SCHEDULING NOTE

Title: **DISCUSSION OF MEDICAL USES OF RADIOACTIVE MATERIALS (Public Meeting)**

Purpose: The purpose of the briefing is to provide the Commission with an update on the NRC's program for medical uses of radioactive materials, a status of recent activities related to the licensing and oversight of medical uses of radioactive materials, the views of stakeholders on recent NRC initiatives, and suggestions regarding transformation/innovation opportunities.

Scheduled: **January 28, 2020**
9:00 a.m.

Duration: Approx. 3 hours

Location: Commissioners' Conference Room, 1st fl OWFN

NRC Staff Panel **40 min.***

Steven West, Deputy Executive Director for Materials, Waste, Research, State, Tribal, Compliance, Administration, and Human Capital Programs
- Overview of the NRC's program for medical uses of radioactive materials

Kevin Williams, Deputy Director, Division of Materials Safety, Security, State, and Tribal Programs (MSST), Office of Nuclear Materials Safety and Safeguards (NMSS)
- Status of recent NRC staff activities

Lisa Dimmick, Team Leader of the Medical Radiation Safety Team, MSST, NMSS
- Innovation opportunities and initiatives

Katherine Tapp, PhD, Medical Radiation Safety Team, MSST, NMSS
- Efforts to prepare for the review of emerging medical technologies

Donna Janda, Chief, Medical and Licensing Assistance Branch, Division of Nuclear Materials Safety, Region I
- Regional perspectives on licensing and oversight of medical licensees

Commission Q & A **40 min.**

Break **5 min.**

External Stakeholder Panel **40 min.***

Murray Sheldon, MD, Associate Director for Technology and Innovation, Center for Devices and Radiological Health, U.S. Food and Drug Administration **8 mins.***

- Stakeholder suggestions regarding transformation/innovation opportunities for the NRC to explore – federal perspective

Terry Derstine, Chair, Organization of Agreement States **8 mins.***

- Emerging issues regarding the national program for the regulation of medical uses of radioactive materials

Thomas Eichler, MD, President, American Society for Radiation Oncology **8 mins.***

- Stakeholder suggestions regarding transformation/innovation opportunities – medical community perspective

Vasken Dilsizian, MD, President, Society of Nuclear Medicine and Molecular Imaging **8 mins.***

- Perspectives on recent NRC staff initiatives related to medical uses of radioactive materials

Josh A. Mailman, President, NorCal CarciNET Community **8 mins.***

- Stakeholder suggestions regarding transformation/innovation opportunities for the NRC to explore – patient perspective

Commission Q & A **40 min.**

Discussion – Wrap-Up **5 min.**

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

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Discussion of Medical Uses of Radioactive Materials

Commission Meeting

January 28, 2020

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Overview of the NRC's Program for Medical Use

Steven West
Deputy Executive Director for Materials, Waste, Research, State, Tribal, Compliance, Administration and Human Capital Programs

NRC Panel will Address the Following Topics

- Status of NRC Staff Activities
- Innovation Opportunities and Initiatives
- Efforts to Prepare for the Review of Emerging Medical Technologies
- Regional Perspective on Licensing and Inspecting Medical Uses

Meeting the Medical Uses Policy Statement Objectives

Regulate to provide for radiation safety of workers and the general public.

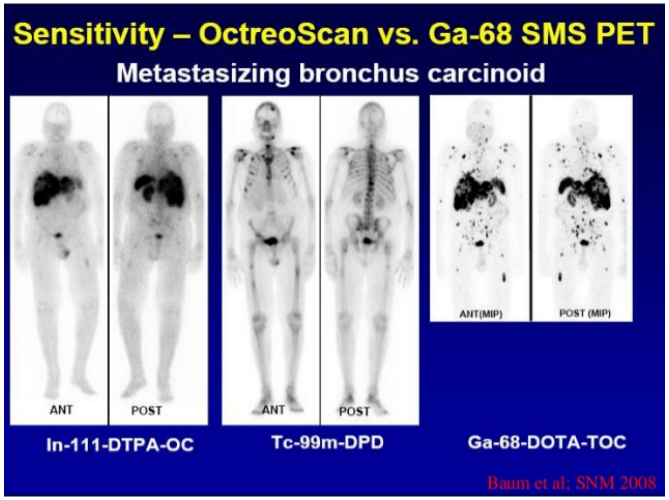
Not intrude into medical judgements, except as necessary to protect radiation safety of workers and the general public.

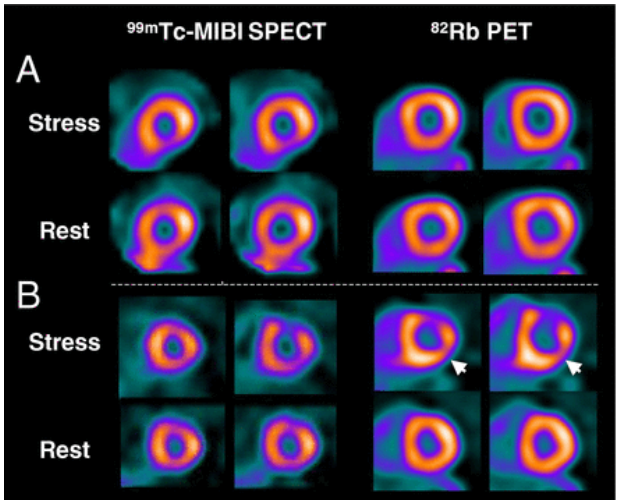
When justified by the risk to patients, regulate radiation safety of patients primarily to assure medical use is in accordance with the physician's directions.

In developing a specific regulatory approach, consider industry and professional standards that define acceptable approaches of achieving radiation safety.

Two Categories of Medical Use

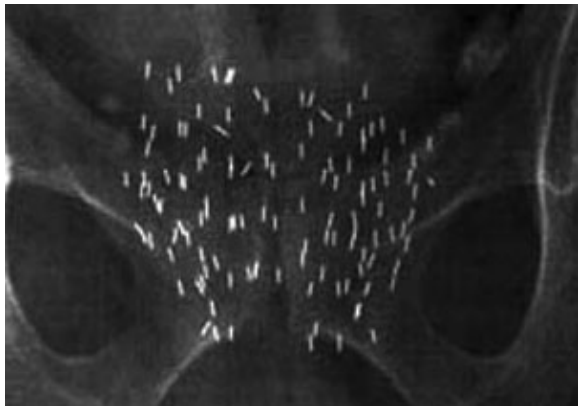
- Diagnostic
  - Imaging organs, systems, and functions
  - Gamma camera, PET, PET/CT, or SPECT
  - Nuclear medicine, nuclear cardiology, endocrinology, diagnostic radiology





Two Categories of Medical Use

- Therapeutic
  - Radiopharmaceutical therapy, teletherapy, brachytherapy, gamma stereotactic radiosurgery
  - Nuclear medicine, endocrinology, radiation oncology, interventional radiology



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Status of NRC Staff Activities

Kevin Williams, Deputy Director
Division of Materials Safety, Security, State, and Tribal Programs
NMSS

Ensuring an Effective Medical Program through Coordination

- Training and experience
- Patient release
- Prevention of medical events
- Medical AO thresholds
- Extravasations

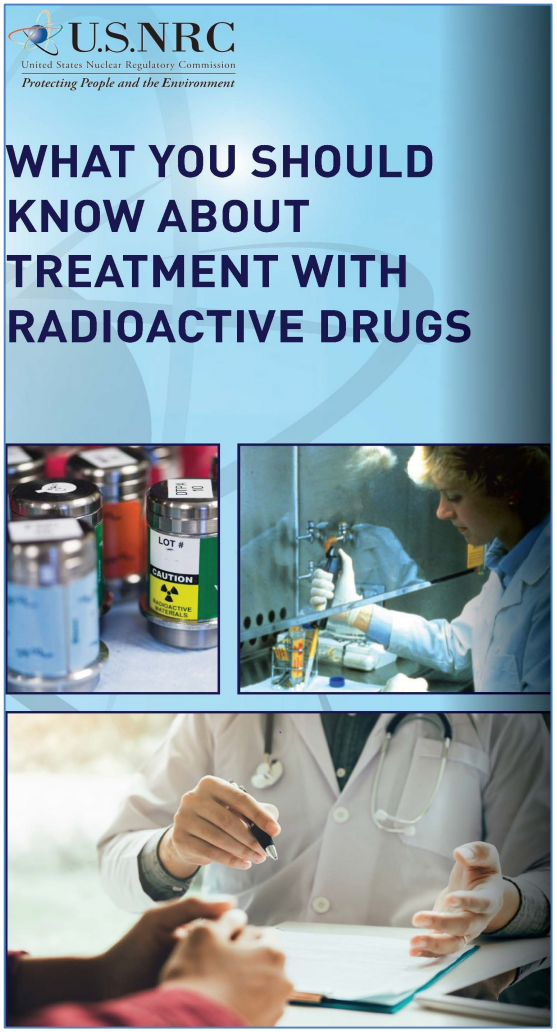
Gathering Stakeholder Input on Training and Experience

Outreach for the staff's evaluation of T&E for radiopharmaceuticals under 10 CFR 35.300 included

- Three *Federal Register* notices
- Two public comment periods
- Six public meetings
- Five online newsletter articles published
- Four conferences attended
- Three medical list server announcements
- 200+ letters to solicit input

Informing the Public About Treatment with Radioactive Drugs

- Phase 1 revision to RG 8.39, "Release of Patients Administered Radioactive Material" expected April 2020
- Phase 2 update to RG 8.39 began in October 2019



Preventing Medical Events

IN-2019-06
Patient Skin Contamination Events with I-131 MIBG

IN-2019-07
Methods to Prevent Medical Events

IN-2019-11
Sr-82/Rb-82 Generator Elution Events

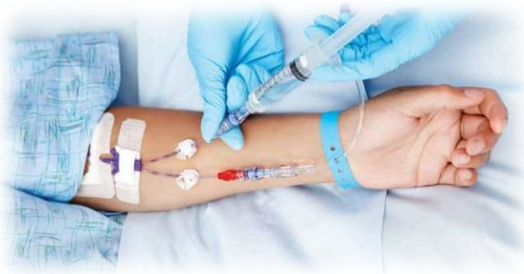
IN-2019-12
Y-90 Medical Events

Evaluating Medical Abnormal Occurrence Thresholds

- Staff reviewed medical event AOs
- Concluded that medical event AO criteria may capture events that are not significant from the standpoint of public health and safety
- Recommended in SECY-19-0088 that AO criteria be revised

Evaluating Extravasations

- ACMUI subcommittee recommendations on extravasations and infiltrations in April 2019
  - Extravasation is a practice of medicine issue, not an item that needs to be regulated by the NRC
  - Extravasation should not be considered a medical event unless there is unintended permanent functional damage
- NRC staff is conducting an independent evaluation



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Innovation Opportunities and Initiatives

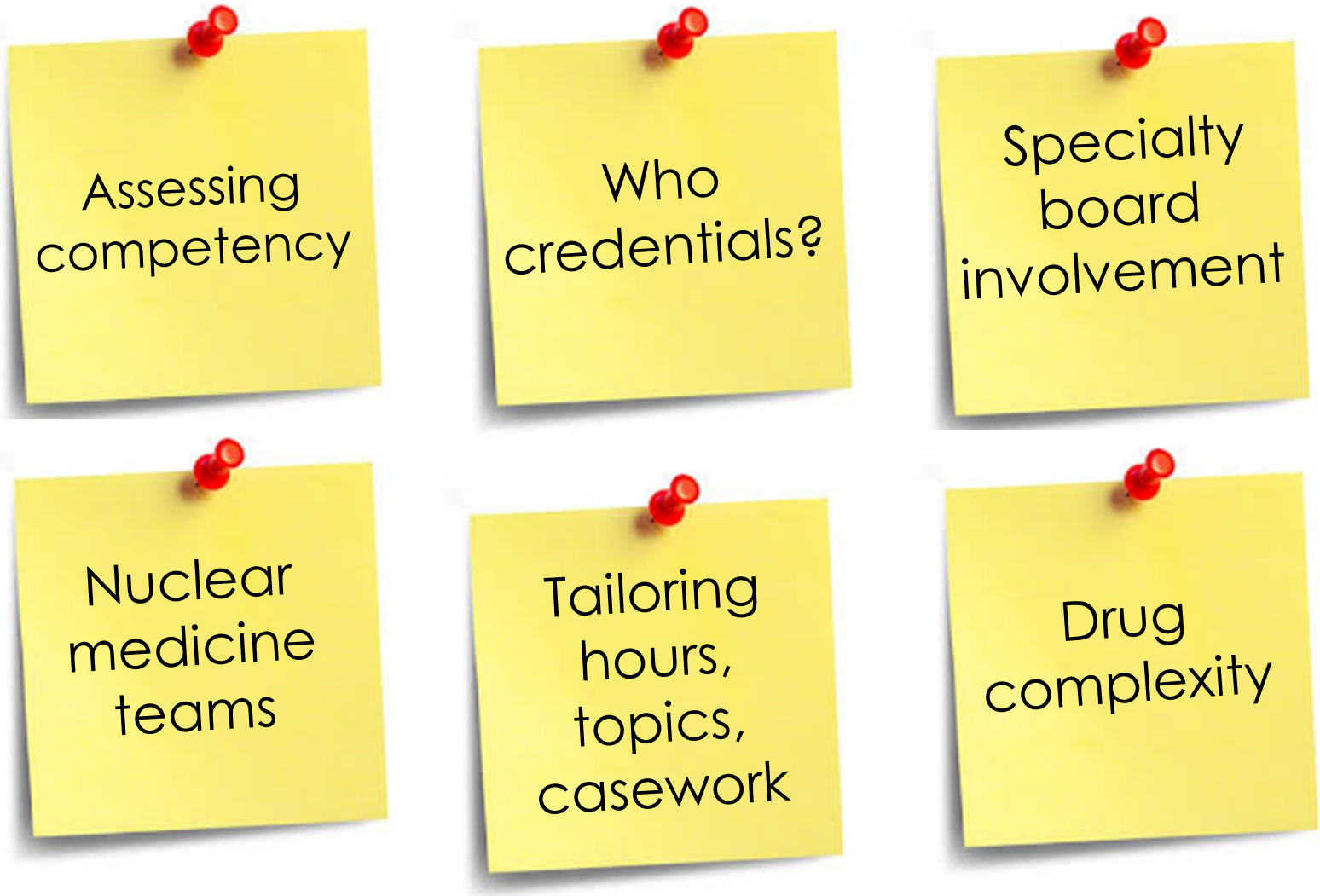
Lisa Dimmick, Team Leader
Medical Radiation Safety Team

Reconsidering the Training and Experience Requirements

- TASK: Determine whether and how to tailor the T&E requirements for different categories of radiopharmaceuticals
- CHALLENGES: Current regulatory framework is prescriptive; NRC and Agreement States must review and approve T&E for AUs

What if we changed the framework?

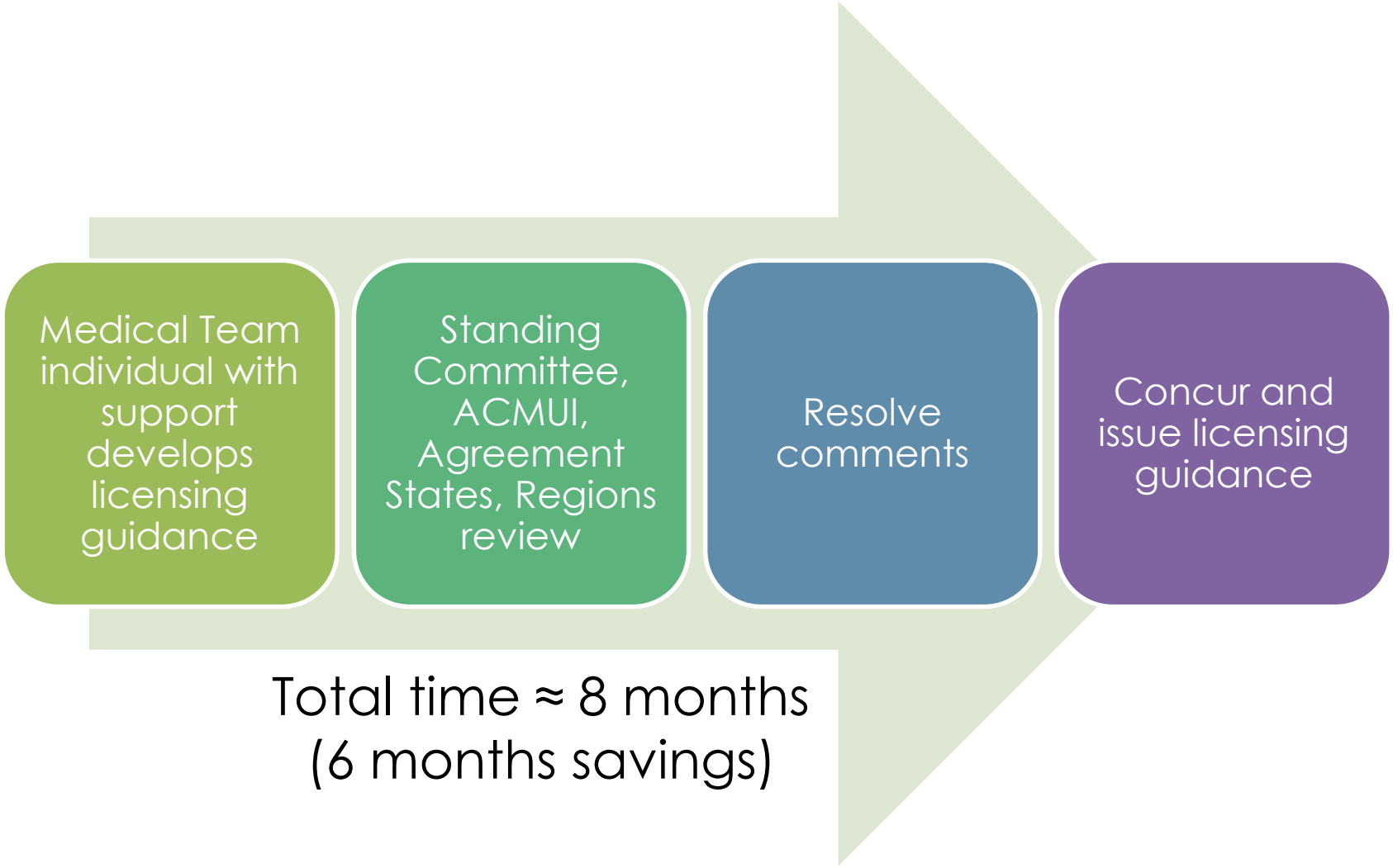
Thinking About Transformation



Proposing to Change the Regulatory Framework

- Removal of prescriptive T&E for AUs of unsealed byproduct material
- NRC and Agreement States no longer review and approve T&E
- AUs must be credentialed by a recognized medical specialty board
- Maintain high-level board recognition criteria

Streamlining our Process for Reviewing Emerging Technologies



Total time ≈ 8 months
(6 months savings)

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Efforts to Prepare for the Review of Emerging Medical Technologies

Katie Tapp, Ph.D., Medical Physicist
Medical Safety and Events Assessment Branch

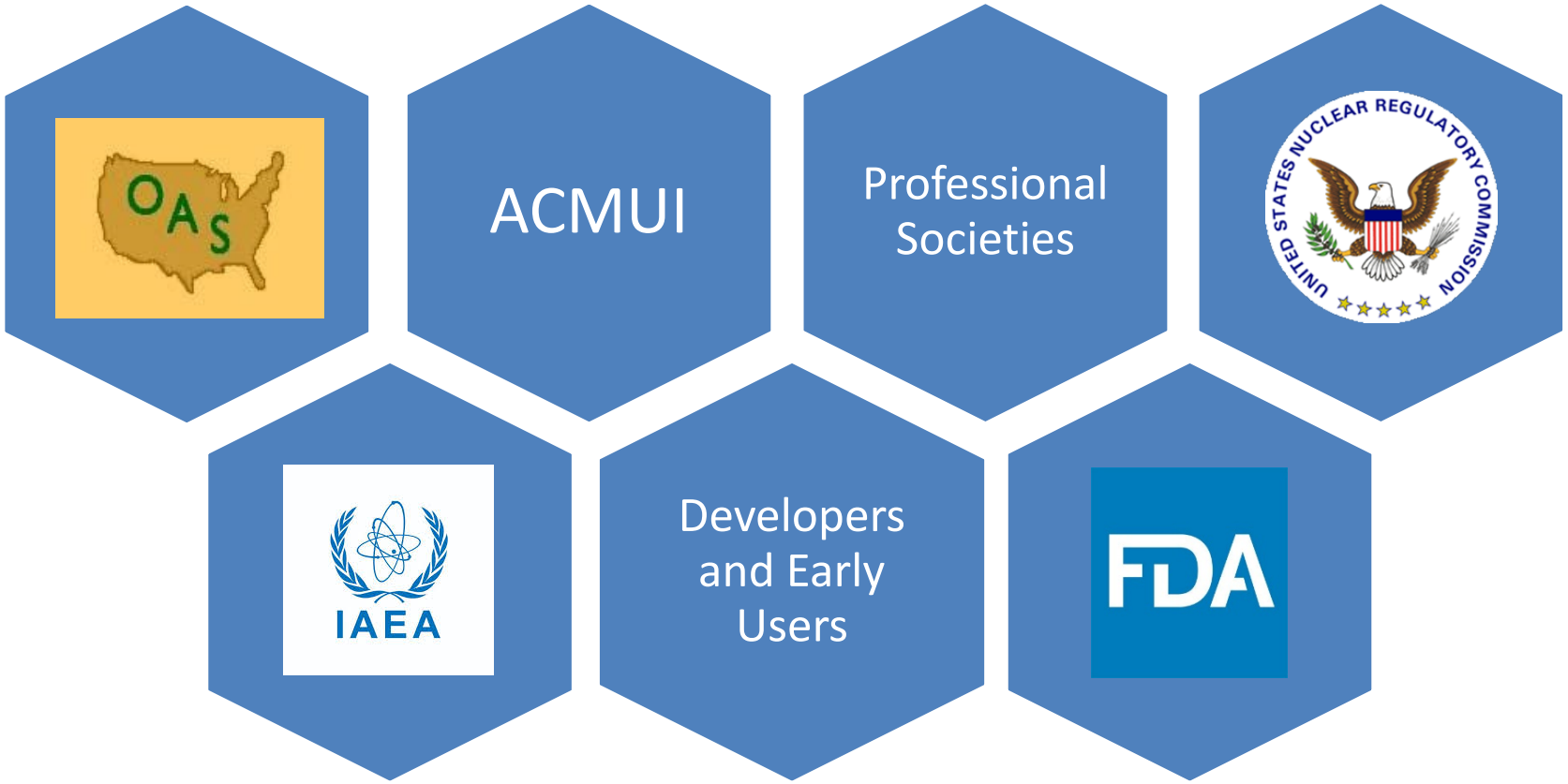
Flexible Regulatory Framework for Emerging Medical Technologies

- 10 CFR Part 35, Subpart K – Other Medical Uses of Byproduct Material or Radiation from Byproduct Material (10 CFR 35.1000)
- Supports efficient licensing of emerging technologies

Evaluation Process of Emerging Medical Technologies

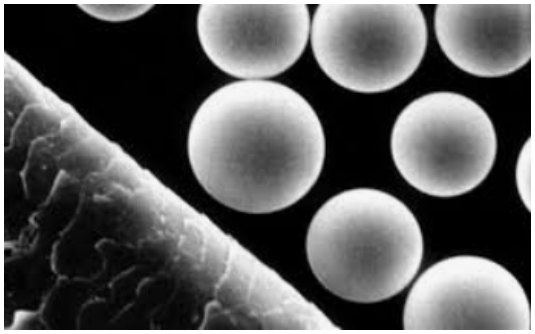
- Evaluate if medical use is addressed in 10 CFR 35 Subparts D through H
  - If no, staff develops recommended conditions of use and 10 CFR 35.1000 licensing guidance
  - If yes, staff may still provide licensing and inspection guidance on specific radiation safety aspects

Effective Stakeholder Engagement on Emerging Technologies



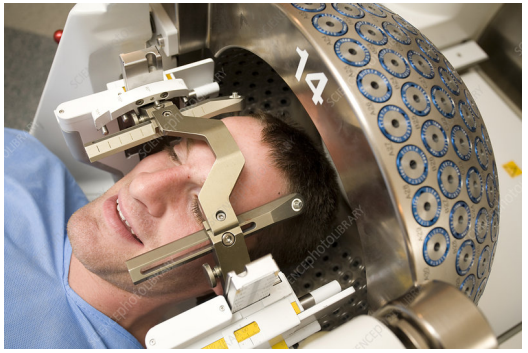
Yttrium-90 Microsphere Brachytherapy

- Permanent implant brachytherapy for treatment of liver lesions
- Several new manufacturers developing microsphere and micro-particle devices



Gamma Stereotactic Radiosurgery Units

- Original regulations developed for Gamma Knife, which treated the brain using stationary sources, helmet collimators, and a frame
- Newer units – Perfexion, Icon, GammaPod, Infini, Galaxy, Orbiter, Vertex

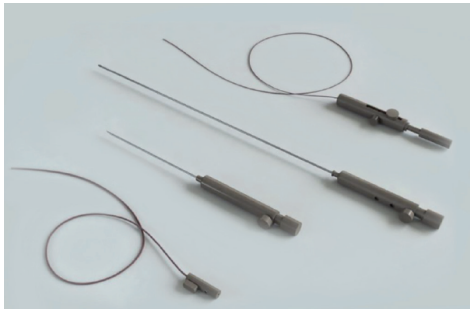


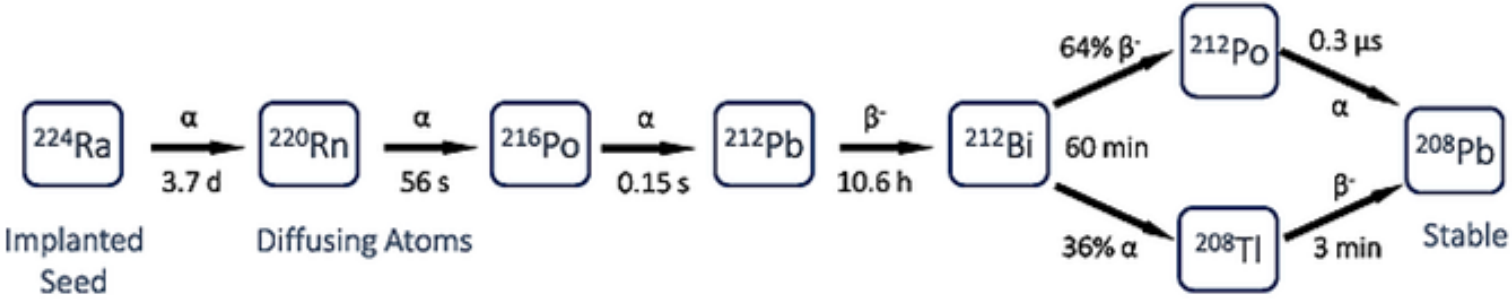
Response to Evolving Medical Landscape

- Updates for Emerging Medical Technologies Rulemaking would incorporate medical uses approved under 10 CFR 35.1000 into relevant subparts of 10 CFR Part 35
- Joint NRC/OAS WG working to complete the rulemaking plan by Summer 2020

Alpha DaRT (Diffuse Alpha Radiation Therapy)

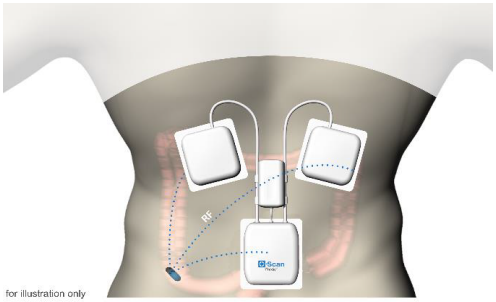
- Brachytherapy utilizing alpha-emitting daughters of Ra-224
- Device evaluation performed by Massachusetts





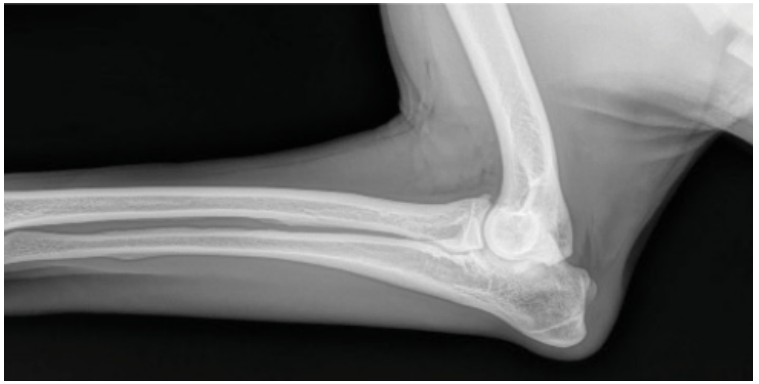
Check-Cap

- Colorectal cancer screening
- Sealed source for diagnosis (35.500 vs. 35.1000)
- Authorized user T&E
- Waste disposal



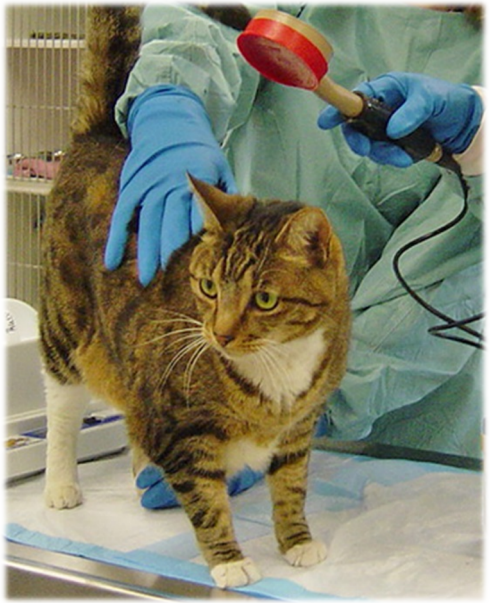
Increase in Veterinary Uses of Byproduct Material

- Sn-117m colloid for treatment of osteoarthritis of canine elbow
- Y-90 particles for treatment of pet sarcomas



Different Public Dose Limits for Animal Release

- Higher public dose limits for the release of human patients
- Release of animals must comply with 10 CFR Part 20 public dose limits



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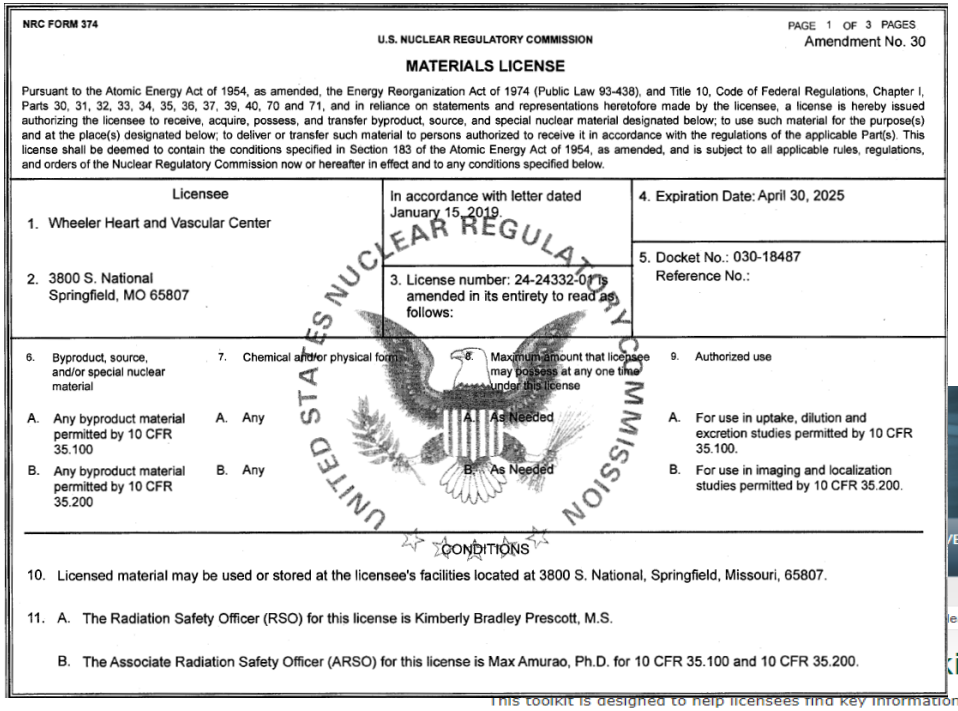
Regional Perspective on Licensing and Inspecting Medical Uses

Donna Janda, Branch Chief
Medical Licensing Assistance Branch
Division of Nuclear Materials Safety, Region I

Regional Experiences with the Part 35 Changes



NRC FORM 374 — U.S. NUCLEAR REGULATORY COMMISSION — PAGE 1 OF 3 PAGES

Amendment No. 30

MATERIALS LICENSE

Pursuant to the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974 (Public Law 93-438), and Title 10, Code of Federal Regulations, Chapter I, Parts 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 70 and 71, and in reliance on statements and representations heretofore made by the licensee, a license is hereby issued authorizing the licensee to receive, acquire, possess, and transfer byproduct, source, and special nuclear material designated below; to use such material for the purpose(s) and at the place(s) designated below; to deliver or transfer such material to persons authorized to receive it in accordance with the regulations of the applicable Part(s). This license shall be deemed to contain the conditions specified in Section 183 of the Atomic Energy Act of 1954, as amended, and is subject to all applicable rules, regulations, and orders of the Nuclear Regulatory Commission now or hereafter in effect and to any conditions specified below.

Licensee	In accordance with letter dated January 15, 2019.	4. Expiration Date: April 30, 2025
1. Wheeler Heart and Vascular Center 2. 3800 S. National Springfield, MO 65807	3. License number: 24-24332-01 is amended in its entirety to read as follows:	5. Docket No.: 030-18487 Reference No.:

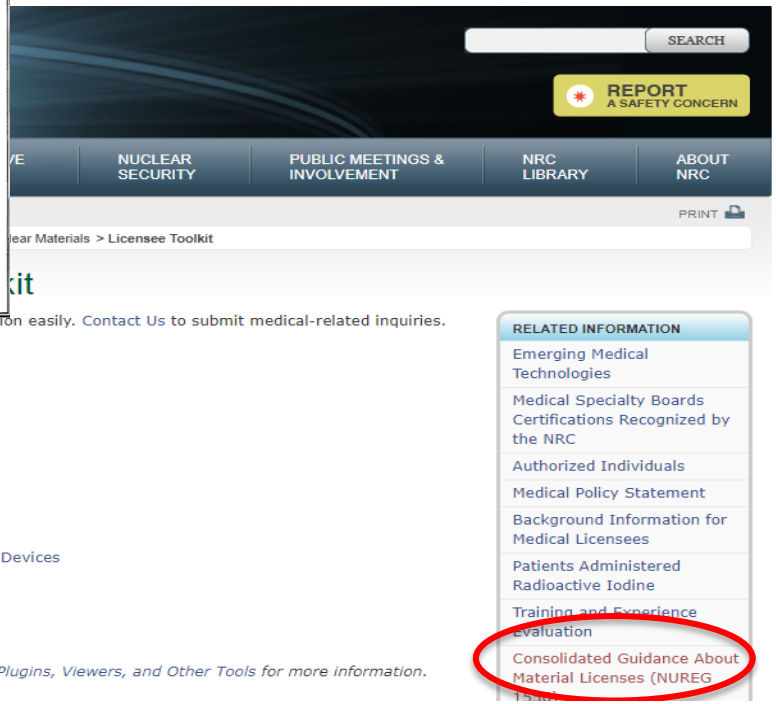
6. Byproduct, source, and/or special nuclear material	7. Chemical and/or physical form	8. Maximum amount that licensee may possess at any one time under this license	9. Authorized use
A. Any byproduct material permitted by 10 CFR 35.100	A. Any	A. As Needed	A. For use in uptake, dilution and excretion studies permitted by 10 CFR 35.100.
B. Any byproduct material permitted by 10 CFR 35.200	B. Any	B. As Needed	B. For use in imaging and localization studies permitted by 10 CFR 35.200.

CONDITIONS

10. Licensed material may be used or stored at the licensee's facilities located at 3800 S. National, Springfield, Missouri, 65807.

11. A. The Radiation Safety Officer (RSO) for this license is Kimberly Bradley Prescott, M.S.

B. The Associate Radiation Safety Officer (ARSO) for this license is Max Amurao, Ph.D. for 10 CFR 35.100 and 10 CFR 35.200.



SEARCH

REPORT A SAFETY CONCERN

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PRINT

...lear Materials > Licensee Toolkit

...kit

This toolkit is designed to help licensees find key information easily. Contact Us to submit medical-related inquiries.

On this page:

- Announcements
- Medical List Server
- Evaluation of Training and Experience
- Regulations
- Guidance
- Generic Communications
- Inspection
- Medical Events
- High Dose-Rate Remote Afterloader Brachytherapy Devices
- Licensing
- Fees
- Forms

This page includes links to files in non-HTML format. See Plugins, Viewers, and Other Tools for more information.

RELATED INFORMATION

- Emerging Medical Technologies
- Medical Specialty Boards Certifications Recognized by the NRC
- Authorized Individuals
- Medical Policy Statement
- Background Information for Medical Licensees
- Patients Administered Radioactive Iodine
- Training and Experience Evaluation
- Consolidated Guidance About Material Licenses (NUREG ...

Inspection of Patient Release

U.S.NRC
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Protecting People and the Environment

NUREG-1556
Volume 9, Rev. 3

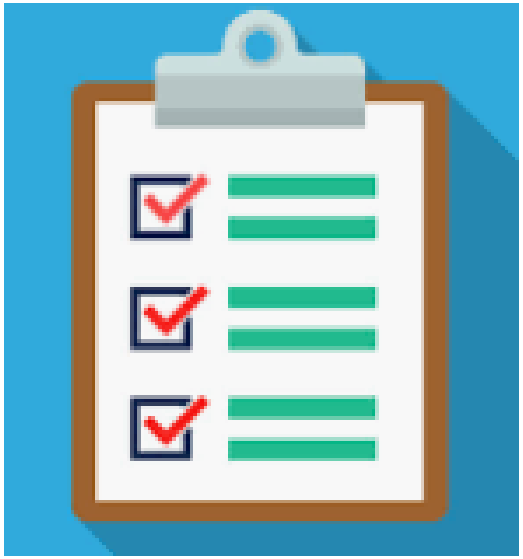
Consolidated Guidance About Materials Licenses

Program-Specific Guidance About Medical Use Licenses

Final Report

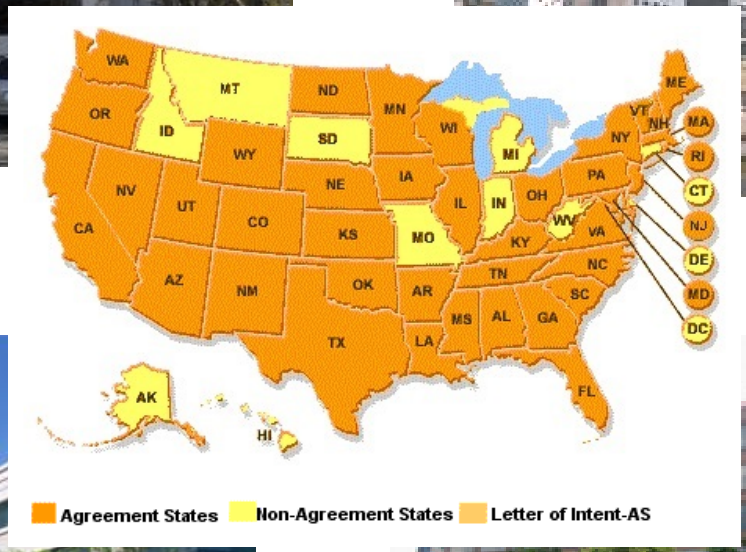
$$D(t) = \frac{34.6\,\Gamma\,Q_0\,T_p\,(1-e^{-0.693t/T_p})}{r^2}$$

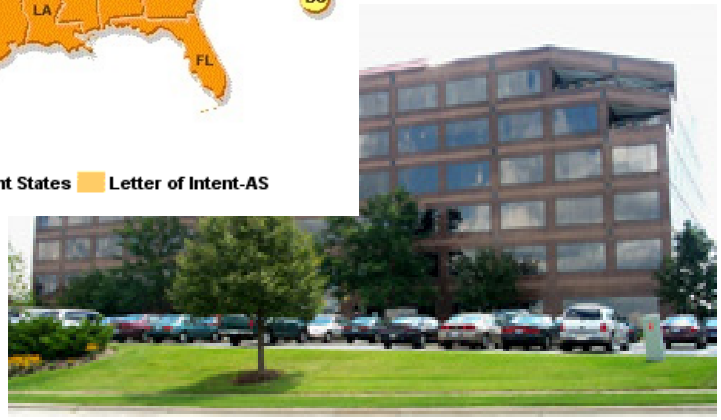
Review of Medical Events



Samples from two manufacturers of yttrium-90 (Y-90), SIR-Spheres® (left) and TheraSphere® (right); these vials contain millions of Y-90 microspheres used to treat liver cancers.

Coordination with Agreement States and Headquarters





Acronyms

ACMUI – Advisory Committee on the Medical Uses of Isotopes

AO – Abnormal Occurrence

AU – Authorized User

CFR – Code of Federal Regulations

CRCPD – Conference of Radiation Control Program Directors

CT – Computed Tomography

DaRT – Diffuse Alpha Radiation Therapy

FDA – U.S. Food and Drug Administration

Acronyms

GSR – Gamma stereotactic radiosurgery
I-131 MIBG – Iodine-131 Metaiodobenzylguanidine
IAEA – International Atomic Energy Agency
IN – Information Notice
NRC – U.S. Nuclear Regulatory Commission
OAS – Organization of Agreement States
PET – Positron-emission tomography
Ra-224 – Radium-224

Acronyms

Rb-82 – Rubidium-82

RG – Regulatory Guide

Sn-117m – Tin-117m

SPECT – Single-Photon Emission Computerized Tomography

Sr-82 – Strontium-82

T&E – Training and Experience

WG – Working Group

Y-90 – Yttrium-90

Transformation/Innovation Opportunities for the NRC to Explore

Federal Perspective

Murray Sheldon, MD
Center for Devices and Radiological Health
U.S. Food and Drug Administration

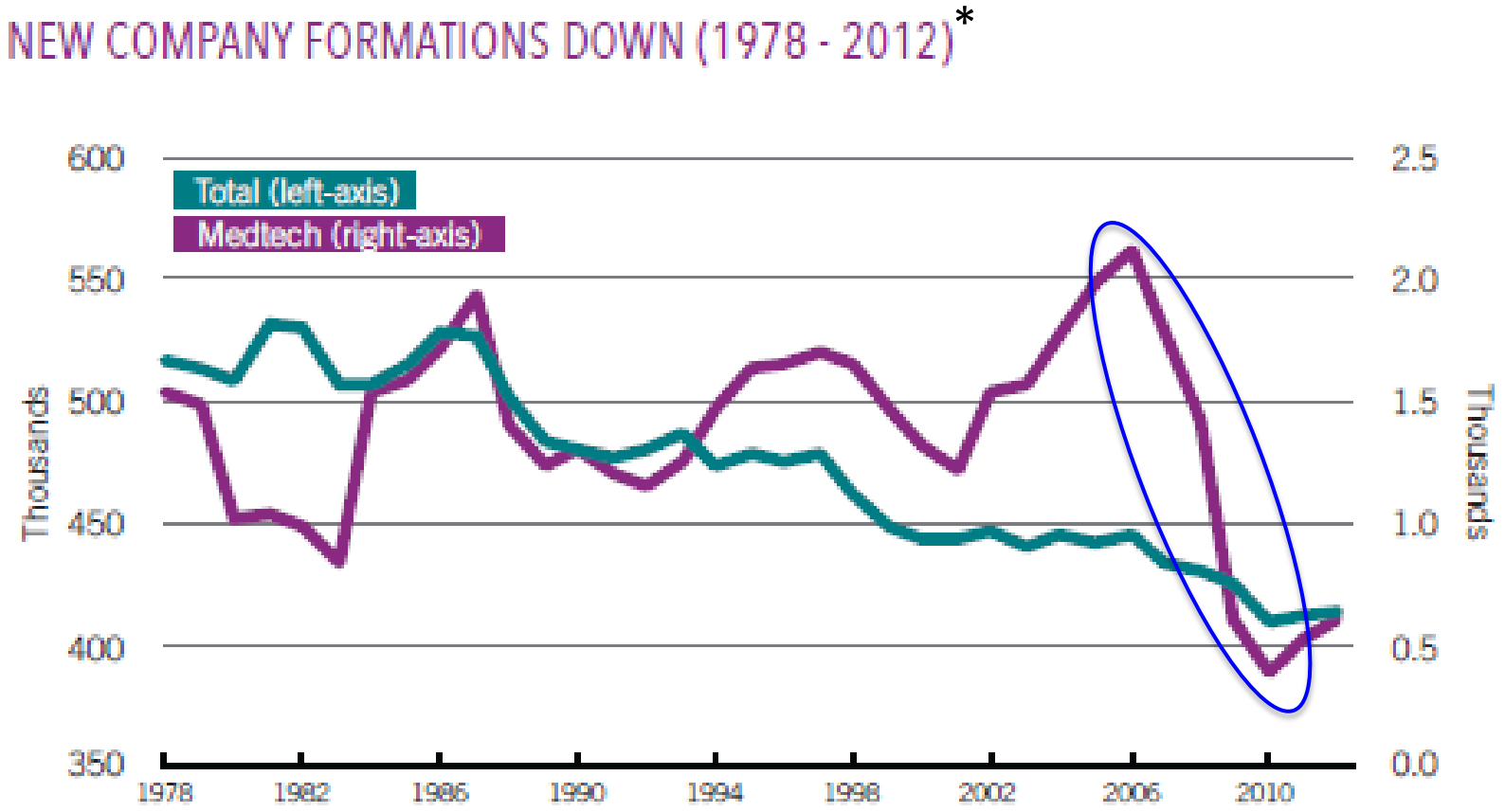
Nuclear Regulatory Commission
Discussion of Medical Uses of Radioactive Materials (public meeting)
Rockville, MD
January 28, 2020

CDRH Mission and Vision

<u>MISSION:</u> To Protect and Promote the Public Health. Assure that patients and providers have timely and continued access to safe, effective, and high-quality medical devices

<u>VISION:</u> Patients in the US have access to high quality, safe and effective medical devices of public health importance first in the world

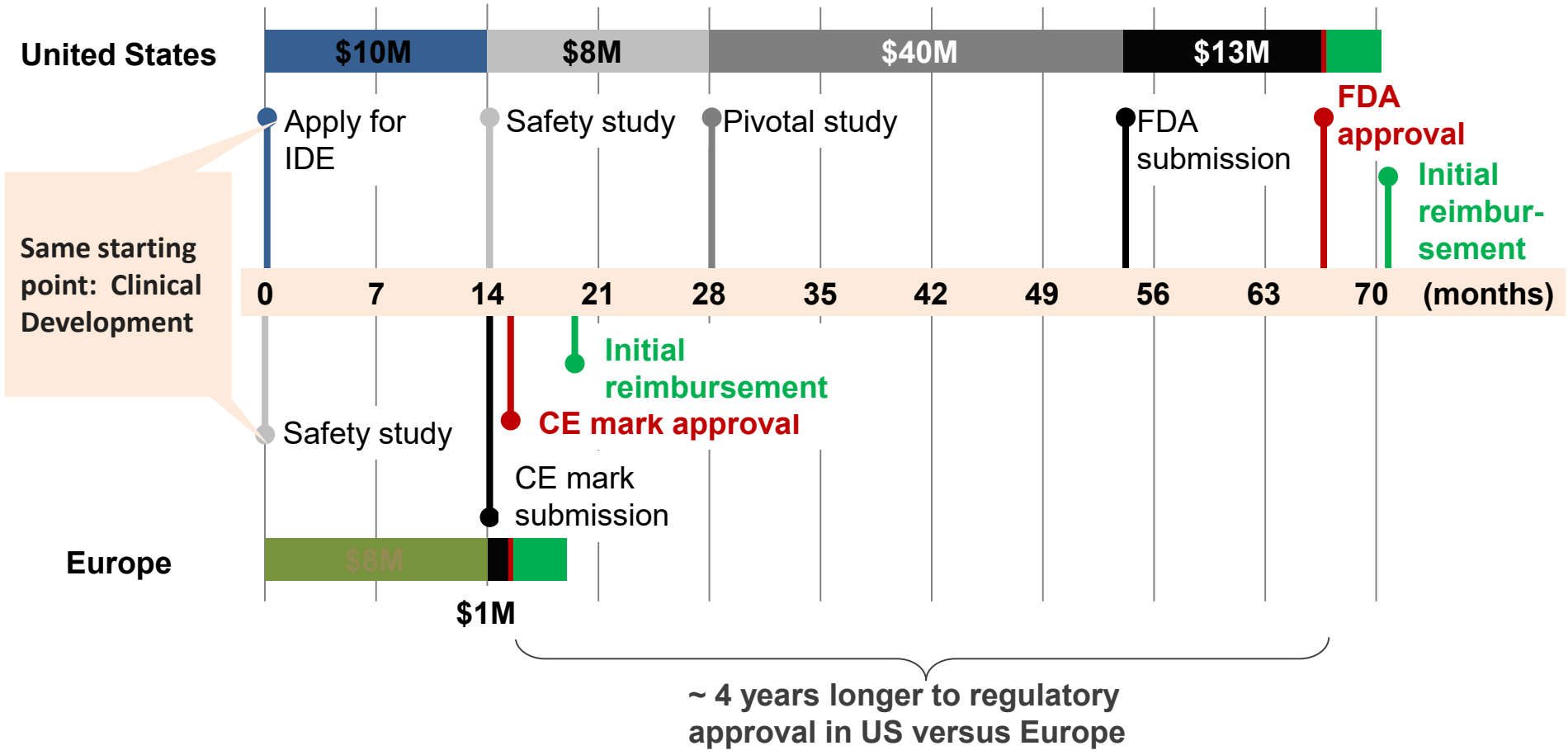
Long-term Decline in Start-up Density Since 1988



Stark decline in Medtech since 2006 to ~600 in 2012

*from: A Future At Risk: Economic Performance, Entrepreneurship, and Venture Capital in the U.S. Medical Technology Sector. Written by Innovation Counsellors LLC with support from AdvaMed Accell October, 2016
https://www.advamed.org/sites/default/files/resource/a_future_at_risk_advamed_october_2016.pdf

Makower Report (2010):
FDA Impact on US Medical Technology Innovation



Adapted from: Josh Makower white paper, "FDA Impact on US Medical Technology Innovation", November 2010

Entrepreneurs-in-Residence
Program One (Oct 2011 – May 2012)

Overview: The Entrepreneurs-in-Residence (EIR) program at CDRH is a time-limited recruitment of world-class entrepreneurs and innovators to join highly-qualified internal government employees in the development of solutions in areas that impact innovation

Goal: The EIR goal is to deliver transformational change by combining the best internal and external talent applying the principles of lean engineering in rapidly testing, validating and scaling new approaches

Focus: To better understand the drivers for the CDRH vision and to develop a new expedited pathway to improve patient access to innovative medical devices

- ESRD Innovation Challenge (2013 – 2016)
- Breakthrough Devices Program (2018)

Source: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHInnovation/InnovationPathway/ucm286138.htm

US Medical Device Industry: Innovation Challenges

Factors cited as having the highest impact on decisions to move medical device investment outside of U.S.*

Regulatory Challenges - 38%

Reimbursement Concerns - 18%

Clinical Trial Time and Costs - 14%

* from National Venture Capital Association/Medical Innovation & Competitiveness Coalition survey of 259 NVCA member firms investing in the healthcare sectors; 60% (156 firms responding) October, 2011

Entrepreneurs-in-Residence
Program Two (Oct 2012 – May 2013)

Focus: The EIR teams confronted the three challenging areas identified by NVCA that have the potential to better support a more robust environment for medical device innovation:

- Streamlining clinical trials
- Streamlining FDA approval to reimbursement
- Striking the right balance between pre- and post-market requirements

Source: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHInnovation/InnovationPathway/ucm286138.htm

FDA Responds to the Challenge

- Clinical Trials Program in ODE based on recommendations from the EiR Program
  - Early feasibility program: 17 approvals in FY 2013; 51 in FY 2019
  - Adaptive and Bayesian design
  - Patient-Centric Benefit/Risk; Patient perspectives
- Payor Communication Task Force to Streamline the path from FDA Approval to Payer Coverage (from EiR)
- Balancing Pre and Post-market Evidentiary Requirements
  - NEST – the use of Real-World Evidence
  - Coordinated Registry Networks (CRNs)

Continuous Innovation

Internal Innovation

- Training visits to innovative incubators/accelerators
- Training visits to payors

Public Private Partnerships

- KHI – American Society of Nephrology and FDA (2012)
- KidneyX – American Society of Nephrology and HHS (2018): Uses prize competitions to accelerate the development of innovative solution that can prevent, diagnose and/or treat kidney diseases

Thank You

ASTRO
TARGETING CANCER CARE

AMERICAN SOCIETY FOR RADIATION ONCOLOGY
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Arlington, VA 22202

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www.astro.org · www.rtanswers.org

Statement of Thomas Eichler, MD, FASTRO
On behalf of The American Society for Radiation Oncology
Before the Nuclear Regulatory Commission
January 28, 2020

Good morning. Thank you very much for inviting me today. My name is Dr. Thomas Eichler and I am a board-certified radiation oncologist at the Sarah Cannon Cancer Institute in Richmond Virginia. I am also the President of the American Society for Radiation Oncology, or ASTRO for short. ASTRO is the largest radiation oncology society in the world, with more than 10,000 members who specialize in treating patients with a variety of radiation therapy techniques. We thank you for your commitment to stakeholder engagement and appreciate the opportunity to collaborate with the NRC.

Before I move on to suggestions regarding transformation and innovation opportunities from the medical community perspective, I want to take a moment to discuss the staff's recent recommendations regarding training and experience for radiopharmaceuticals. The proposal gives us cause for concern. We continue to believe that there is no need to pursue additional rulemaking, as current regulations are appropriate, protect the safety of patients, the public, and practitioners. However, if the Commission ultimately decides to pursue rulemaking, we believe the board recognition criteria must ensure that existing requirements are maintained, and that any criteria for additional boards is equivalent to existing requirements.

You asked me to speak about transformation and innovation opportunities from the medical community perspective, and I would like to highlight a 2017 ACMUI report entitled "Medical Event Reporting and Impact on Medical Licensee Patient Safety Culture." In its report, the ACMUI made two important observations:

1. First, the NRC's medical event reporting criteria are set at conservative levels – which include events that rarely cause patient harm – when compared to other criteria set by The Joint Commission, the Food and Drug Administration (FDA), and the Centers for Medicare and Medicaid Services (CMS). This inconsistency in definitions leads to inconsistent levels of response to a patient safety event and causes confusion in the medical community.
2. Second, despite the recognition that the medical events rarely cause patient harm, a licensee is required to notify the NRC no later than the next calendar day after discovery. After the notification, an inspection occurs looking for violations as the cause of the event.

In other words, the NRC's conservative medical event reporting requirements are inconsistent when compared to other regulatory requirements and current radiation oncology practice, and do not foster a culture of safety.

Based on these observations, as well as the need to consider other ways medical events could be evaluated, the ACMUI made the following recommendations:

- The NRC should establish a program allowing a medical use licensee to evaluate medical events as described in current regulations with an approved patient safety program. The ACMUI describes an approved patient safety program as one or more of the following: a safety program that reports medical events to a Patient Safety Organization (PSO) which has medical expertise in medical use as defined in Part 35; a safety program evaluated by a CMS-approved Accrediting Organization, or; a safety program which is established as part of accreditation by a professional organization for medical use as defined in Part 35.
- NRC licensees with an NRC-approved patient safety program will continue to report medical events as required with certain conditions. These conditions include the NRC not including these events in the Event Notification Report, or, if this is not possible, posting them anonymously. And probably more importantly, the NRC does not conduct a reactive inspection unless the event results in, or will result in death, unintended permanent harm, or unintended significant temporary harm for which medical intervention is required. Additionally, the licensee will write a report describing the event and corrective action taken which will be made available for the next NRC inspection. Finally, the NRC will develop inspection procedures to support a test of this program.
- The NRC should test this program with various medical practice sizes and locations, evaluating the medical event reports with the ACMUI.
- 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.

ASTRO supports the recommendations offered by the ACMUI to promote a culture of safety for medical licensees. The progressive recommendations align with ASTRO's commitment to improving quality and safety in radiation oncology, and support the NRC's Safety Culture Policy Statement, while at the same time maintaining the NRC's regulatory authority to protect patients during the medical use of byproduct materials. We believe that both ASTRO's Accreditation Program for Excellence (APEx®) and RO-ILS: Radiation Oncology Incident Learning System® fulfill the spirit and the requirements set forth by the ACMUI.

First, I would like to discuss APEx. APEx was launched in February 2015 and to date, has accredited more than 150 facilities. The mission of APEx is to recognize facilities by objectively assessing the radiation oncology care team, policies and procedures, and the facility. APEx supports quality improvement and patient safety in radiation therapy practices. Facilities that obtain APEx practice accreditation will have the systems, personnel, policies and procedures that are needed to deliver safe, high-quality patient care.

Obtaining APEx accreditation is a multi-step process beginning with an application and contract, followed by a thorough self-assessment, including a robust medical record review and document upload of relevant processes, procedures and other documents, a facility visit by radiation oncology professionals who are trained as APEx surveyors, and finally a determination made by

ASTRO's APEx committee. The APEx program is constantly evolving with regular quality assurance performed by the APEx committee.

The APEx standards represent the cornerstone of the program and identify systematic quality and safety approaches that build on and reinforce regulatory requirements to add value for practitioners and health care consumers. They are organized around five pillars: The Process of Care in Radiation Oncology; The Radiation Oncology Team; Safety; Quality Management and Assurance in Radiation Oncology; and Patient-centered Care.

Of the 16 APEx standards, the Culture of Safety standard specifically requires that the radiation oncology practice foster a culture in which all team members participate in assuring safety, capitalize on opportunities to improve safety and does not take reprisals upon staff that report safety concerns. This standard ensures that the practice fosters a culture where learning from patient safety events and unsafe conditions is a part of the process of care, and is a mandatory component of the program. We believe that the most effective way for facilities to take action on a safety event or unsafe condition is for them to take ownership of the corrective actions in a non-punitive environment. The facilities are in the best position to make changes and improve safety since they are most familiar with their own processes and procedures. We are pleased that the ACMUI embraced this approach to safety culture, especially when it comes to medical event reporting.

Now I would like to turn your attention to RO-ILS. RO-ILS embodies these same ideals, albeit in a slightly different way. RO-ILS facilitates the collection and reporting of patient safety events from all participating facilities to make suggestions for change. The mission of RO-ILS is to facilitate safer and higher quality care in radiation oncology by providing a mechanism for shared learning in a secure and non-punitive environment. While important legal protections prevent RO-ILS from sharing reported information by a facility, the facility has the ability, and is often required, to share relevant information with the NRC (and other federal and state regulators).

RO-ILS is part of an Agency for Healthcare Quality and Research (AHRQ)-approved PSO. RO-ILS has more than 500 facilities enrolled, and more than 12,000 events have been reported. Approximately 300 of those events involve radioactive materials[1]. Approximately 44% of the reported events are classified by users as "operational/process improvement", which is defined as a non-safety event. This suggests that practices are utilizing the system for more comprehensive quality improvement. An additional 12% of events are classified as therapeutic radiation incidents, where the radiation dose is not delivered as intended, with or without harm, with the majority of those having a less than 5% dose deviation.

The culture of safety in medicine has completely shifted from one of blame to one focused on learning. This has led to an increase in reporting. RO-ILS participants want to identify events and near misses, create interventions to prevent them from happening again, and share safety

[1] Note: this number does not include events using GammaKnife because those are grouped under the broader "stereotactic radiosurgery" events, which include linear accelerators.

risks and solutions with others. Analyzing safety events that were caught before reaching the patient and addressing those error-prone processes is a critical aspect of incident learning in medicine. We believe the current NRC medical event reporting approach does not focus sufficiently on learning, and the ACMUI recommendation holds great promise for improving the process.

To reiterate, ASTRO believes that the NRC could play a greater role in improving safety culture in radiation therapy by implementing the ACMUI's recommendations.

Thank you, and I look forward to answering your questions.

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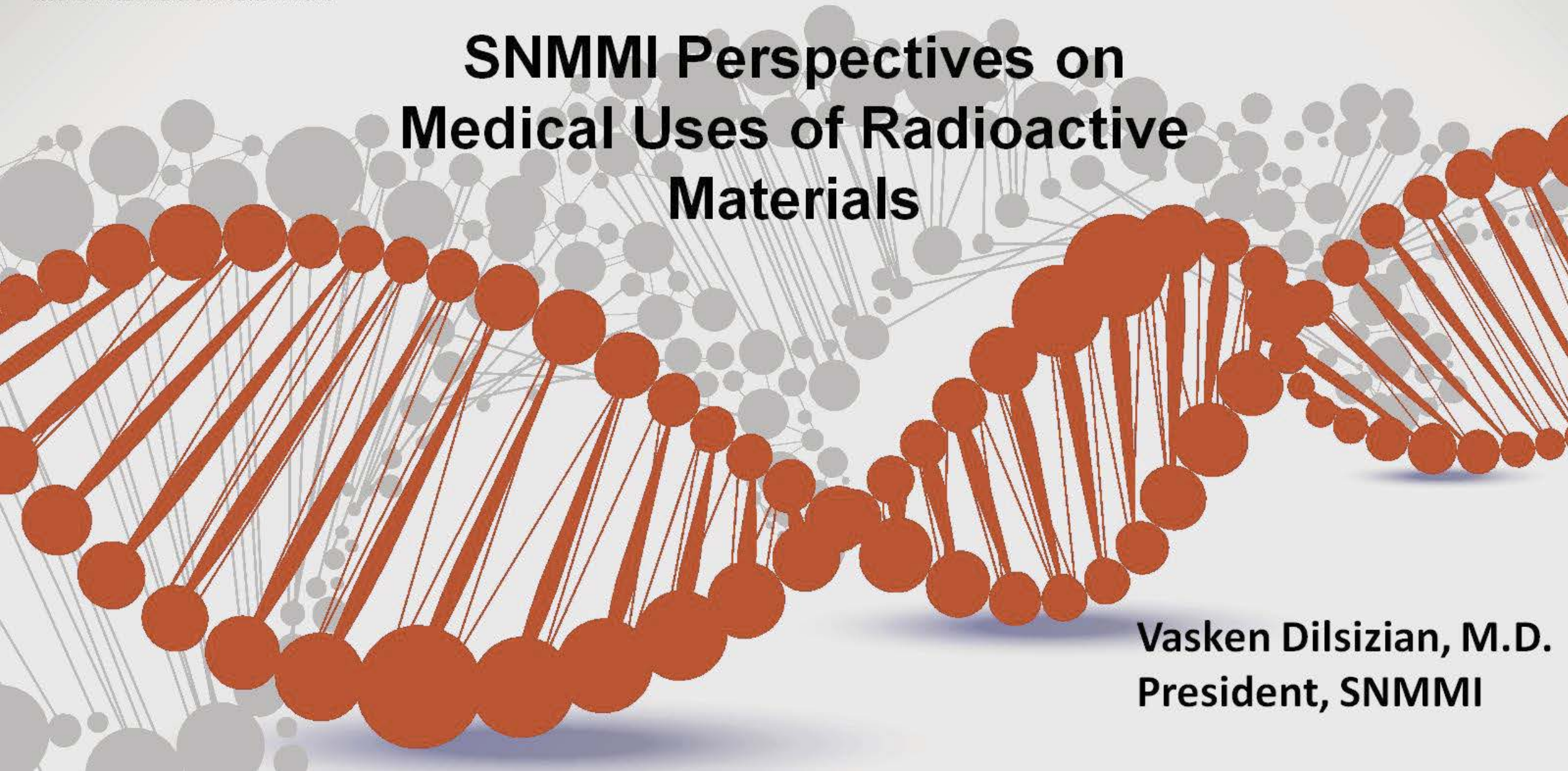
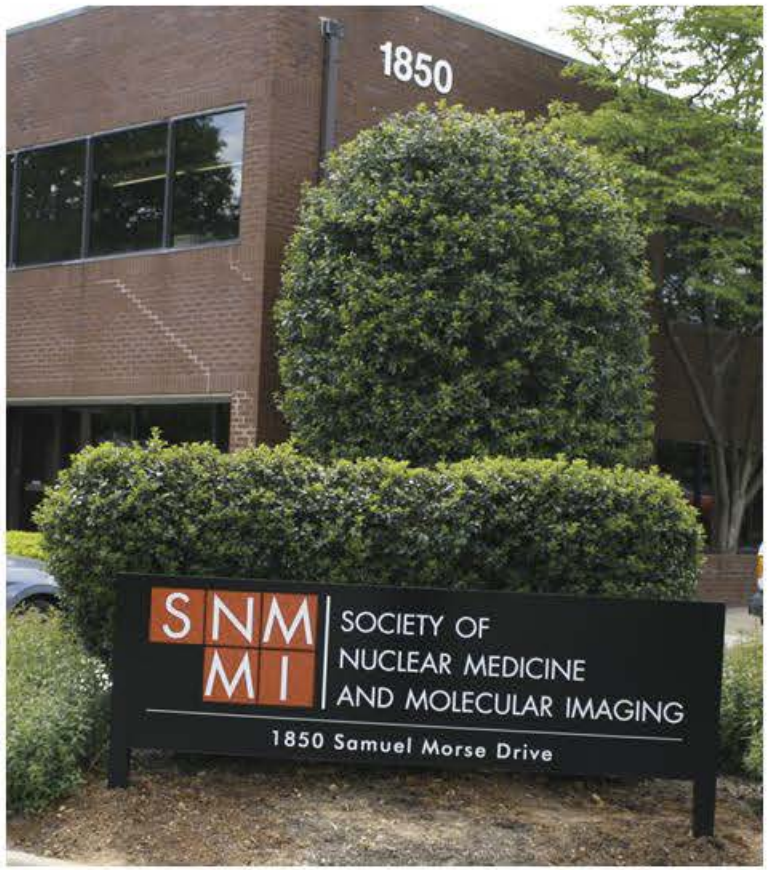
SNMMI Perspectives on Medical Uses of Radioactive Materials



Vasken Dilsizian, M.D.
President, SNMMI

SNMMI's History

- Founded in 1954
- The largest international scientific organization dedicated to nuclear medicine and radionuclide therapy
- A multidisciplinary organization
  - Over 15,000 physicians, scientists, pharmacists and technologists



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Current Pathways for Obtaining AU Status

1. Certification by a medical specialty board whose certificate is recognized by the NRC or an agreement state (American Board of Nuclear Medicine, American Board of Radiology, and American Board of Osteopathic Radiology)
2. Completion of 200 hours of classroom training and 500 hours of supervised work experience in an ACGME accredited program (Nuclear Medicine, Diagnostic Radiology with 16 month NM/NR pathway, or Radiation Oncology)
3. Previous identification as an Authorized User on an NRC or Agreement State license of permit

Training and Experience (T&E) Requirements

NRC-2018-0230: Draft Approaches for Addressing T&E Requirements for Radiopharmaceuticals Requiring a Written Directive

- We thank the NRC for the opportunity to provide feedback
- Our main objective is to emphasize **Patient and Public Safety**, while ensuring **Access to Quality of Care**
- The NRC's advisor board (ACMUI) identified no Authorized User shortage in their revised report (ACMUI July of 2018) and **"strongly supported maintaining current AU pathways"**
- Thus, there seems to be no clearly defined or compelling need to develop a new tailored T&E pathway

NRC staff's SECY-20-0005 paper: SUMMARY

NRC staff's SECY paper, SECY-20-0005: "Rulemaking Plan for Training & Experience Requirements for Unsealed Byproduct Material (10 CFR Part 35),"

- The NRC staff finds that given the expected growth in the field of nuclear medicine and uncertainties in the safety-related characteristics of emerging and future radiopharmaceuticals, such as energy level, dose, half-lives, and administration protocol, **a less prescriptive and more performance-based approach to regulating T&E would be beneficial** because it could cover radiopharmaceuticals beyond those currently known or in use.
- In addition, increased involvement by the medical community in determining the appropriate safety criteria for radiopharmaceuticals and setting the associated T&E requirements could **help accommodate the increasing "interest" of non-nuclear medicine and non-radiation oncology physicians in using radiopharmaceuticals**. While the staff considered **stakeholder concerns** about patient access, the availability and geographic distribution of AUs did not drive the staff's evaluation of T&E.

NRC RULEMAKING PLAN - SECY-20-0005: RECOMMENDATION – 1/13/2020

- NRC staff's recommendation to initiate a rule making **to remove prescriptive T&E requirements and to eliminate the need for NRC review and approval of AUs**. The staff's recommended option would require that physicians be certified by an NRC-recognized or Agreement State-recognized **medical specialty board** to become AUs.
- As part of this recommended rulemaking, the NRC would revise its board recognition criteria so that certification by specialty boards other than the existing nuclear medicine and radiation oncology boards would be an acceptable T&E pathway for the use of radiopharmaceuticals.
- The staff‘s recommended rulemaking option would continue to protect public health and safety, better align the NRC's T&E requirements with the Medical Policy Statement, and position the agency for more effective and efficient regulatory decision making with respect to the expected increase in the number and complexity of emerging radiopharmaceuticals.
- The recommended option would also alleviate regulatory burden for the NRC, Agreement States, and licensees, resulting in an estimated cost savings of $2.4 million per year.

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Other Important Views to Consider

- Who will be training the current oncology, urology, or other medical specialties and how do we ensure that the next generation of residents and fellows in these area receive competency based training? There are no (or perhaps only a handful of) Authorized Users in these medical specialties at the present time.
- Expansion in medical specialty training requires ACGME review committee discussion and approval in each of these medical specialties. **NRC does not have jurisdiction to require changes in medical and surgical residency or fellowship training**.
- Nuclear Medicine, Radiation Oncology and Diagnostic Radiology with 16 month NM/NR pathway are **the only ACGME-approved training programs** that have specific goals and objectives pertaining to administration of radioactive material. These have to be completed **under the supervision of Board Certified physicians** who also have been trained in this area.

Other Important Things to Consider

- **Independent of the medical or surgical specialty board**, the AU candidate must attest to the acquisition of § 35.390 knowledge topics & skills by successfully completing a formal competency assessment with continued formal periodic competency reassessment to maintain his/her limited-scope AU status (competency certification for radionuclide therapy).

- Given that this type of training is not part of standardized program requirements in these medical and surgical subspecialty areas, the question arises as to which organization is best suited to ensure competency and safe administration of these agents from individuals who have sought this additional training?

- Which subspecialty Board would be most qualified to certify these medical specialty candidates as qualified and competent for radionuclide therapy? American Board of Nuclear Medicine or Medical Specialty Boards without adequate mentors or educators to cover the § 35.390 knowledge topics & skills?

- Undoubtedly, organizations that have the most experience and expertise in these areas are Nuclear Medicine, Diagnostic Radiology and Radiation Oncology.

Release of Patients Administered Radioactive Material

NRC-2019-0154: Release of Patient Administered Radioactive Material

- We thank the NRC for the opportunity to provide feedback on the patient release criteria.
- The SNMMI submitted comments for this patient guide in June 2017 and again in September 2019, following the current revision, to provide licensees with more detailed instructions for their patients before and after they have been administered radioactive material
- This revision included new section on “Death of a Patient Following Radiopharmaceutical or Implants Administrations,” and “Dosages of Radiopharmaceuticals that Require Instructions and Records when Administered to Patients who are Breastfeeding an Infant or Child”

Release of Patients Administered Radioactive Material

- SNMMI submitted specific comments related to radiation monitoring of family members, breastfeeding interruption limits and guidance for families and children
- SNMMI agrees that the 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
- **SNMMI is keenly aware of the usage and impact of social media on education**. Accordingly we are planning to develop a video clip that will be available on the Society's website and on **YouTube** for patients to view the entire radioactive material administration procedure and follow instructions in advance of their treatment.

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Targeted Radiopharmaceutical Therapies Growth Areas

- Targeted Radiopharmaceutical Therapies are expected to be an area of tremendous growth in the coming years with several new agents under testing and development, in clinical trials, or in clinical use.
- Some examples of alpha- and beta-emitting targets include:

  1) FDA-approved Radium-223 therapy for metastatic prostate cancer and other cancers in bone

  2) Other alpha-emitting therapeutics targeting a variety of receptors including prostate specific membrane antigen (PSMA)

  3) FDA-approved Lutetium-177-labeled somatostatin analog (Lu-177 dotatate) therapy for neuroendocrine and other somatostatin receptor expressing tumors

  4) Lutetium-177 PSMA therapies for metastatic or treatment-resistant prostate cancer

  5) Iodine-131 labeled antibodies to leukemia targets (such as CD-33)

  6) Other indications in Phase 2 or 3 trials include Colorectal Cancer,

  Non-Hodgkin's Lymphoma and Leukemia

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Potential Barriers to Patient Access

- Addition of new diagnostic and therapeutic isotopes to a Radioactive Material License (RAML) can be time consuming – up to 6 months – and can be variable from state to state
- Rulemaking related to generators can cause delays (decommissioning funding plans)
- Isotope/agent-specific training for targeted therapeutic dosing and patient administration

Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- AU – Authorized User
- ACGME - Accreditation Council for Graduate Medical Education
- FDA - Food and Drug Administration
- NRC – Nuclear Regulatory Commission
- T&E – Training and Experience
- RAML – Radioactive Material License
- PSMA - Prostate Specific Membrane Antigen
- NM/NR – Nuclear Medicine/Nuclear Radiology

Innovation and Education
Medical Use of Isotopes
Patient Perspectives

Josh Mailman
NorCal CarciNET Community

NorCal CarciNet
Strength in Community

Disclosure

NorCal CarciNET receives funding for educational and speaking events from AAA, Curium, IPSEN, Lexicon, Novartis, and Progenics.

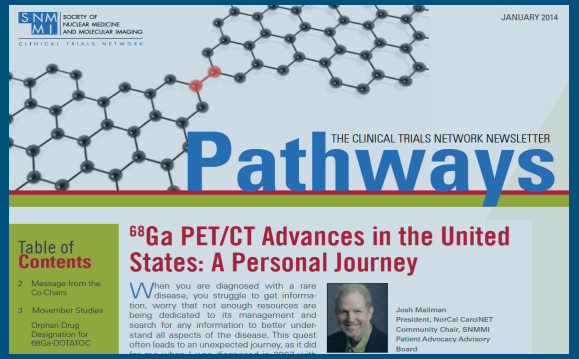
Views expressed during this presentation are solely my own.

Thank you on behalf of patients for this opportunity to participate in this forum

Who am I ?

Diagnosed in 2007 with a Pancreatic Neuroendocrine Tumor

- First nuclear imaging in 2007
- First Ga68 PET/CT in Germany 2008
- First Nuclear Medicine Therapy in Germany 2009



Selected current affiliations:

President - NorCal CarciNET Community

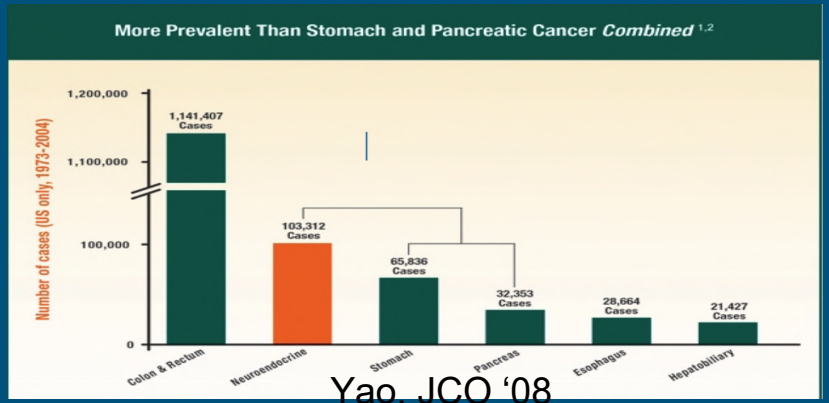
COO - World Association of Radiopharmaceutical and Molecular Therapy

Inaugural president of Patient Advocate Advisory Board and Ga68 Working Group- SNMMI

Treasure and Board Member - Neuroendocrine Tumor Research Foundation

About Neuroendocrine Tumors (NETS)

- Considered a “Rare” or Orphan Disease
  - Low incidence ~7/100k ~21,000
  - Second highest prevalence for GI Cancer ~172k
- Arising from cells of the endocrine (hormonal) and nervous systems.
  - They can occur all over the body
- Often hard to diagnose due to confusing symptoms and imaging challenges (more on that later)
- NETS overexpress naturally occurring somatostatin receptors



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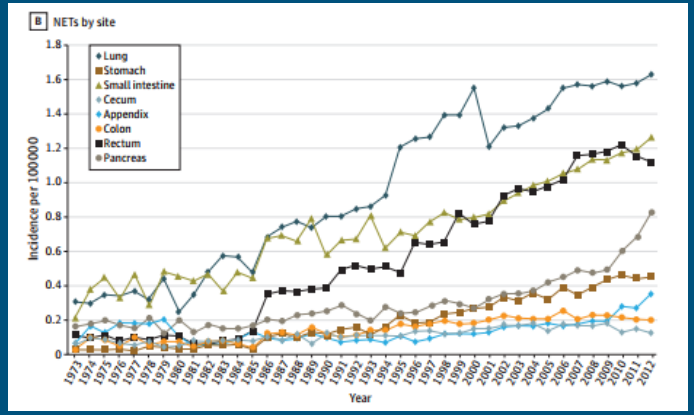

Approvals for Nuclear Medicine for NET Patients

June 2016, NETSPOT - Ga68 Dotatate for Imaging

January 2018, Lutathera - Lu177 Dotatate for Treatment of GEPNETS

July 2018, Azedra - I131 - Para/Pheo

June 2019, Ga68 Dotatoc for imaging

Future Isotopes under Consideration

We concur with the SNMMI, EANM and WARMTH on the promising use of Alpha emitters and Copper 67 for several disease indications beyond NETS

- Actinium-225 (^{225}Ac) * - α
- Lead-212 (^{212}Pb)* - α
- Copper-67 (^{67}Cu) - β
- Thorium-227 (^{227}Th) – α
- Terbium-149 (^{149}Tb) – α
- Bismuth-213 (^{213}Bi) – α
- Astatine-211 (^{211}At) -α

Patients Overjoyed with Availability

- Were desperately seeking any Ga 68 imaging since 2012
- Facebook on NETSPOT approval generated over 100 comments on approval date
- Little understanding of the complexity of delivery
- Lutathera approval has allowed a therapeutic option availability that was limited to only those who could afford to travel overseas

With Availability Comes New Opportunities for Education.

New Options in a New Era of Information

- Overwhelming response is positive to these approvals - but information challenges for patient, providers, and payers are magnified by the use of social media
- Concerns, confusion and misinformation regarding “Patient release instructions”
  - DIffers by treatment facility
  - Fear of the unknown with Radiation
  - Some families (and pets) are separated from each other for weeks
- Desire to work those that are trained are experienced with new drugs
  - Mis reads or mis understanding of imaging
  - Wanting to use an “experienced center”
- Challenge of getting this paid for

All magnified in the lens of Facebook, and private patient support portals

Areas Where the NRC Can Help

Patient Release Criteria

Maintaining Education Standards

Managing Regulatory Challenges

Patient Release Criteria

NorCal CarciNET responded to Docket ID-NRC-2019-0154

Our response asked the NRC to consider adding isotope to tables 1 and 2 even if below threshold value with NA or “*” to indicate that the instructions do not apply as below threshold.

Consider a patient friendly version of the Release Criteria so that patient can use this in discussion with their provider

Confirm all values and best practice with stakeholders prior to final approvals

Training and Education Standards

NorCal CarciNET Community responded to Docket ID NRC-2018-0230 in January 2019. Our position was:

1. There is no shortage in the number of Authorized Users (AUs) for medical uses under 10 CFR 35.300.
2. There is adequate Geographic coverage of AUs where sufficient demand for therapy exists.
3. Current NRC regulations on AU Training & Education (T&E) requirements do not limit patient access to procedures involving radiopharmaceuticals.
4. Current NRC regulations on AU T&E requirements do not limit research and development in nuclear medicine.

We are reviewing proposed rulemaking that was issued on 1-17-2020

Managing Regulatory Challenges

We want to again thank the NRC for updating giudice in 2017 and again in 2019 in the matter of germanium-68/gallium-68 (Ge-68/Ga-68) pharmaceutical-grade generators

We were involved in at least 2 calls over 2015/16 in regards to Ge68 being left of one table and the impact that might have to facilities that did not currently have a decommissioning plan in place.

While we can not predict the next regulatory challenge we know that one will occur and steps to mitigate the resolution time should be considered

NorCal CarciNet
Strength in Community

Thank You!

Josh@norcalcarcinet.org