

## SCHEDULING NOTE

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

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

**Scheduled:** March 17, 2016  
9:30 a.m.

**Duration:** Approx. 1 hour and 45 minutes

**Location:** Commissioners' Conference Room, 1<sup>st</sup> fl OWFN

**Participants:** **Presentation**

**ACMUI Panel** **50 mins.\***

**Philip Alderson, M.D., ACMUI Chair**

Topics:

- Overview of ACMUI Activities

**Pat Zanzonico, Ph.D., ACMUI Vice Chair**

Topic:

- ACMUI's Comments on the NRC's Patient Release Project

**Laura Weil, ACMUI Patients' Rights Advocate**

Topic:

- Patients' Rights Advocate's Comments on the NRC's Patient Release Project

**Christopher Palestro, M.D., ACMUI Nuclear Medicine Physician**

Topic:

- ACMUI's Comments on the Training and Experience Requirements for Authorized Users of Alpha and Beta Emitters

**Steven Mattmuller, ACMUI Nuclear Pharmacist**

Topic:

- Decommissioning Funding Plan Requirements for the Medical Use of Germanium-68/Gallium-68 Generators

**Philip Alderson, M.D., ACMUI Chair**

Topics:

- Enhancing ACMUI Communications

**Commission Q & A**

**40 mins.**

**Discussion – Wrap-up**

**5 mins.**

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



# **Overview of ACMUI Activities**

**Philip O. Alderson, M.D.**  
**ACMUI Chairman**  
**March 17, 2016**

# **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**

## **Some topics addressed by the ACMUI in the last year**

- **Refining some aspects of the 10 CFR Part 35 Rulemaking, including NUREG-1556, Vol. 9,**
- **Revising the NRC's Abnormal Occurrence Criteria as the criteria relate to medical events,**

# **ACMUI Topics (Continued)**

- **Medical events, for all medical applications with particular attention to those involving yttrium-90-labeled microspheres,**
- **The T&E requirements for 10 CFR 35.390 AUs of Alpha and Beta Emitters,**

# **ACMUI Topics (Continued)**

- **Revisions to the NRC's Radioactive Seed Localization licensing guidance,**
- **The decommissioning funding plan requirements for the medical use of Ge-68/Ga-68 generators,**



# **ACMUI Topics (Continued)**

- **Clarification of the term “patient intervention” , and**
- **Review and consideration of three Petitions for Rulemaking related to the LNT Model and Standards for Protections Against Radiation.**

# **Current ACMUI Topics**

- **Continuing discussions involved:**
  - **Patient release**
  - **Review of medical events**
  - **Medical event reporting for all modalities**
  - **T&E for AUs of Alpha and Beta Emitters**

## **Current ACMUI Topics (Continued)**

- Radioactive Seed Localization Licensing Guidance,**
- Addressing the decommissioning funding plan requirements for the medical use of Ge-68/Ga-68 generators,**
- Leksell Gamma Knife Icon Licensing Guidance.**

## **Current ACMUI Topics (Continued)**

- **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 – The Food and Drug Administration**

**LNT – Linear-No-Threshold**

**NRC – The U.S. Nuclear Regulatory Commission**

**T&E – Training and Experience**



# **ACMUI's Comments on the NRC's Patient- Release Project**

**Pat Zanzonico, PhD, DABR  
ACMUI Vice Chairman**

**March 17, 2016**

# **Prologue**

## **Dose- vs Activity-Based Release Criteria**

- **Medical use of radionuclides**
  - **Widely recognized health benefits**
  - **Public doses  $\approx$  Background levels**
  - **Avoid burdensome regulatory control**



# **Prologue**

## **Dose- vs Activity-Based Release Criteria**

- **Dose: A more meaningful and direct metric of radiation risk than activity**
  - **The amount of radioactive material (activity) does not predict dose to other individuals from the patient**

## **Prologue**

# **Dose- vs Activity-Based Release Criteria**

- **ACMUI endorses current  
10 CFR 35.75 dose-based  
release criterion**

# **NRC's Patient Release Project**

**Develop a patient-directed web site and brochure providing information on release of radionuclide ( $\text{Na}^{131}\text{I}$ )-therapy patients and related radiation-safety issues**

# **ACMUI Comments**

- **Wide variability in quantity and quality of radiation-safety precautions and related information conveyed to radionuclide therapy patients**
  - **Some of this variability due to differences among patients and their circumstances**

# **ACMUI Comments**

- **Pressing need for systematic dissemination of clear, consistent, and scientifically based radiation-safety information to such patients**
- **Such information is already available in the peer-reviewed medical literature**

# Example

NCRP REPORT No. 155

MANAGEMENT OF  
RADIONUCLIDE  
THERAPY PATIENTS



2006

## ➤ Freely available companion EXCEL file

- Patient-specific time of release and duration of post-release precautions

## ➤ Populates patient-specific instruction sheet

## ➤ Distributed to 53 centers to date

Disclosure: Co-Author of Report

## **ACMUI Comments cont.**

- **Inadequacy and inconsistency in radiation-safety information conveyed to radionuclide therapy patients is a matter of professional education - eg Professional societies' "Practice Guidelines"**

# **ACMUI Comments cont.**

- **Patient-directed web site and brochure are inappropriate because they interpose a regulator (ie the NRC) between the patient and his/her physician**
  - **Concerned this may exacerbate patient confusion and anxiety by failing to account for differences among patients**



# **Acronyms**

- **ACMUI: Advisory Committee on Medical Uses of Isotopes**
- **CFR: Code of Federal Regulations**
- **NCRP: National Council on Radiation Protection and Measurements**



**Patients' Rights Advocate's  
Comments  
on the NRC's  
Patient- Release Project**

**Laura Weil**

**ACMUI Patients' Rights Advocate**

**March 17, 2016**



# **Comments on Training and Experience Requirements for Authorized Users of Alpha and Beta Emitters**

**Christopher J. Palestro, M.D.  
ACMUI Nuclear Medicine Physician  
March 17, 2016**

# Background

- **RIT of lymphoma with beta emitters approved about 14 years ago.**
- **Two agents**
  - $^{90}\text{Y}$  ibritumomab tiuexetan (Zevalin®)**
  - $^{131}\text{I}$  tositumomab (Bexxar®).**

# **Background**

## **Use of both agents**

**Peaked shortly after introduction**

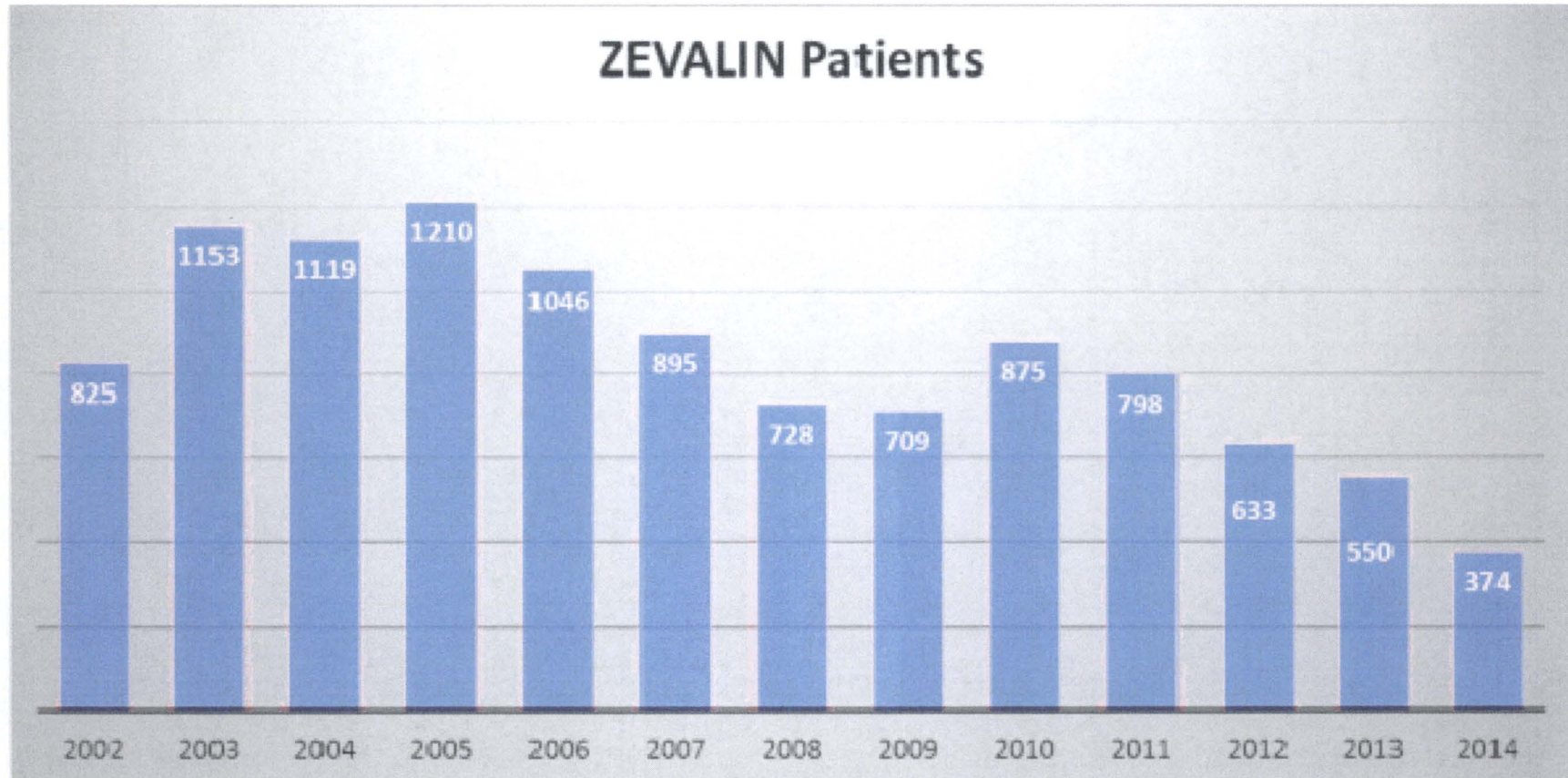
**Steady decline since**

**Bexxar® withdrawn in 2014**

**Lack of use**

**< 75 patients treated in 2014**

# Background



Adapted from Spectrum Pharmaceuticals, ACMUI meeting October 2015

# **Background**

**Why has RIT use declined despite favorable clinical results?**

**-Direct effect of the change in AU T&E requirements that went into effect in 2006?**

**-ACMUI subcommittee formed**

# **ACMUI Subcommittee on T&E**

## **Charge 1**

**Determine if current requirement (700 hours for T&E) for AU of alpha & beta emitters places hardship on patient community & make recommendations for ACMUI action.**



# **ACMUI Subcommittee on T&E**

## **Charge 2**

**Establish recommendation for total number of hours of T&E for AU's of such emitters that appropriately balances safety with reasonable patient access**

# **Factors Possibly Accounting for Decreased RIT Use**

- **Lack of knowledge**
- **Competition**
- **Shortage of AU's**

# Factors Possibly Accounting for Decreased RIT Use

Institution	Time Period	Total number of Therapies
Memorial Sloan Kettering Cancer Ctr. (NY)	2009-2014	190
University of Maryland (Baltimore)	2002-2014	25
North Shore LIJ Health System (NY)	2005-2014	49
Washington University/Barnes-Jewish Hospital (St. Louis)	2004-2014	55

Adapted from Palestro ACMUI meeting Oct 2015

# **Factors Possibly Accounting for Decreased RIT Use**

- **Explanation for decreased RIT use likely multifactorial**
- **Shortage of AU's not the only explanation**

**Regardless, why not reduce T&E requirements?**

# **Reducing AU T&E Requirements for Alpha and Beta Emitters**

- **Excellent safety record for RIT  
80 hours T&E for  $^{131}\text{I}$  therapy**
- **Consequences of  
misadministration of RIT vs  $^{131}\text{I}$**

# **ACMUI Subcommittee on T&E**

## **Charge 1**

**Determine if current requirement (700 hours for T&E) for AU of alpha & beta emitters places hardship on patient community ...**

**No change in T&E requirements**

# **ACMUI Subcommittee on T&E**

## **Charge 2**

**Establish recommendation for total number of hours of T&E ...**

**Time for thorough review of T&E**  
**Nearly 15 years since last review**  
**New radiopharmaceuticals**  
**New educational paradigm**

# **ACMUI Subcommittee on T&E**

## **Subcommittee Recommendation**

**Establish standing subcommittee  
to periodically review T&E  
requirements currently in  
effect making recommendations  
for changes as warranted**

**Subcommittee established Feb 2016**



# **ACMUI's Position**

- **The report and its recommendations were unanimously approved by the full Committee on March 10, 2016.**

# **Acronyms**

**ACMUI: Advisory Committee on  
Medical Uses of Isotopes**

**AU: Authorized user**

**$^{131}\text{I}$ : Iodine-131**

**RIT: Radioimmunotherapy**

**T&E: Training and experience**

**$^{90}\text{Y}$ : Yttrium-90**



# **Decommissioning Funding Plan (DFP) Requirements for the Medical Use of Germanium-68/Gallium-68 Generators**

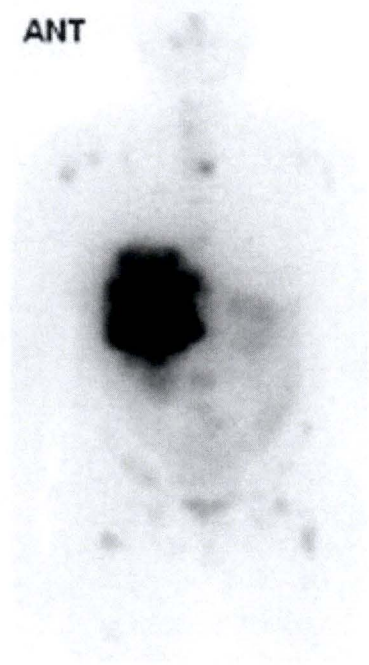
**Steve Mattmuller**  
**ACMUI Nuclear Pharmacist**  
**March 17, 2016**

# **Ga-68 PET**

## **Radiopharmaceuticals**

$^{111}\text{In}$ -DTPA-Octreotide

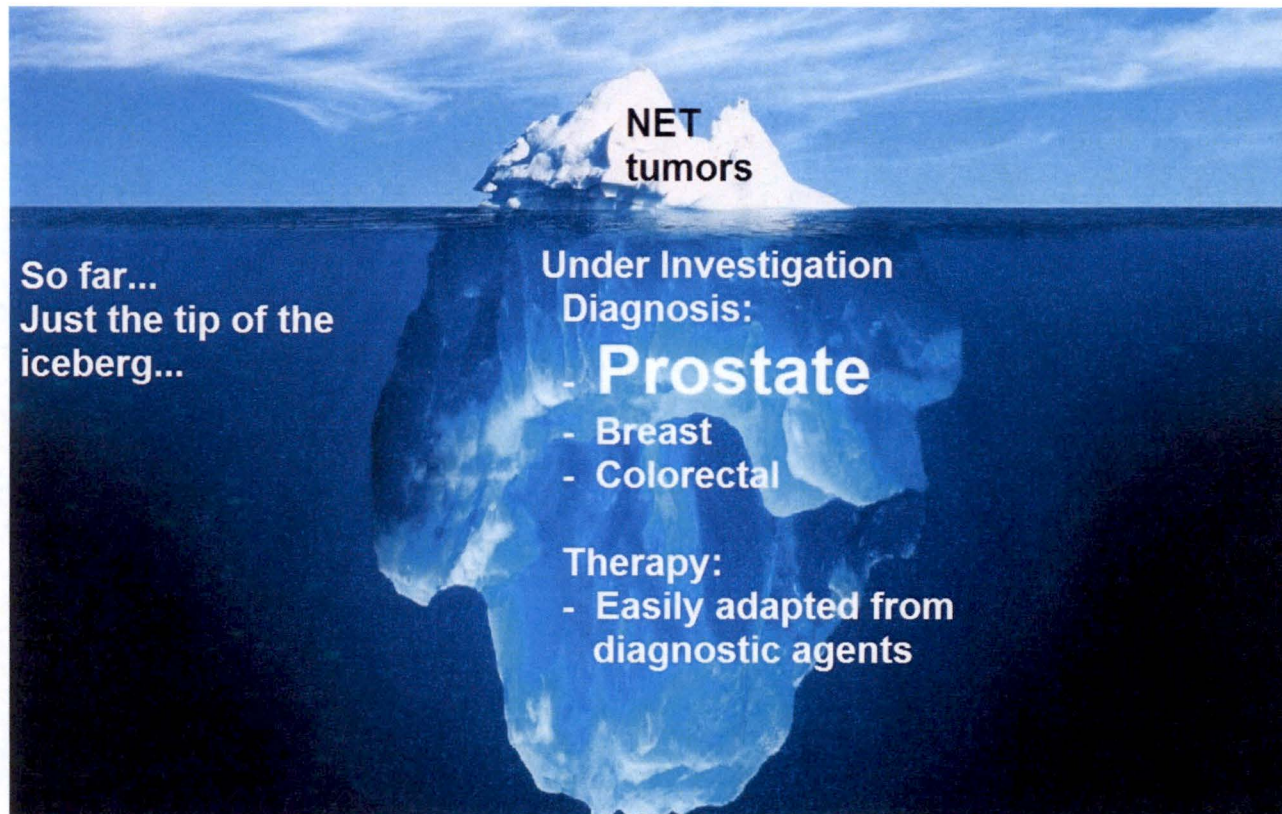
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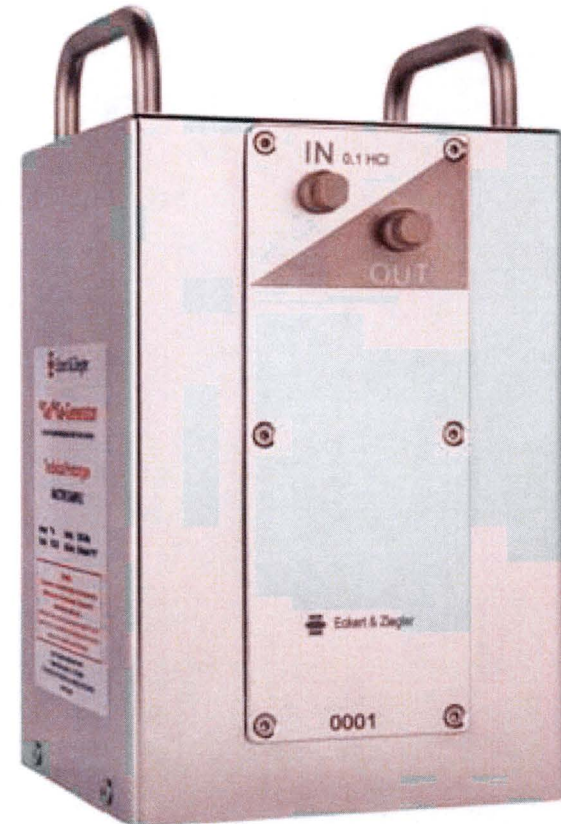
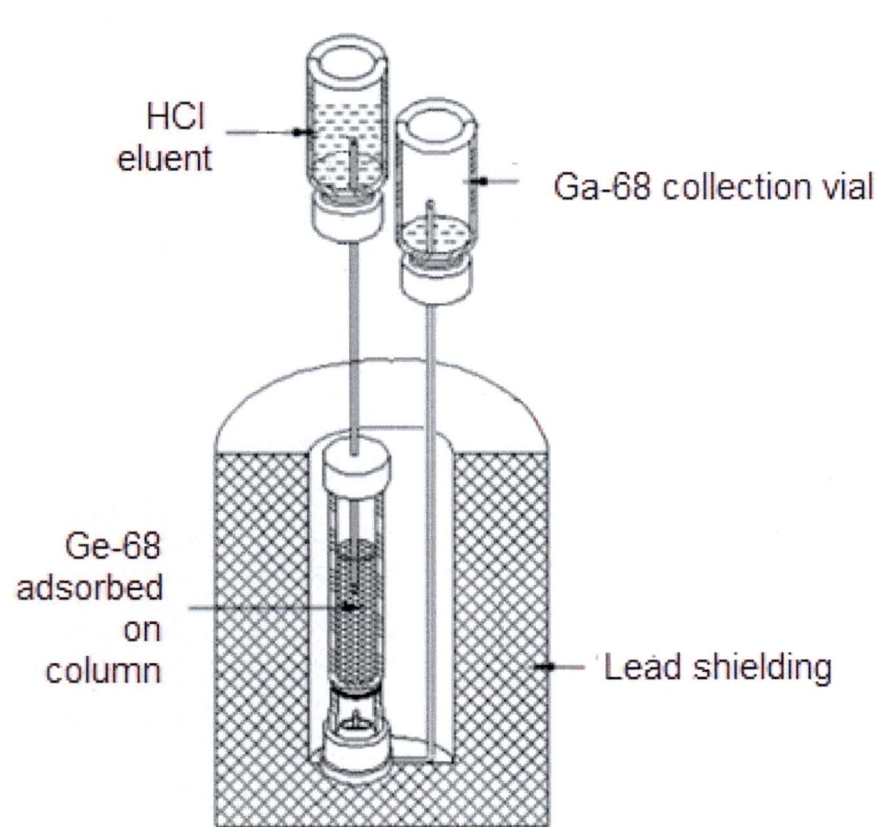
$^{68}\text{Ga}$ -DOTA-TOC



# Ga-68; now and in the near future



# Ga-68 Generator



# **Decommissioning Funding Plan (DFP)**

- **Triggered by the derived default value for unlisted radionuclides in Appendix B of Part 30. Ge-68's trigger level = 10 mCi.**
- **DFP is “extensive and expensive.”**

-John Keklak, MS, CHP, RSO Thomas Jefferson University and Hospitals

# **Decommissioning Funding Plan (DFP)**

- **“Every patient in need would not have equal access to these radiopharmaceuticals, most especially those in smaller and/or more rural markets.”**

-Fred Gattas, PharmD, FAPhA, BCNP, Director of Quality and Safety for Triad Isotopes



# **ACMUI's Proposed Relief**

- **The cost of decommissioning a medical use Ga-68 generator does not warrant the need for a DFP.**
- **The current DFP requirements have already and will continue to limit patient access to Ga-68's use.**

# **ACMUI's Proposed Relief**

**The Committee recommends the following language be added as a footnote to Appendix B Part 30 – Quantities of Licensed Material Requiring Labeling:**

**<sup>3</sup>This does not include Ge-68 in a Ge-68/Ga-68 medical use generators (limit less than  $10 \mu\text{Ci} \times 10^5$ ) that are returned to the manufacturer at end of use.**

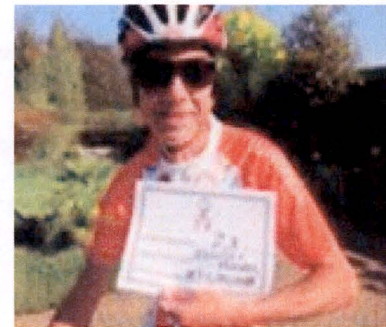
# NRC's Responsibility to Patients



11/08/14  
Diane McElheny



10/30/14  
Ang Fran



10/19/14  
Kristina Kiekens

# **Acronyms**

- **ACMUI – Advisory Committee on the Medical Uses of Isotopes**
- **DFP – Decommissioning Funding Plan**
- **Ga-68 – Gallium-68**
- **Ge-68 – Germanium-68**
- **NET – Neuroendocrine Tumor**



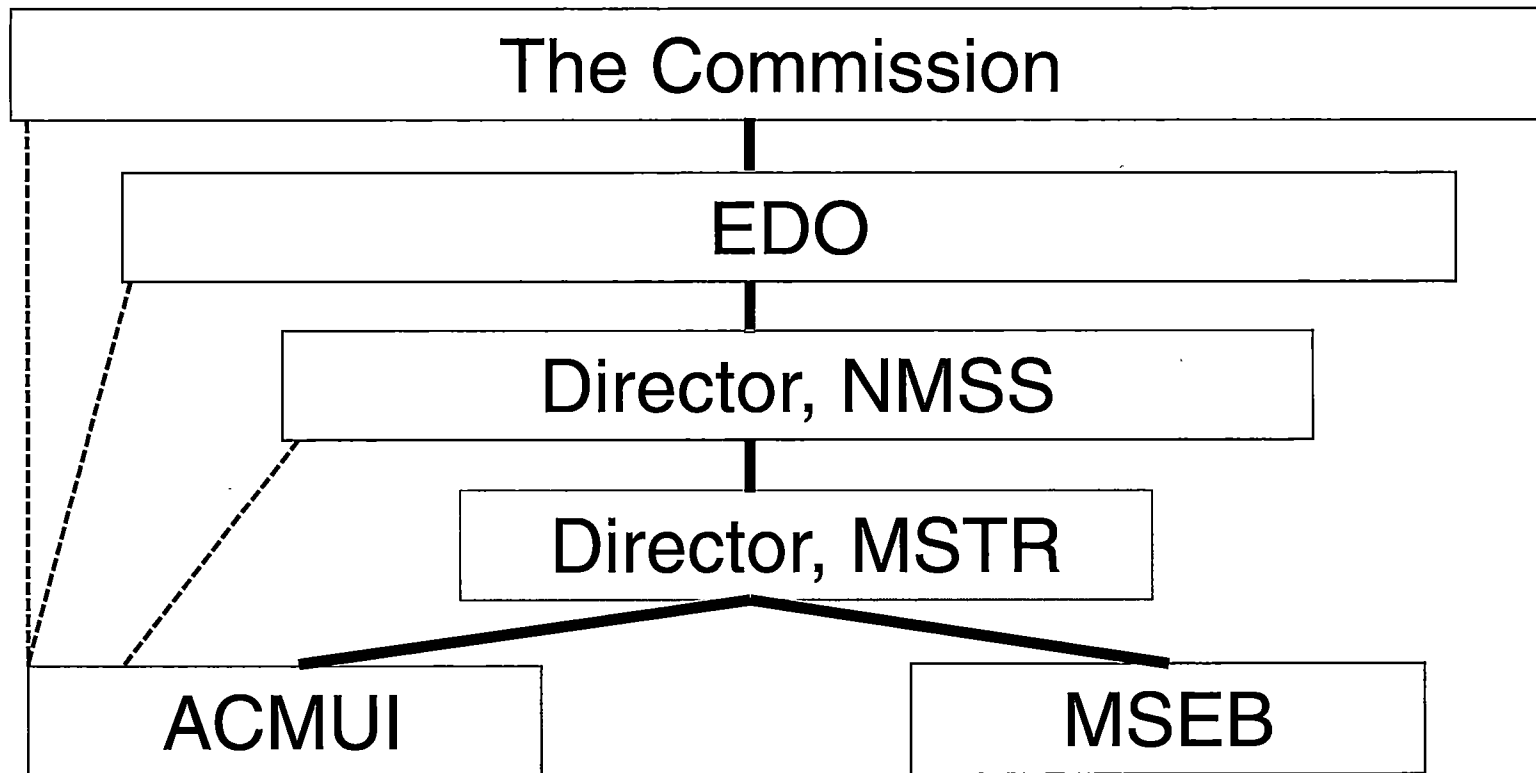
# **Enhancing ACMUI Communications**

**Philip O. Alderson, MD**  
**ACMUI Chairman**  
**March 17, 2016**

# **Reporting Structure**

- **The ACMUI reports to Director, NMSS/MSTR.**
- **NMSS/MSTR/MSEB supports the ACMUI with day-to-day activities.**

# Reporting Structure



# **Communications with NRC**

- **The ACMUI meets at NRC HQ 2x/yr, holds ad hoc teleconferences, and meets with the Commission on an annual basis.**
- **The ACMUI Coordinator is the primary conduit for transmitting and receiving communications.**



# **Communications with NRC**

- **The ACMUI informs NRC staff about emergent medical issues.**
- **NRC seeks input from the ACMUI on medical-related topics, including rulemaking and licensing actions.**

# **Communications with NRC**

- **For various items, through NMSS P&P 2-5, the ACMUI is provided with 60-90 days for review and comment.**

# **Communications with NRC**

- **The ACMUI produces subcommittee reports, which provide recommendations on various topics.**
- **The ACMUI's unfettered opinions are captured in papers to the Commission... then what?**

# **Improving Communications with NRC**

- **Staff should provide additional explanation(s) to the ACMUI on why certain recommendations are not accepted or no action is being taken.**

# **Improving Communications with NRC**

- **Staff should inform the ACMUI on internal processes (i.e. rulemaking, guidance, generic communications) in order to facilitate better-informed recommendations.**

# **Improving Communications with the Medical Community**

- **The ACMUI has members of numerous professional societies/organizations.**
- **Members, with an NRC staff person, should speak at relevant annual societal meetings (i.e. AAPM, ASTRO, SNMMI).**

**Thank you**

# Acronyms

- **AAPM – American Association for Physicists in Medicine**
- **ACMUI – Advisory Committee on the Medical Uses of Isotopes**
- **ASTRO – American Society for Radiation Oncology**
- **EDO – Executive Director for Operations**
- **MSEB – Material Safety and Events Assessment Branch**



# Acronyms

- **MSTR – Division of Material Safety, State, Tribal and Rulemaking Programs**
- **NMSS – Office of Nuclear Material Safety and Safeguards**
- **P&P – Policy and Procedure**
- **SNMMI – Society of Nuclear Medicine and Molecular Imaging**