healthcare

- CMS-Approved Accrediting Organizations (AO) – e.g. The Joint Commission.

- Patient Safety Organizations (PSO) – e.g. Department of Health and Human Services (HHS).

Identity

NRC	Accrediting or Patient Safety Organizations
Reporting information, including licensee identity, is posted on the NRC website and remains even if the event is later determined by the NRC not to be a medical event.	Reporting is anonymous to those outside the hospital, the patient or patient advocate, and the AO or PSO.

Information Sharing

NRC	Accrediting or Patient Safety Organizations
Besides posting event report on NRC website, NRC posts inspection reports and notices of violations and licensee responses. If similar events occur, NRC may issue regulatory summary document alerting licensees or may initiate rulemaking to prevent future events.	AO or PSO provides database to track events, and provide education or tips on tools, best practices to prevent errors, and general patient safety initiatives to improve safety culture.

Recommendation for NRC Policy and Regulatory Changes for ME Reporting

1) Define "High" vs "Low" Impact Medical Events.
2) High Impact events will require timely notification to NRC, NRC reactive inspection, and timely written report to NRC.
3) Low Impact events will not require notification to NRC.

Recommendations Cont.

4) Low Impact events will undergo self-evaluation and corrective action reporting through NRC or NRC-approved Patient Safety Organizations, Accrediting Organizations or institutional robust patient safety program.

5) Ideally, only high impact events should be made public. Low impact events should be anonymous to licensee information and location.

Reactor Oversight Process (ROP)

The NRC staff suggested that the ACMUI explore the ROP program and the way in which the NRC and reactor community developed and tested this change in regulatory oversight for possible methods of implementing NRC ME oversight improvements using current Part 35 reporting regulations.

Short-Term Recommendation

NRC to develop and test a program (like done with ROP) to allow medical use licensee to evaluate MEs (10 CFR 35.3045, 35.1000 guidance, 35.3047) perhaps with an approved patient safety organization (PSO) or CMS-approved AO

NRC Patient Safety Program

- Licensee to report MEs per current requirements.
- NRC will not post event report on its website, or will make posting anonymous.
- NRC will not conduct reactive inspection except in special "High Impact" medical events.

NRC Patient Safety Program Cont.

- Licensee will develop written report of "Low Impact" ME review for next NRC inspection.
- NRC to develop temporary inspection procedures for report reviews and to evaluate enforcement manual changes for MEs to support test program.
- Number of participants and length of time to be determined
- Evaluate MEs and reports with the ACMUI

NRC Patient Safety Program Cont.

After the test period is completed, NRC should consider opening the program to:

- All NRC medical use licensees who request approval of their patient safety program, and
- Agreement States who request to implement the program with their medical licensees.

Acronyms

- ACMUI – Advisory Committee on Medical Uses of Isotopes
- AO – CMS-approved Accrediting Organization
- CFR – Code of Federal Regulations
- CMS – Centers for Medicare & Medicaid Services
- HHS – Department of Health and Human Services

Acronyms

- ME – medical event (includes 10 CFR 35.3045, 35.1000 guidance, and 35.4047)
- NRC – Nuclear Regulatory Commission
- PSO – Patient Safety Organization
- ROP – Reactor Oversight Process

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Patients' Rights Advocacy Perspectives

Laura Weil

ACMUI Patients' Rights Advocate

March 8, 2018

Training and Experience (T&E)

- Ethical Tensions

  Patient safety ⟺ Unnecessary regulatory control

  Allow professional associations to determine T&E requirements for alternate pathways?

  Potential for financial conflict of interest, bias

Training and Experience (T&E)

Arguments for alternate pathway:

"Turf" issues are potentially driven by financial considerations

Possibility of unnecessarily limited patient access to treatment

Chilling Pharma interest in research and development of new drugs with limited and decreasing number of physicians to administer

Training and Experience (T&E)

Argument for status quo:

Safety, uniformity, comprehensiveness

To consider:

How well has alternate pathway worked for I-131? Are the release instruction issues related to a lack of awareness and respect for the potential dangers of radionuclide therapy?

Patient Release SECY Paper

"The data indicates the spread of contamination from the patient to other persons can be minimized by following instructions"

Patient Release SECY Paper

"...family members of patients receiving the highest activity I-131 administrations often received some of the lowest doses. This points to the importance of behavior patterns and following ALARA (as low as reasonably achievable) guidance and instructions provided by the licensee."

Patient Release SECY Paper

"For cancer patients...all [transportation] exposure scenarios indicate that transportation situations pose a radiation concern for members of the public."

"licensee's assessment of the patient's likely behavior after release."

Patient Release SECY Paper

"The decision to release the patient should be reviewed before starting treatment to determine the conditions under which the patient is expected to be released, and whether the living arrangements, modes of transportation, and staying at a hotel are such that releasing the patient is unlikely to result in doses above 5 mSv (500 mrem)."

Patient Release SECY Paper

"dominant factor in determining both internal and external doses to members of the public from exposure to a patient that has been administered I-131, is the behavior of the patient after release."

ACMUI Subcommittee Recommendations

"Written and oral instructions must be provided to the patient far enough in advance of treatment, without compromising patient care, to ensure that the patient has sufficient time to determine whether or not he/she can actually comply with the instructions and to make whatever arrangements may be necessary for compliance."

Financial Issues

- 1997 Patient Release rule created environment where health insurers can deny coverage for hospitalizations
- Difficult/impossible to get insurance coverage for hospitalization
- Patients or healthcare facilities on the hook for cost when patient requires hospital isolation

What's Needed

In addition to dose or activity limits that must be considered for patient release, clear and formal regulatory language for assessing behavioral or logistical parameters should be required to justify patient release, or to justify insurance covered hospitalization, in order keep radiation exposures to caregivers and the public ALARA.

Public Health

It has been argued that when to provide release instructions, when and how to assess the likelihood of patient adherence, and when to require hospitalization or delayed release is a "clinical" and "practice of medicine" issue."

It needs to be seen as a public health issue, and well within the purview of NRC regulation.

Safety Culture

Two paradigms

1. Identified/required regulatory reporting

2. De-identified/voluntary, self-reporting

Safety Culture

Identified/Regulatory required reporting fosters a culture of hiding errors and hinders proactive use of experiences for education and enhanced patient safety

De-Identified/voluntary reporting fosters a cooperative culture of shared information re near misses and events with the goal of increasing safety on a global scale

Safety Culture

ACMUI Subcommittee suggests limited trial of required but de-identified reporting to PSO in lieu of existing regulatory process.

Acronyms

- ACMUI: Advisory Committee on Medical Uses of Isotopes
- ALARA: as low as reasonably achievable
- I-131: iodine 131
- mSv: milliseivert
- mrem: millirem
- PSO: patient safety organization
- RAI: radioactive iodine
- SECY: Commission Paper
- T&E: training and experience