MEETING AGENDA
ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

March 19-20, 2015
Two White Flint North Building (T2-B3), 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.

Thursday, March 19, 2015 OPEN SESSION			
8:30 – 8:45	**1.**	**Opening Statements** Mr. Fuller will formally open the meeting and Ms. Dudes will provide opening comments.	**M. Fuller, NRC** **L. Dudes, NRC**
8:45 – 9:00	**2.**	**Old Business** Ms. Holiday will review past ACMUI recommendations and provide NRC responses.	**S. Holiday, NRC**
9:00 – 9:15	**3.**	**Open Forum** The ACMUI will identify any medical topics of interest.	**ACMUI**
9:15 – 10:00	**4.**	**Additional Medical Meeting** Mr. Costello and Dr. Langhorst will discuss various options for an additional medical-related meeting.	**F. Costello, ACMUI** **S. Langhorst, ACMUI**
10:00 – 10:15		**BREAK**	
10:15 – 10:45	**5.**	**Patient Release Tasks** Ms. Cockerham and Dr. Howe will provide an update on the staff's efforts related to the release of patients administered radioactive material.	**A. Cockerham, NRC** **DB. Howe, NRC**
10:45 – 11:30	**6.**	**Patient Intervention** Dr. Gabriel will provide the history and background of the term "patient intervention." Mr. Costello will provide the perspective from an Agreement State inspector point of view.	**S. Gabriel, NRC** **F. Costello, ACMUI**
11:30 – 1:00		**LUNCH**	
1:00 – 2:00	**7.**	**ACMUI Comments on NUREG-1556, Volume 9** Ms. Cockerham will lead discussions on the proposed changes to NUREG-1556, Volume 9.	**A. Cockerham, NRC**
2:00 – 3:00	**8.**	**Medical Related Events** Dr. Howe will provide the latest update on medical-related events.	**DB. Howe, NRC**
3:00 – 3:30		**BREAK**	
3:30 – 4:15	**9.**	**Radioactive Seed Localization** Mr. Sheetz and Dr. Langhorst will lead discussions on proposed changes to the existing 35.1000 licensing guidance for radioactive seed localization.	**M. Sheetz, Univ. of Pittsburgh** **S. Langhorst, ACMUI**

4:15 – 5:00	**10. Ge/Ga-68 Subcommittee Report** Mr. Mattmuller will discuss the subcommittee's recommendations regarding the decommissioning funding plan for Ge/Ga-68 generators.	**S. Mattmuller, ACMUI**

Friday, March 20, 2015 OPEN SESSION		
8:30 – 9:00	**11. Yttrium-90 Microspheres and Radionuclides in Cadavers** Dr. Zanzonico will discuss the handling and disposal of yttrium-90 microspheres and other radionuclides found in cadavers.	**P. Zanzonico, ACMUI**
9:00 – 9:45	**12. Compatibility Category for Permanent Brachytherapy Reportable Medical Events** Mr. Costello will discuss the compatibility category for permanent brachytherapy medical events from an Agreement State perspective.	**F. Costello, ACMUI**
9:45 – 10:15	**13. Status of the Abnormal Occurrence Criteria** Dr. Tapp will provide a status update on the proposed changed to the Abnormal Occurrence Criteria.	**K. Tapp, NRC**
10:15 – 10:30	**BREAK**	
10:30 – 11:00	**14. Perfexion Gamma Knife and AU Physical Presence** A representative from Elekta will provide an overview of the Perfexion Gamma Knife and discuss the need for AU physical presence.	**Elekta**
11:00 – 11:15	**15. 10 CFR Part 35 Rulemaking Update** Mr. Danna will provide an update on the status of rulemaking for 10 CFR Part 35.	**J. Danna, NRC**
11:15- 11:30	**16. Committee Reporting Structure** Members will discuss the reporting structure of the Committee and provide feedback to NRC staff.	**S. Holiday, NRC**
11:30 – 12:00	**17. Open Forum** The ACMUI will discuss any medical topics of interest.	**ACMUI**
12:00 – 12:15	**18. Administrative Closing** Ms. Holiday will provide a meeting summary and propose dates for the Fall 2015 meeting.	**S. Holiday, NRC**
12:15	**ADJOURN**	

Opening Statements

NO HANDOUT

2007 ACMUI RECOMMENDATIONS AND ACTION ITEMS

	ITEM	DATE	STATUS	
2	NRC staff should remove the attestation requirement for board certified individuals and rewrite the attestation requirement for individuals seeking authorization under the alternate pathway. The rewritten attestation should not include the word “competency” but should instead read “has met the training and experience requirements.”	6/12/07	Accepted	Open
3	NRC staff should revise the regulations so that board certified individuals, who were certified prior to the effective date of recognition or were certified by previously recognized boards listed in Subpart J of the previous editions of Part 35, are grandfathered.	6/12/07	Accepted	Open
6	NRC staff should add the words “or equivalent” so it is clear that information included in a letter is the same as that which would have been submitted in NRC Form 313A (35.12(c))	6/13/07	Accepted	Open
7	NRC staff should revise 10 CFR 35.50(c)(2) to include AUs, AMPs, or ANPs identified on any license or permit that authorizes similar types of use of byproduct material. Additionally, the AU, AMP, or ANP must have experience with the radiation safety aspects of similar types of use of byproduct material for which the individual is seeking RSO authorization.	6/13/07	Accepted	Open
8	NRC staff should remove the attestation requirement from 10 CFR 35.50(d) for AUs, AMPs, and ANPs seeking RSO status, if the AU, AMP, or ANP seeking RSO status will have responsibilities for similar types of uses for which the individual is authorized.	6/13/07	Accepted	Open

2007 ACMUI RECOMMENDATIONS AND ACTION ITEMS

	ITEM	DATE	STATUS	
10	a) NRC staff should allow more than one RSO on a license with a designation of one RSO as the individual in charge. b) NRC should create a Regulatory Issue Summary (RIS) to inform the regulated community of NRC's interpretation. The RIS should be sent to ACMUI and the Agreement States for review and comment.	6/13/07	a) Accepted b) Accepted	a) Open b) Closed
25	NRC staff should revise the current regulations to include Canadian trained individuals who have passed the ABNM certification exam.	8/16/07	Accepted	Open
30	The Elekta Perfexion® should be regulated under 10 CFR 35.1000 until 10 CFR 35.600 is modified to be performance-based, which would allow the Perfexion® to be regulated under 10 CFR 35.600.	10/22/07	Accepted	Open *Delayed*
31	NRC staff should require experienced RSOs and AMPs to receive additional training, if the individual is seeking authorization or responsibility for new uses.	10/22/07	Accepted	Open
32	NRC staff should not require experienced RSOs to obtain written attestation to become authorized or have responsibility for new uses.	10/22/07	Accepted	Open
34	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	Accepted	Open *Delayed*
35	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	Partially Accepted	Open *Delayed*

	ITEM	DATE	STATUS	
36	NRC staff should not require medical licensees regulated under 10 CFR 35.400, 500, or 600, as applicable, to only use the sealed sources and devices for the principle use as approved in the SSDR.	10/22/07	Accepted	Open
37	NRC staff should revise 10 CFR 35.290 to allow physicians to receive training and experience in the elution of generators and preparation of kits under the supervision of an ANP.	10/22/07	Accepted	Open

2008 ACMUI RECOMMENDATIONS AND ACTION ITEMS

	ITEM	DATE	STATUS	
2	NRC staff should pursue rulemaking to allow more than one RSO on a medical use license with the indication of one RSO as the individual in charge.	4/28/08	Accepted	Open
5	NRC staff should incorporate the subcommittee's recommendations for the Gamma Knife® Elekta Perfexion™ in future rulemaking.	4/28/08	Accepted	Open *Delayed*
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	Pending	Open *Delayed*
22	ACMUI encouraged NRC staff to begin the rulemaking process to move the medical use of Y-90 microspheres from 10 CFR 35.1000 to another section of the regulations, so that the training and experience requirements for AUs can be vetted though the public review process instead of residing in guidance space.	10/27/08	Partially accepted	Open *Delayed*
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	Accepted	Open *Delayed*

2008 ACMUI RECOMMENDATIONS AND ACTION ITEMS

	ITEM	DATE	STATUS	
27	NRC staff should revise 10 CFR 35.40 to clarify that an AU, not the 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	Accepted	Open *Delayed*
28	NRC staff should revise 10 CFR 35.65 to clarify it does not apply to sources used for medical use; however, NRC should not require licensees to list the transmission sources as a line item on the license. NRC staff should also revise 10 CFR 35.590 to permit the use of transmission sources under 10 CFR 35.500 by AUs meeting the training and experience requirements of 10 CFR 35.590 or 35.290.	10/28/08	Accepted	Open
29	NRC staff should revise 10 CFR 35.204(b) to require a licensee that uses Mo 99/Tc-99m generators for preparing a Tc-99m radiopharmaceutical to measure the Mo-99 concentration of each eluate after receipt of a generator to demonstrate compliance with not administering to humans more than 0.15 microcurie Mo-99 per millicurie Tc-99m.	10/28/08	Accepted	Open
30	NRC staff should require licensees to report to the NRC events in which licensees measure molybdenum breakthrough that exceeds the regulatory limits.	10/28/08	Accepted	Open

2009 ACMUI RECOMMENDATIONS AND ACTION ITEMS

	ITEM	DATE	STATUS	
2	NRC staff should revise 35.390(b)(1)(ii)(G)(3) to read "parenteral administration requiring a written directive for any radionuclide that is being used primarily because of its beta emission, or low energy photo-emission, or auger electron; and/or" and revise 35.390(b)(1)(ii)(G)(4) to read "parenteral administration requiring a written directive for any radionuclide that is being used primarily because of its alpha particle emission"	5/7/09	Accepted	Open
10	ACMUI recommends NRC staff delete the phrase "at a medical institution" from 10 CFR 35.2, 35.490(b)(1)(ii), 35.491(b)(2) and 35.690(b)(1)(ii).	10/19/09	Accepted	Open

	ITEM	DATE	STATUS		1st/2nd	Vote
1	ACMUI endorsed the draft response to NRC comments, as reflected in the meeting handout (ML110600249). ACMUI agreed if NRC believes the release criteria should be changed from a per release criteria to an annual criteria, this change would require new rulemaking, as stated in Regulatory Issue Summary (RIS) 2008-07. ACMUI recommended rulemaking to clarify that the release under 10 CFR 35.75 is per release and not per year	1/5/11	Pending	Open	Langhorst/Gilley	9, 1, 0
6	ACMUI created an action item to reevaluate its satisfaction with the reporting structure annually.	1/12/11	ACMUI Action	Open indefinitely	Welsh/Zanzonico	
11	(1) ACMUI feels ASTRO's approach to Permanent Implant Brachytherapy (handout) is correct approach for patient welfare (2) ACMUI recommends that the NRC require Post-Implant dosimetry following brachytherapy treatment (3) ACMUI believes that prostate brachytherapy is a unique subset of brachytherapy and should therefore require a separate set of rules from non-prostate brachytherapy.	4/11/11	Partially Accepted	Open	Welsh/Mattmuller	11, 0, 0
13	ACMUI recommends to eliminate the written attestation for board certification pathway, regardless of date of certification	4/12/11	Accepted	Open	Zanzonico/Guiberteau	11, 0, 0

	ITEM	DATE	STATUS		1st/2nd	Vote
14	ACMUI recommends the attestation to be revised to say … has received the requisite training and experience in order to fulfill the radiation safety duties required by the licensee	4/12/11	Accepted	Open	Langhorst/Thomadsen	11, 0, 0
15	ACMUI supports the statement that residency program directors can sign attestation letters, representing consensus of residency program faculties, if at least one member of the faculty is an AU in the same category as that designated by the applicant seeking authorized status, and that AU did not disagree with the approval.	4/12/11	Accepted	Open	Thomadsen/Welsh	11, 0, 0
16	ACMUI continues to assert that the current regulations are based on a per release limit. ACMUI does not recommend any change to the regulation and does not recommend the NRC consider this topic during the current rulemaking process, as there is no clinical advantage or advantage to members of the public for using an annual limit.	4/12/11	Pending	Open	Langhorst/Welsh	11, 0, 0
32	ACMUI reaffirms the 2008 AO Criteria as stated in the handout with the amendment that (s) be added to the end of physician, to read "consultant physician(s)"	12/15/11	Accepted	Closed	Guiberteau/Mattmuller	11,0,1

	ITEM	DATE	STATUS	
9	ACMUI requested that reporting structure reviews remain on an annual basis.	9/20/12	Accepted	Open

	ITEM	DATE	STATUS		1st/2nd
1	ACMUI recommended NRC staff allow use of total source strength as a substitute for total dose for determining medical events for permanent implant brachytherapy until the Part 35 rulemaking is complete.	3/5/13	NRC Action	Open	
2	ACMUI recommended that NRC staff solicit feedback from stakeholders, in Supplementary Information section IV.D, on whether the proposed ME definition for permanent implant brachytherapy would discourage licensees from using this form of therapy. This recommendation was modified the caveat that NRC may utilize the language that they think is appropriate for gaining this type of information from its stakeholders	3/5/13	NRC Action	Open	Zanzonico/Langhorst
3	ACMUI recommended the draft rule re-defining medical events in permanent implant brachytherapy be designated as Compatibility Category B.	3/5/13 3/12/13	NRC Action	Open	
4	ACMUI recommended replacing the phrasing in the literature in terms of support for the 5 cubic centimeters of contiguous normal tissue provision of the ME definition, to the specific reference cited as, Nag, et al 2004	3/5/13	NRC Action	Open	

	ITEM	DATE	STATUS		1st/2nd
5	ACMUI recommended that licensees approved to use generator systems show specific training on the requirement now listed under 35.290 (c)(1)(ii)(G) for those individuals (Authorized Users and others) who are responsible for proper operation and testing of the generator as part of their license conditions. ACMUI further recommended that Authorized Nuclear Pharmacists who have the adequate training and experience (T&E) are able to provide the supervised work experience for Authorized Users on the elution of generators.	3/5/13	NRC Action	Open	
6	ACMUI endorsed the language in the proposed rule for preceptor attestations that states a candidate is able to independently fulfill the radiation safety related duties for which authorization is being sought.	3/5/13	NRC Action	Open	
7	ACMUI recommended that the work experience for parenteral administrations under Sections 35.390 (b)(1)(2)(g), and 35.396 not be separated between parenteral administrations of a beta gamma emitting radiopharmaceutical versus an alpha emitting radiopharmaceutical, as proposed in the proposed rule.	3/12/13	NRC Action	Open	Zanzonico/Guiberteau
8	ACMUI recommended that the date of recognition of a certifying board should not impact individuals seeking to be named as an Authorized User, Authorized Radiation Safety Officer, Authorized Medical Physicist, or Authorized Nuclear Pharmacist through the certification pathway.	3/12/13	NRC Action	Open	Zanzonico/Thomadsen
9	ACMUI recommended that the NRC adopt the FDA approved package insert for breakthrough limits for radioisotope generators	3/12/13	NRC Action	Open	Zanzonico/Mattmuller

	ITEM	DATE	STATUS		1st/2nd
10	ACMUI recommended licensee reporting of out-of-tolerance generator breakthrough results to the NRC	3/12/13	NRC Action	Open	Zanzonico/Weil
11	ACMUI recommended requiring testing of molybdenum breakthrough on every elution of a molybdenum-technetium generator, rather than after only the first elution.	3/12/13	NRC Action	Open	
12	ACMUI recommended that the addition of Associate Radiation Safety Officers (ARSOs), and Temporary RSOs also be included in these exemptions in the same manner as AUs, ANPs, and AMPs.	3/12/13	NRC Action	Open	Zanzonico/Langhorst
13	In reference to the plain language requirement, the ACMUI suggested that the rule “could be shortened and improved by eliminating redundancies and consolidating related sections and eliminating identical or nearly identical passages appearing multiple times throughout the draft rule. A further improvement would be the inclusion of a detailed “executive summary”-style section summarizing, perhaps in a bullet format, the key changes introduced in the draft rule.”	3/12/13	NRC Action	Open	
21	The ACMUI recommended that NRC provides regulatory relief from the decommissioning funding plan requirements for the use of a Germanium-68/Gallium-68 generator.	4/16/13	NRC action	Open	Mattmuller/Zanzonico
25	The ACMUI recommended to reestablish the Rulemaking Subcommittee to review and address staff's response to the subcommittee's recommendations for the draft proposed expanded 10 CFR Part 35 Rulemaking.	9/10/13	ACMUI Action	Open	Mattmuller/Zanzonico

	ITEM	DATE	STATUS		Assigned	1st/2nd
6	Dr. Thomadsen formed a subcommittee on May 8, 2014 to provide staff with the background information to justify the recommendation for the regulatory relief from the DFP of Ge-68. The subcommittee is specifically charged with evaluating the cost of a DFP for the use of Ge-68, its effect on the future clinical use of new Ga-68 radiopharmaceuticals and how appropriate regulatory relief may be gained. Subcommittee members include Mr. Mattmuller (chair), Dr. Langhorst, Mr. Costello, Dr. Palestro and Dr. Zanzonico.	5/8/14	ACMUI Action	Open	S. Holiday	
10	The ACMUI recommended that the total treatment activity of yttrium-90 microspheres to be administered should be the required compliance measure for organs and tissues other than the treatment site.	9/29/14	NRC action	Open		
11	The ACMUI recommended that the implantation of the microsphere brachytherapy sources is considered to be in accordance with the written directive if the total administered/infused activity does not vary from the activity prescribed in the written directive by 20% or more; except in situations in which the activity administered is limited by the termination of procedure due to stasis.	9/29/14	NRC action	Open		
12	The ACMUI recommended that (a) these recommendations be incorporated into the NRC guidance for yttrium-90 microsphere brachytherapy and that (b) the NRC staff, in consultation with ACMUI, compose and disseminate explanation of these recommended revisions in a manner best suited to both the NRC as well as to AUs and other stakeholders tasked with compliance.	9/29/14	NRC action	Open		

	ITEM	DATE	STATUS		Assigned	1st/2nd
13	The ACMUI endorsed the yttrium-90 microsphere brachytherapy medical event reporting criteria subcommittee report.	9/29/14	ACMUI Action	Closed		
14	The ACMUI endorsed the revisions to the ACMUI Bylaws presented on September 29, which includes the proposed language in section 1.3.5 and 3.1 and changes to reflect the new office structure.	9/29/14	ACMUI Action	Closed		
17	Dr. Thomadsen tasked Dr. Langhorst and Mr. Costello with creating a proposal to present to the Committee and staff regarding the costs and logistics for an additional face-to-face meeting and/or a medical regulatory information conference.	9/29/14	ACMUI Action	Open		
18	The ACMUI have tentatively scheduled the Spring 2015 Meeting for March 19-20, 2015. The back-up date is March 24-25, 2015	9/30/14	ACMUI Action	Closed		
19	Dr. Thomadsen formed a subcommittee to review the advanced notice of proposed rulemaking for Title 10 Code of Federal Regulations Part 20, “Standards for Protection Against Radiation.” Subcommittee members include: Dr. Langhorst (chair), Mr. Costello, Dr. Dilsizian, Mr. Mattmuller, and Dr. Zanzonico. The subcommittee will present their recommendations at a future teleconference.	9/30/14	ACMUI Action	Closed		

	ITEM	DATE	STATUS		Assigned	1st/2nd
20	Dr. Thomadsen tasked Dr. Suh and Dr. Welsh to work with the American Society for Radiation Oncology for their proposed changes to the language in the Draft FY15 Water and Energy Bill. Dr. Ennis will serve as a consultant to Drs. Suh and Welsh until he assumes the role of the ACMUI's Brachytherapy Radiation Oncologist in February 2015. Drs. Ennis, Suh, and Welsh will present the language to the Committee at the spring 2015 meeting.	9/30/14	ACMUI Action			
21	The ACMUI endorsed the ANPR for Part 20 subcommittee report.	12/10/14	ACMUI Action	Closed		
22						
23						
24						
25						
26						

Open Forum

NO HANDOUT

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

Additional Medical Meeting

Enhancing Medical Community and Regulator Communications

Susan M. Langhorst
Francis M. Costello
Said Daibes

Charge to the group

Provide a concrete proposal for a meeting, possibly more, to focus on enhancing medical regulatory information communication. Include

- **a cost estimate for future NRC budgetary consideration, and**
- **how it should be organized.**

2

Who would/should participate?

Medical Community – organizations associated with Specialty Boards recognized by the NRC, others?

Regulators – NRC, Agreement States, Non-Agreement States, FDA, others?

3

What would be the objective?

Enhanced communication to improve understanding of how medical use of radiation is different.

- **Who decides what is the specific objective?**
- **Would/should each meeting have the same objective?**

4

3,000 participants from over 30 countries

2015 was 27th year

Future RIC dates

- **28th Annual RIC - March 8-10, 2016**
- **29th Annual RIC - March 14-16, 2017**
- **30th Annual RIC - March 13-15, 2018**

5

NRC RIC

Co-sponsored by the Office of Nuclear Reactor Regulation and the Office of Nuclear Regulatory Research.

- **Designed to encourage informal, open dialogue**
- **Provide unique opportunity to interact with counterparts to gain and share valuable insights and perspectives**

6

OAS Annual Meeting

Membership – 37 Agreement States

Annual meetings

- **2015 Boston, MA (8/23-27)**
- **2014 Chicago, IL (8/25-28)**
- **2013 Reno, NV (8/19-22)**
- **2012 Milwaukee, WI (8/27-30)**
- **2011 Richmond, VA (8/22-25)**

7

Other meetings/models

- **ACMUI meetings**
- **NRC rulemaking workshop meetings**
- **NRC/Stakeholders meetings**
- **NRC outreach to and attendance at professional organization meetings**

8

NRC Staff Outreach Initiatives

- NRC exploring various outreach initiatives to enhance communications with medical licensees, regulators, stakeholders and other regulating agencies.
- Goals – education; information exchange; regulatory process participation

9

If you build it, will they come?

10

11

If they help you build it, will they be more willing to participate?

AMERICAN ASSOCIATION of PHYSICISTS IN MEDICINE
SNMMI SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING
ASTRO TARGETING CANCER CARE
American Pharmacists Association APhA
ACR AMERICAN COLLEGE OF RADIOLOGY QUALITY IS OUR IMAGE
HPS Health Physics Society Specialists in Radiation Safety
THE CANADIAN COLLEGE OF PHYSICISTS IN MEDICINE
NCRP National Council on Radiation Protection & Measurements
CBNC Certification Board of Nuclear Cardiology
U.S.NRC United States Nuclear Regulatory Commission Protecting People and the Environment
NEI NUCLEAR ENERGY INSTITUTE
American Nuclear Society

12

Medical regulatory information meeting added to OAS meeting?

Co-sponsored by the Office of Nuclear Material Safety and Safeguards and ??

- **Designed to encourage informal, open dialogue**
- **Provide unique opportunity to interact with counterparts to gain and share valuable insights and perspectives**

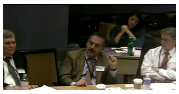
13

Medical regulatory information meeting added to OAS meeting?

- **How to fund and for how long?**
- **What kinds of topics are of interest?**
- **Who to decide and develop program each year?**
- **How to encourage medical community participation?**
- **What kind of "products" should be expected?**

14

What does ACMUI think?



15

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

Status of Patient Release Project

Ashley Cockerham
Medical Radiation Safety Team

Overview

- Commission direction
- Current status
- Path forward

2

Tasks

- Brochure
- Website
- Standardized guidelines
- Commission paper on rulemaking
- Update guidance
  - Regulatory Guide (RG) 8.39
  - NUREG-1556 Volume 9

3

Current Status

- Staff drafted Office of Management and Budget (OMB) clearance package for publication in the *Federal Register*

4

2015 Milestones

- OMB publication (60 days)
- NRC issue FRN to solicit information (60 days)
- NRC hold workshops to solicit information (several months)
- Develop website

5

2016+ Milestones

- NRC hold workshops to solicit information on potential rulemaking and guidance
- Draft Commission Paper
- Revise RG 8.39 and NUREG-1556 Volume 9

6

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

History and Background of the Term "Patient Intervention"

Sandy Gabriel, Ph.D.
NRC Medical Radiation Safety Team
March 19, 2015

10 CFR 35.2

Patient intervention **means actions by the patient or human research subject, whether intentional or unintentional, such as dislodging or removing treatment devices or prematurely terminating the administration.**

2

History

<u>Concept</u> of patient intervention has been used since misadministration was defined in Part 35 in 1980, however the <u>term</u> was not added to the regulation until 2002.

3

1980 Misadministration Rule

Letter to licensees used the term "patient intervention" in discussion of hypothetical situations involving intentional patient action such as pulling off a treatment mask or stopping attending treatment sessions.

4

1980 Letter to Licensees

"If the patient stops attending treatment sessions and the total prescribed dose is not delivered, has a misadministration occurred?

No, patient intervention in the treatment plan is not a misadministration under the rule."

5

1992 QM Rule

- **Silent on patient intervention.**
- **Letter to licensees included no examples involving patient intervention.**
- **Determinations of patient intervention were made on a case-by-case basis.**

6

SOC for 1998 Proposed Rule

- **Identified patient intervention as problem area in implementing misadministration reporting requirements.**
- **"The licensee is expected to act reasonably, in accordance with prevailing standards of care, to prevent a medical event....In cases where patient intervention is probable, the licensee should take reasonable actions (e.g., extra suture, taping, or more frequent checks by the nursing staff) to avoid a medical event."**

7

1998 Proposed Rule

- **Proposed wording: "A licensee shall report any administration, except for administrations resulting from a direct intervention of a patient or human research subject that could not have been reasonably prevented by the licensee....."**
- **Federal Register Notice requested specific input from the public on whether the proposed changes adequately addressed patient intervention.**

8

SOC for 2002 Final Rule

- **Phrase "that could not have been reasonably prevented by the licensee" was deleted; commenters said it was ambiguous, subjective and infringed on the practice of medicine.**
- **Requirement added to report events caused by patient intervention that resulted in serious consequences (unintended permanent functional damage, as determined by a physician)**

9

SOC for 2002 Final Rule

- **Defined patient intervention to mean "intentional or unintentional actions taken by a patient or human research subject, such as dislodging or removing treatment devices or prematurely terminating the administration."**
- **Reiterated the expectation that licensees should continue to act reasonably to prevent medical events caused by patient intervention.**

10

2002 Final Rule

10 CFR 35.3045(a)

A licensee shall report any event, except for an event that results from patient intervention, in which the administration of byproduct material or radiation from byproduct material results in.....

11

2002 Final Rule

10 CFR 35.3045(b)

A licensee shall report any event resulting from intervention of a patient or human research subject in which the administration of byproduct material or radiation from byproduct material results or will result in unintended permanent functional damage to an organ or a physiological system, as determined by a physician.

12

Examples: Formal Case Reviews

- Most common:
  - Patient prematurely removed brachytherapy applicator.
  - Implant ribbon or applicator was accidentally dislodged due to patient motion.
- Unusual:
  - Patient surreptitiously removed I-131 capsule from mouth and concealed it.

13

IN 2006-11

"Applicability of Patient Intervention in Determining Medical Events for Gamma Stereotactic Radiosurgery and Other Therapy Procedures"

- Displacement of head frame by patient movement resulted in dose to unintended site.
- Two cases described
  - Head frame was displaced by 7 cm in Z-axis dimension when patient moved "vigorously."
  - Treatment performed using 3-pin technique to avoid collision with 4th pin. Patient coughed, with isocenter shift of 6 mm.

14

IN 2006-11

- Both licensees believed patient movement constituted patient intervention.
- NRC viewed events as resulting primarily from patient equipment setup.
- NRC suggested that licensees consider:
  - Monitoring patient and/or source placement at frequent intervals.
  - Taking prompt and appropriate actions when displacement is identified.
  - Having trained personnel present or available to prevent or mitigate patient actions that may impact treatment.

15

2014 Proposed Rule

No changes related to patient intervention.

16

Acronyms

- **CFR – Code of Federal Regulations**
- **I-131 – Iodine-131**
- **QM – Quality Management**
- **SOC – Statements of Consideration**

17

Patient Intervention
NRC and ACMUI in Alignment?

Frank Costello
ACMUI Meeting
March 19, 2015

Patient Intervention: Past Experience

- “Patient intervention" has been viewed by the NRC as involving patient behavioral actions (intentional or unintentional) rather than physiological phenomena.
- The fact that a patient’s anatomy may have resulted in radioactive materials going to unanticipated locations does not constitute “patient intervention”.

ACMUI Expressed Thoughts

- Official definition of “patient intervention”… is another case of regulatory terms not being in alignment with the various connotative and denotative meanings of the same term as used in the medical community.
- As an example, what do “actions” and ”intentional” or ”unintentional” mean?

ACMUI Expressed Thoughts

- Are these always patient physical actions or may they apply to physiological "actions" within the patient, such as hypotension, cardiac arrest or sudden flow changes in a vessel or yes, unexpected changes in patient anatomy (such as a "latent" vessel opening after vascular skeletalization)? These are surely unintentional, but may lead to a suboptimal treatment result.
- Such occurrences are neither the fault of the patient nor the AU/administering physician. What value is there in reporting them as medical events if they are unpredictable and nothing could be done to correct such events in the future?

ACMUI Expressed Thoughts

- If, during injection of microspheres, the patient's artery contracts and the spheres flow retrograde into the gastrointestinal artery, that too would be patient intervention.
- If the patient's lung shunt fraction was one value during the work-up and changed for the treatment, that also would be patient intervention.

Conclusions

- NRC and its Advisory Committee on the Medical Use of Isotopes seem to be in misalignment on the meaning of “patient intervention”.
- Important because this could lead to miscommunications when discussing medical events.
- Does whether the AU and/or the medical team did something wrong solely determine whether there was a medical event?

Acronym

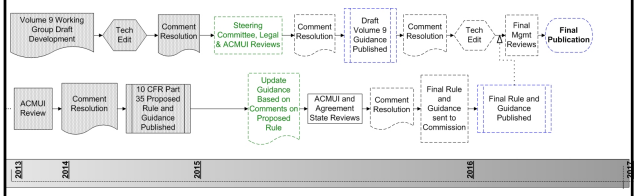
AU – Authorized User

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

NUREG 1556 Volume 9

Ashley Cockerham
Medical Radiation Safety Team

Timelines



Summary of Significant Changes

- **Comments received but not addressed during Revision 2**
- **Comments received from regulatory staff and the public since the publication of Revision 2**
- **Updates to references and other guidance documents in NUREG 1556 Volume 9**
- **Updates to reflect the general move from hard copy to electronic-based systems**

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

Status of Medical Events FY 2013

Donna-Beth Howe, Ph.D.
Medical Radiation Safety Team
March 19, 2015

1

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

Medical Events 2014

- **43 Medical events reported - FY 2013**
- **46 Medical events reported - FY 2014**

	FY13	FY14
35.200	0	1
35.300	2	3
35.400	15	5
35.600	10	10
35.1000	16	27

2

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

Medical Events

The dose threshold for diagnostic events precludes reportable events most years.

Each year there are approximately 150,000 therapeutic procedures performed utilizing radioactive materials.

3

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

Medical Events 2014

35.200 Medical events **1**

Technetium-99m

- Administered entire multi dose vial 140 mCi to single patient
  - 6-7 cGY (rad) whole body

4

Medical Events 2014

35.300 Medical events **3**

Samarium 153 1

- Administered 39 microcuries to skin of arm
- Intended 100 microcuries intravenously

Radium – 223 1

- Error in writing millicuries in written directive
- administered micro curies

5

35.300 Medical Events

I-131 1

- 30 millicuries delivered to wrong patient
- Patient was given bracelet id of another patient
- Authorized User did not use another identifier to confirm the patient was correctly identified
- 728 cGy(rad) to the thyroid

6

Medical Events 2014

35.400 Medical events **5**

Gynecological 1

Prostate 4

7

35.400 Medical Events

Gynecological Cs-137 1

- Dislodged applicator
- Treatment time 49.5 hours – planned 63.1
- Treatment site received 78% of intended dose
- inner thighs received up to 1,509 cGy (rad) expected 652 cGy (rad).

8

35.400 Medical Events

Prostate 4

- Air Kerma - received 18,400 cGy (rad) instead of the prescribed 14,500 cGy (rad) medical physicist mistakenly ordered using mCi instead of the air kerma value.
- Some seeds inadvertently implanted into the scar tissue - 54% of prescribed dose delivered to treatment site

9

35.400 Medical Events

Wrong Site - Ultrasound Issues 2

- Seeds implanted 3.5 cm inferior from the target location 29.31% of the prescribed dose was delivered to the target tissue.
- 88 seeds were implanted in penile bulb 34 seeds prostate gland attending urologist mistook the penile bulb for the prostate gland

10

Medical Events 2014

35.600 Medical events **10**

HDR 9

- Skin 2
- Bronchial 1
- Not designated 2
- Pelvic 1
- OBGYN 3

Gamma knife 1

11

Medical Events 2013

35.600 Medical events

HDR **9**

- Wrong Site 3
- Wrong Patient 1
- Decay correction 1
- Right patient wrong treatment plan 1
- Source Retraction 1
- Wrong dwell time 1
- Wrong interpretation of dose per fraction 1

12

35.600 Medical Events

HDR Wrong Site 3

- **OBGYN** - wrong location during three treatment fractions of 700 cGy (rad) per fraction
- During follow-up visit burns observed to the skin on the patient's thighs and labia.
- The estimated skin dose received by the patient was 4,200 cGy (rad).
- the source was 100 mm short of the intended treatment site due to Source reference length error,.

13

35.600 Medical Events

HDR Wrong Site cont.

- **Broncial/tracheal -** each fraction had two segments, a distal portion using a simple catheter and a proximal portion using a centering catheter.
- In 1st fraction the centering catheter was positioned incorrectly
- Treatment offset of 9 cm superior to the intended treatment site

14

35.600 Medical Events

HDR Wrong Site cont.

- **OBGYN** - first of three fractions vaginal cylinder position checked with planar digital x-ray image and unusual inferior cylinder placement was noted, attributed to special patient anatomy.
- On next fraction vaginal cylinder was approximately 5 cm superior to the first treatment..
- dose in 1st fraction to unintended tissue was 900 cGy (rad) and 100 cGy (rad) was to the intended tissue.

15

35.600 Medical Events

HDR Wrong Patient – Skin 1

- physicist selected a different patient's treatment plan with shorter channel length
- The correct site and applicator were used
- Recognized error when time was too long – manually stopped procedure
- Intended treatment site received less than half of the 500 cGy (rad) intended dose,
- Area adjacent to the intended site received a maximum dose of 2,300 cGy (rad) to a single point and 1,000 cGy (rad) to a 1 cm radius and 4.5 mm depth

16

35.600 Medical Events

HDR Decay correction – Skin 1

- Decay corrected value for the source activity was used in data entry for the treatment plan.
- HDR software also corrected for decay in determining the exposure time for the fraction
- patient received approximately twice the prescribed 600 cGy (rad) during a skin treatment

17

35.600 Medical Events

HDR Wrong Treatment Plan – 1

- Two Ir-192 high dose rate (HDR) fractions of 700 cGy (rad) each
- The patient returned for the second fraction and treatment plan for the first fraction instead of the second fraction was loaded.
- 700 cGy (rad) to 60% of intended dose received by planned volume.

18

35.600 Medical Events

HDR Source retraction – Pelvic 1

- Received 5.94 cGy (rad) of the prescribed 300 cGy (rad),
- First fractions, unexpected resistance detected in moved to the second dwell position.
- HDR unit detected a delay and automatically retracted the source.
- The dummy source wire could not traverse the pathway and the treatment was abandoned.

19

35.600 Medical Events

HDR Dwell time – unspecified 1

- Before third of six fractions an error was identified in planning the correct dwell position for the first two fractions.
- Corrective actions included updating procedures to provide all catheter measurements, producing a checklist of necessary equipment for the operating room, briefing staff physicists in utilizing the equipment, and hiring additional staff.

20

35.600 Medical Events

HDR Wrong interpretation of dose per fraction – OBGYN 1

- Intended treatment was three fractions of 500 cGy (rad) each
- During the second of three fractions error noted
- Treatment plan was set to deliver three fractions for a total of 500 cGy (rad)
- Cause was attributed to human error.

21

35.600 Medical Events

Gamma knife 1

- Two similar patients arrived and had head frames attached
- Scheduling change to treat only patient 2 was made with out communicating the change to nursing staff
- Patient identification was not checked
- Physician realized mistake 2 minutes into the treatment
- 175 cGy (rad) to the wrong site.

22

Medical Events 2014

35.1000 Medical events 28

Perfexion		**1**
I-125 Seed localization		**1**
Y-90 Microspheres		**24**
SirSphere®	15	
Therasphere®	9	
Gliasite		**1**

23

35.1000 Medical Events

Perfexion 1

- Treatment prescribed for left side of brain.
- Treatment planner set up plan for right side of brain as done for two previous treatments
- Incorrect treatment plan was reviewed and signed
- The treatment stopped at 1.72 minutes into the 19.14 minute procedure.
- Approximately 1,800 cGy (rad) deliver to wrong site.

24

35.1000 Medical Events

I-125 Seed localization 1

- received two I-125 seeds when only one was intended.
- The patient had two marker clips, one for benign biopsy site and other for a papilloma.
- the benign site was marked with a 9.32 MBq (252 µCi) I-125 seed
- The unintended dose from two days seed placement was 61 cGy (rad) at 0.5 cm

25

35.1000 Medical Events

Y-90 Microspheres **24**

SirSphere ® **15**

- Wrong site 2
- Written Directive 1
- 3-Way Stopcock 2
- Bubbles 1
- Contamination 1
- Transfer error 1
- Occluded /kinked catheters 6
- No Information 1

26

35.1000 Medical Events

SirSphere® Wrong Site **2**

- **Duodenal Ulcer**
  - First of 3 treatments – 36.2 mCi (1,339 MBq)
  - Duodenum lesion and an ulcer that had developed seemingly as a result of microspheres migrating to the stomach.
  - A biopsy of the affected region revealed synthetic beads.
  - Aberrant hepatic arterial vasculature supplying the stomach.

27

35.1000 Medical Events

SirSphere® Wrong Site cont.

- **Gastric fundus**
  - 1,100 cGy (rad) to the gastric fundus
  - Prescribed microspheres to the right liver lobe
  - Stopped when unanticipated shunting was identified.

28

35.1000 Medical Events

SirSphere® Written Directive 1

- **Over dose 36,300 rad instead of 10,200 rad**
  - Authorized user provided radiopharmacist with an incorrect version of the written directive treatment form
  - failure to follow all procedures and the defeat of normal checks and balances that should have identified the incorrect dosage

29

35.1000 Medical Events

SirSphere® 3 Way Stopcock 2

- **45.8 % under Dose**
  - Majority of undelivered Y-90 in and around the 3-way stop
  - 3-way stop system was defective
- **29.7% under dose**
  - Microspheres in the tubing near the stop cock valve
  - Dextrose not Saline

30

35.1000 Medical Events

SirSphere®

- **75 % under Dose**
  - Noticed bubbles in the administration line during the treatment and stopped.
- **44.7 % under dose**
  - elevated readings at the catheter/vial interface - coagulation of microspheres.
  - contamination on physician's glove and table

31

35.1000 Medical Events

SirSphere®

- **34 % under Dose**
  - Error transferring microspheres from the delivery vial to the dosing via.
- **22.7 % under dose**
  - Larger than expected amount of microspheres remained in the needle and tubing and did not reach the patient.

32

35.1000 Medical Events

SirSphere®

- **22.5 and 30 % under Dose**
  - Split dose, not detected until end of both.
  - Blockage in the delivery system.
- **25 % under dose**
  - catheter clogged halfway through the procedure
  - catheter removed, replaced, and remaining microspheres administered

33

35.1000 Medical Events

SirSphere®

- **41% under Dose**
  - Same lobe but two different arterial pathways.
  - No microspheres delivered to second part.
  - Short arterial segment and the acute angle at the arterial origin, with possible manipulation or patient movement, resulted in a kink or fold

34

35.1000 Medical Events

SirSphere®

- **41.1% under Dose**
  - blockage
  - Not problem with administration kit .
  - Significant number of kinks, bends, clots, and other blockages at catheter tip
- **32.2 under Dose**
  - last bolus could not be pushed through

35

35.1000 Medical Events

SirSphere®

- **38% under Dose**
  - No information provided

36

35.1000 Medical Events

Y-90 Microspheres cont.

Therasphere ® 9

- Wrong site 2
- Reflux & Precipitated out 1
- Dosage error 1
- Remained in vial 1
- Settle out /kink 4

37

35.1000 Medical Events

Therasphere® Wrong Site 2

- **SHUNTING** - Two tumors right and left lobes
  - Tested right hepatic artery found shunting - intended 370 cGy (rad) to lung
  - Treated left lobe through left hepatic artery – untested shunting
  - lungs received 3,450 cGy (rad)
  - Patient died 5 months later

38

35.1000 Medical Events

Therasphere®

Wrong site - Catheter Position Error

- Could not properly position the catheter for Segment IV
- Bilateral disease that would eventually require the treatment of both lobes
- 0.81 GBq (21.8 mCi) to Segment IV and 0.91 GBq (24.5 mCi) in the right lobe.

39

35.1000 Medical Events

Therasphere®

Reflux & Precipitated out

- 24 % under dose – noted some reflux into the common hepatic artery/gastroduodenal artery.
- reduced flow rate during administration process, which resulted in the precipitation of microspheres along the outflow tube

40

35.1000 Medical Events

Therasphere®

Dosage error over dose

- Written directive for 20 % less activity.
- Reviewed treatment plan but verified standard activity not prescribed activity

41

35.1000 Medical Events

Therasphere®

- **20% remained in vial**
- **44% under dose**
  - Targeting vessel was flowing slowly
  - Microspheres to settle out prior to reaching the target.
- **73 % under dose**
  - Wrong catheter - kinking

42

35.1000 Medical Events

Therasphere®

- **23.5% under dose**
  - Microspheres adhered to the connector and first one inch of manufacturer supplied tubing
- **28.7% under dose**
  - kink in the delivery catheter - created blockage
  - thinner, more flexible catheter walls and a small internal catheter diameter were contributing factors.

43

35.1000 Medical Events

GliaSite

- **No dose to treatment site**
  - The balloon had not inflated incorrectly positioning a three-position stopcock
  - I-125 saline solution being diverted to another syringe instead of filling the balloon.
  - The stopcock was not part of the vendor's kit

44

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

Acronyms

- FY – Fiscal Year
- HDR – High Dose Rate Remote Afterloader
- mCi – millicurie
- MBq – Mega Becquerel
- Pts - Patients
- Y – Yttrium
- I-131 – Iodine-131

45

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

QUESTIONS?

46

Radiation Safety and Regulatory Issues for Radioactive Seed Localization (RSL) of Non-Palpable Lesions

Michael Sheetz
Radiation Safety Officer
University of Pittsburgh

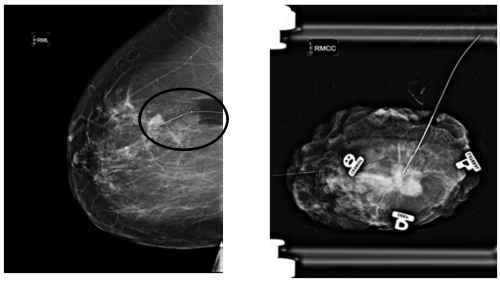
Purpose

- Initiated RSL program under broad scope license in 2011 - Currently performing over 100 RSL procedures each month at six different sites
- Feedback from user community that strict compliance with NRC RSL licensing guidance makes it difficult to establish program
- Revisions to licensing guidance will make it more relevant to RSL procedure and increase access for patients

Background

- Advances in screening mammography have led to increased detection of microscopic breast lesions
- Traditional method to pinpoint non-palpable lesion for surgical excision is Wire Localization Breast Biopsy (WLBB)
- Radioactive Seed Localization (RSL) developed as an alternative technique
- Studies have shown benefits of RSL over WLBB

Wire Localization Breast Biopsy

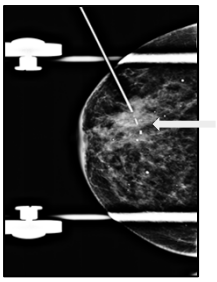


RSL Iodine-125 Seed

- Same seed used for brachytherapy
- Available in individual preloaded sterile 18 ga needle
- FDA approved for RSL
- Assayed activity ≈ 200 µCi

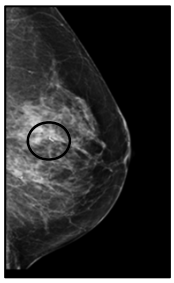
Radioactive Seed Localization

- Seed implanted by radiologist under ultrasonic or mammographic guidance
- Seed cannot be repositioned
- Rare incidence of seed migration



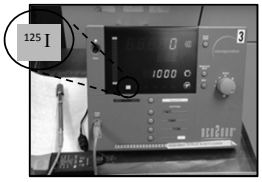
I-125 Seed Implant

- Confirmatory mammogram to verify seed placement
- Survey of patient and implant area
- Surgery typically scheduled within 5 days



Surgical Excision of I-125 Seed

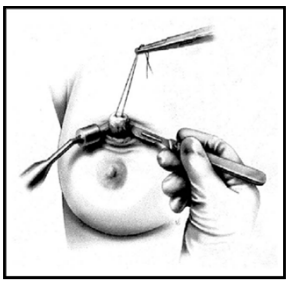
- Gamma probe used to localize seed and lesion
- Surgeon determines best incision site



Ann Surg Oncol, Vol. 10, No. 9, Oct 2003, p. 1039-1047

Surgical Excision of I-125 Seed

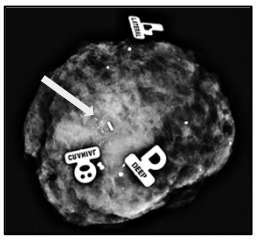
- Gamma probe provides audible feedback to guide excision of lesion
- Tissue specimen surveyed to confirm presence of radioactive seed



Ann Surg Oncol, Vol. 10, No. 9, Oct 2003, p. 1039-1047

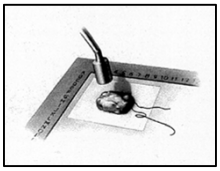
Steps After Resection of Lesion

- Specimen radiograph taken to confirm presence of seed(s)
- Specimen transported to pathology for sectioning and seed removal

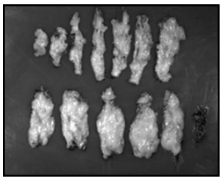


Pathology

- Seed(s) located in specimen using gamma probe
- Specimen sectioned using scalpel

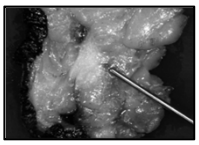


Ann Surg Oncol, Vol. 10, No. 9, Oct 2003, p. 1039-1047



Seed Retrieval

- Seed removed with reverse action tweezers
- Placed into container and labeled with patient tracking number
- Specimen scanned before release



Benefits of RSL

- Reduced incidence of positive margins compared to wire localization
- Improved surgical approach with better cosmetic outcomes
- Less pain and discomfort for patient
- Eliminates scheduling conflicts between surgeon and radiologist

Regulatory Oversight

- RSL covered under 10 CFR 35.1000 or Agreement State equivalent
- NRC licensing guidance:

  "I-125 and Pd-103 Low Dose Rate Brachytherapy Seeds Used for Localization of Non-palpable Lesions"

- Must meet other applicable requirements in Part 35

Issues for Compliance with NRC Part 35.1000 RSL Guidance Document

- Training and Experience Requirements for Authorized User
- Written Directive
- Radiation Surveys
- Medical Event
- Survey Instrumentation
- Commitments to Certain Safety Precautions

Training and Experience Requirements for Authorized User (AU)

- Radiologist vs Radiation Oncologist
  - Supervised in 3 cases by 35.490 approved AU
  - Work experience in surgical excision and seed removal
- Only AU may implant seed?
  - Work under the "supervision" of AU (35.27)

Written Directive

- RSL is a diagnostic procedure and not intended for therapeutic dose – 35.40(a)
  - 9 days to deliver 50 rem at 1 cm for 200 µCi seed
- Documentation requirements in 35.40(b)(6) for manual brachytherapy are not applicable
- Use of a "prescription" to define procedure

Radiation Surveys

- Documentation of surveys after seed implant and removal
- Interference from Tc-99m sentinel node injection
- Confirmatory specimen radiograph satisfies survey requirements

Medical Event

- Dose threshold of 50 rem to tissue unlikely
- No prescribed dose (limit of 5 days)
- Patient does not return – patient intervention?

Time Since Implant (days)	Rem	
	r = 1 cm	r = 3 cm
1	6	0.4
2	11	0.8
3	17	1.2
4	22	1.6
5	28	2.0

Peak Radiation Dose to Breast After Implant of 200 µCi I-125 Seed

Survey Instrumentation

- Thin crystal NaI vs GM vs Gamma Probe
- Gamma Probe calibration

Commitment to Requirements for Certain Safety Procedures

- Verification of Seed Activity – Provision for 32.72 licensee assay
- Annual training on topics in 35.410 – Patient meets release criteria in 35.75
- Change in physical conditions of use – Now FDA approved
- Emphasis on emergency response to cut or leaking source – Rare occurrence with minimal radiological impact

Other RSL Adverse Events

- Loss of radioactive seed
- Implant of a radioactive seed in the wrong location or patient
- Inability to locate an implanted seed during surgery
- Patient implanted with radioactive seed does not return for scheduled surgery

Conclusions

- RSL of non-palpable breast lesions offers clinical and patient care advantages over WLBB
- Strict compliance with current NRC licensing guidance is difficult
- Revision of licensing guidance will allow increased patient access to RSL procedure while maintaining high level of safety

Acronyms

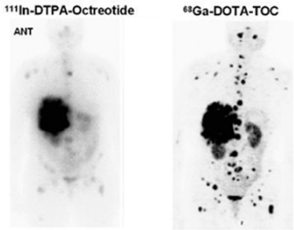
- AU – Authorized User
- FDA – U.S. Food and Drug Administration
- GM – Geiger Muller
- I-125 – Iodine-125
- NaI – Sodium Iodide
- Pd-103 – Palladium-103
- RSL – Radioactive Seed Localization
- WLBB - Wire Localization Breast Biopsy

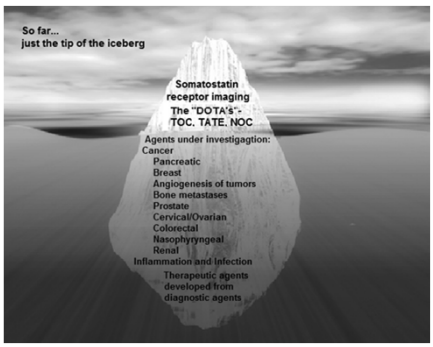
ACMUI Ge/Ga-68 Subcommittee Report

Susan Langhorst, PhD
Pat Zanzonico, PhD
Chris Palestro, MD
Frank Costello
Steve Mattmuller, Chair

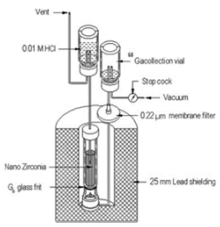
March 19-20, 2015

Ga-68 Radiopharmaceuticals





Ge-68/Ga-68 Generator



Ge-68/Ga-68 Regulatory Issue

§ 30.35 Financial Assurance and recordkeeping for decommissioning.

(a)(1) Each applicant for a specific license authorizing the possession and use of **unsealed** byproduct material of half-life greater than **120 days** and in quantities exceeding **10^5 times** the applicable quantities set forth in **appendix B** to part 30 shall submit a decommissioning funding plan as described in paragraph (e) of this section.

5

Lost in Translation*; 1991 vs. 1993 vs. 2005?

Quantities of Licensed Material Requiring Labeling		
Byproduct Material	Appendix C to Part 20 (uCi)	**Appendix B to Part 30 (uCi)**
F-18 T-$^1/_2$ 110 min	1,000	**1,000**
Mo-99 T-$^1/_2$ 2.8 days	100	**100**
Ge-68 T-$^1/_2$ 271 days	10	

*Redesignated at 56 FR 23391, May 21, 1991, and further redesignated at 58 FR 67659, Dec. 22, 1993.
2005: Definition of byproduct material is expanded to include accelerator produced radionuclides

6

Ge/Ga-68 Subcommittee: Charges

- **Evaluate the cost of a Decommissioning Financial Plan (DFP) for the use of Germanium-68**
- **Provide examples/recommendations on how regulatory relief may be gained**
- **Evaluate how this DFP will affect the future clinical use of new Gallium-68 pharmaceuticals**

7

Evaluate the cost of a DFP

Requests: - Nuclear Pharmacy Chains
- Health Physics Consulting Firms

D.I.Y.: NUREG-1757, Vol. 3, Rev.1: Consolidated Decommissioning Guidance Financial Assurance, Recordkeeping, and Timeliness

DFP: Covers not just the use of Ge-68, but all uses of radioactive material at all locations of use under the license.

8

DFP experience: large, multi-site university hospital

"extensive and expensive"

- "Resource demands go far beyond the costs associated with the generation and maintenance of a financial assurance instrument itself, which can be in the thousands of dollars in creation fees and more thousands in annual maintenance fees."
- "Most substantial costs are in manpower demands in the generation of the DFP itself."

  "140 person-hours"

  "I am probably underestimating this"

9

DFP experience: large, multi-site university hospital

- "Manpower costs to the institution from other areas."
- "Once submitted, the DFP is reviewed by the State with a site visit."

  "significant resource demands on regulatory agencies related to review and ultimate approval of DFP's"
- "State's initial review resulted in comments that required further demands on institutional resources."

  "site visit interactions and plan revisions cost at least another 30 person-hours"
- "Financial assurance instrument in the amount of $1,125,000 would be needed."

10

DFP experience: large, multi-site university hospital

"Many hospitals will not have the in-house expertise to deal with the DFP issue, and if they do have to pursue DF planning, will likely need to hire consultants, adding further to their costs."

"The restrictive aspects arising from the current Part 30 situation may therefore prevent or deter use of promising imaging agents for patients due to the decommissioning funding burden."

11

Regulatory Relief: Rulemaking

- Add the same value for Ge-68 of 10 uCi that exists in appendix C Part 20 to appendix B Part 30!
- Direct Final Rulemaking (DFR)
- Problem: This is not a safety concern or a security concern, this is a patient concern. Due to an unintentional omission of a value in appendix B Part 30 for Ge-68, a DFP is now required for the possession of a Ga-68 generator. The cost of a DFP can be a prohibitive financial barrier to a licensee and will deter the safe and effective use of Ga-68 in patients.

12

Regulatory Relief: Rulemaking

- What has changed that causes the current regulation or policy to be insufficient?

  "Increase in use of Ga-68"
- What new information causes the NRC to question the current regulation or policy?

  "DFP's deleterious effect"
- What is the regulatory insufficiency or gap that needs to be addressed?

  "Missing value in appendix B"

13

Regulatory Relief: Rulemaking

- Why does the insufficiency or gap warrant being addressed?

  "Patient access"
- Why is a change needed if there is no regulatory gap to be addressed?

  "Gap does exist and it has very expensive consequences."

14

Alternate: Revise Guidance

- Revise NUREG-1556 Vol.3, Rev.1 Consold. Guidance About Materials Licenses: "Sealed Sources and Devices"
- Fit under a "custom sealed source or device"
- Fit under "sealed sources and devices for medical uses"

-- § 32.74 Manufacture and distribution of sources or devices containing byproduct material for medical use. (a)(2)(iii) Procedures for, and results of, prototype tests to demonstrate that the source or device will maintain its integrity under stresses likely to be encountered in normal use and accidents;

-- § 35.1000 Other medical uses of byproduct material or radiation from byproduct material.

15

DFP affect clinical use Ga-68

- A regulatory "quirk" a "unintentional omission"
- DFP's negative effect on three licensees in regards to research, the most recent a large university based hospital.

"The restrictive aspects arising from the current Part 30 situation may therefore prevent or deter use of promising imaging agents for patients due to the decommissioning funding burden."

16

DFP affect clinical use Ga-68

- In the US, NET patients are treated on an average of 3-7 years for the wrong disease. Most are diagnosed when the cancer has already spread.
- http://netcancerday.org/support-us/net-cancer-day-selfies
- Tip of the iceberg:

17

Summary…

- Evaluate the cost of a DFP:
  - "Prohibitive"
- Regulatory relief:
  - "DFR or a revised Guidance"
- Affect future clinical use of new Gallium-68 pharmaceuticals:
  - "Yes it will, first NET patients, then prostate cancer patients"

18

Acronyms

- **DFP – Decommissioning Funding Plan**
- **DFR – Direct Final Rulemaking**
- **DIY – Do It Yourself**
- **F-18 – Fluorine-18**
- **FR – Federal Register**
- **Ga-68 – Gallium-68**
- **Ge-68 – Germanium-68**
- **Mo-99 – Molybdenum-99**
- **NET – Neuroendocrine Cancer**

19

Yttrium-90 Microspheres and Radionuclides in Cadavers

Pat Zanzonico, PhD, DABR
ACMUI

Outline

- General considerations
- Pertinent properties of radionuclide-therapy and brachytherapy isotopes
- "To-Do" immediately post-expiration
- Final-disposition scenarios
- Guidance and Standards
- Concluding remarks

General Considerations

- Death of radionuclide therapy or brachytherapy patient immediately post-treatment is rare - Moribund patients excluded

^{125}I seed brachytherapy for prostate cancer, Japan:
0.3% early deaths
(within 12 months of Tx)

Satoh et al. Brachytherapy, 2011

- Any single mortuary, funeral home, or crematorium: 1 to at most several radioactive cadavers annually

General Considerations cont

- General radiation protection principles - time, distance, shielding, and contamination control - apply
- Radiation risks case-dependent but generally minimal

General Considerations cont

- **No precautions/special handling post-diagnostic administrations**
- **Sensitivity to deceased's family and their wishes - Address pre-treatment**
- **Guidance of RSO critical @ hospital, funeral home, crematorium**

Death of Patient Outside Treating Facility

- **Contact treating facility for guidance**
  - **Patient's wallet card**
  - **RSO, Treating physician**
- **For current outpatients, retained activities likely do not warrant precautions**

Radionuclide Therapy: Unsealed Sources

	Radionuclide	Physical Half-life	Radiations	Diseases Treated	Form	Route of Administration	Administered Activity (mCi)
	^{131}I	8.04 d	364-keV γ-rays	Hyperthyroidism	Iodide	Oral, iv	10
			606-keV β-rays	Thyroid cancer	Iodide	Oral, iv	30 - ≥100
				Neuroblastoma	MIBG	iv	≥100
				Lymphoma	Tositumomab (Bexxar®)	iv	100
No external hazard	^{90}Y	2.7 d	2.3-MeV β-rays	Arthritis	Colloid	Intra-articular	5-10
	Long-lived radiocontaminants!			Liver cancer	Resin microspheres (Sir-Spheres®)	Intra-hepatic	20-40
					Glass microspheres (TheraSpheres®)	Intra-hepatic	60-100
				Lymphoma	Ibritumomab (Zevalin®)	iv	25-30
				Carcinoid	Lanreotide	iv	200-250
	^{32}P	14.2 d	1.7-MeV β-rays	P vera	Phosphate	iv	5
	^{89}Sr	51 d	1.5-MeV β-rays	Bone metastases	Chloride (Metastron®)	iv	4
	^{153}Sm	46.2 h	100-keV γ-rays	Bone metastases	EDTMP (Quadramet®)	iv	60-80
			600- to 800-keV β-rays				
Minimal external hazard	^{223}Ra	11.4 d	12- to 270-keV γ-rays	Bone metastases	Radium dichloride (Xofigo®)	iv	0.1
			5-MeV α-rays				

Brachytherapy: Sealed Sources

Radionuclide	Physical Half-life	Radiations	Half-value Layer (mm lead)	Exposure rate Constant, Γ (R cm2/hr/mCi)	Form	Comment
Temporary → **Remove post-mortem - No subsequent hazard**						
^{226}Ra	1600 y	83-keV photons	12	8.3	Tubes, needles	Intracavitary, intraluminal; No longer used
^{137}Cs	14.2 d	662-keV photons	6.5	3.2	Tubes, wires, seeds	Intracavitary, intraluminal
		1.2-MeV β-rays				
^{192}Ir	51 d	0.14- to 1.1-MeV photons	3	4.6	Seeds in ribbons, wires	Intracavitary, intraluminal, interstitial including afterloading
		670-keV β-rays				
^{90}Sr + ^{90}Y	28.7 y	2.3-MeV β-rays	NA	NA	Plaques	Topical: malignant, benign eye diseases
^{106}Ru	11.4 d	3.4-MeV β-rays	NA	NA	Plaques	Topical: malignant, benign eye diseases
^{60}Co	5.25 y	1.3-MeV photons	12	13	Plaques, needles	Intracavitary, intraluminal
^{169}Yb	32 d	93-keV photons	0.48	3.3	Seeds	Intracavitary, intraluminal, interstitial including afterloading; Future use
Permanent → **Post-mortem radiation hazard**						
^{222}Rn	1600 y	83-keV photons	12	8.3	Tubes, needles	Interstitial; No longer used
^{125}I	60.1 d	20- to 40-keV photons	0.025	1.5 *Minimal external hazard*	Seeds	Interstitial; Widely used in prostate cancer
^{103}Pd	17 d	20-keV photons	0.008	0.86	Seeds	Interstitial including afterloading
^{198}Au	2.7 d	412-keV photons	3.3	2.4	Seeds	Interstitial; No longer in common use
		For comparison, ^{131}I:	3.0	2.2		

Immediately Post-Expiration

- **Notify RSO and Nuclear Medicine/ Radiation Oncology**
- **For radionuclide Tx, place cadaver in body bag to contain radioactive fluids**
- **Document radioisotope, administered activity, date and site of administration, and treating institution's contact information**
  - **On body bag**
  - **On cadaver ("toe tag")**

Immediately Post-Expiration cont

- **Radiation survey (RSO)**
  - **Exposure rates (mR/hr) @ contact, 30 cm, and 1 m**
- **Formulate short-term precautions (RSO)**
  - **Permissible procedures and duration of procedures to maintain doses < MPDs**

		Exposure Rate in Air (mR/hr)		Time to Reach 100 mrem (hr)		Time to Reach 500 mrem (hr)	
Radioisotope	Activity (mCi)	30 cm	1 m	30 cm	1 m	30 cm	1 m
^{103}Pd (implant)	40	33	3	3.0	33	15	167
^{125}I (implant)	9	11	1	9.1	100	45	500
^{131}I	33	78	7	1.3	14	6.4	71
	150	355	32	0.3	3	1.4	16

Classic. In Handbook of Autopsy Practice, 4th ed, 2009.

Immediately Post-Expiration cont

- **Remove**
  - **Radioactive solutions/suspensions from accessible cavities (Nuclear Medicine) / Disposal down drain**
  - **Temporary implants (Radiation Oncology)**

If cadaver still radioactive

- **Document radioisotope, administered activity, date and site of administration, treating facility's contact information, and exposure rates**
  - **On body bag**
  - **On cadaver ("toe tag")**
- **Place cadaver in posted, isolated area in mortuary**

Final Disposition of Radioactive Cadavers

- **Autopsy**
- **Transplantation**
- **Embalming**
- **Visitation (wake)**
- **Burial**
- **Cremation**

Autopsy

- **Follow RSO guidance**
- **Avoid or consider limited autopsy**
- **PPE: Doubled disposable gloves, face shield, face mask, and apron (Radionuclide Tx)**
- **Shielded receptacles for sources and contaminated items**
- **Removal of high-activity organs? Case-specific but generally not recommended**

Transplantation

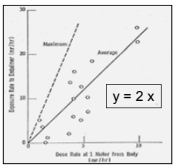
- **Post-therapy activity not a contraindication**
  - **Targeted/diseased organs excluded**
- **RSO guidance**
  - **Dose to transplanted organ: Doses to heart, kidney, liver sub-toxic**
  - **Doses to recipient**
- **Transplantation life-saving and donor organs in short supply → No dose limit for recipient**

Embalming

- **Follow RSO guidance**
- **PPE**
- **≤ 25 mrem per embalmed cadaver (NCRP No 155)**
- **Dose rate @ 30 cm < 50 mrem/h: No restrictions (NCRP No 155)**
- **Brachytherapy patients**
  - **No restrictions generally**
- **Radionuclide-therapy patients**
  - **Embalming fluid down drain**

Embalming cont

	Dose to Embalmer (mrem/mCi)		Activity to Reach (mCi)			
			100 mrem		500 mrem	
Radioisotope	mean	maximum	mean	maximum	mean	maximum
^{192}Ir	1.7	7.1	59	14	294	70
^{198}Au	0.48	2.1	208	48	1,042	238
^{131}I	0.54	2.3	185	43	926	217



Survey-meter measurement @ 1 m is a reliable metric of mean embalmer dose rate

Laughlin et al. Health Physics 15, 1968.

Visitation (Wake)

- **Dose limit: 500 mrem (NCRP No 155)**
- **Brachytherapy patients**
  - **Current permanent-implant isotopes, ^{125}I and ^{103}Pd, emit low-energy photons**
  - **100 mrem: 10s of hours @ ≤ 1 m**
  - **No restrictions generally**
- **Radionuclide-therapy patients**
  - **β-emitting (^{90}Y, ^{32}P, ^{89}Sr) and α-emitting isotopes (^{223}Ra): No restrictions**
  - **^{131}I problematic: Possible time and distance restrictions**
    RSO guidance
    Compliance?

Burial

- **Brachytherapy patients**
  - **No restrictions**
- **Radionuclide-therapy patients**
  - **No restrictions**

Cremation – The Most Problematic Final Disposition

- **Modern cremation**
  - **~2000 °F @ ~2000 cfm for ~2.5 h, 1-h cooling: Total air volume released = 11,000 m^3**
  - **Up to 10 lb of remains (ash)**
- **Sealed sources rupture Any activity dispersed**
- **Follow RSO guidance**
- **PPE**

Cremation - ^{125}I

- **Gaussian Plume Model (NCRP No 123)**
- **Example**

60 mCi ^{125}I in body, [^{125}I] @ stack: 6 μCi/m^3
All ^{125}I released: 5.6 μCi/s
10-m high stack, 2-m/s wind speed
→ Max [^{125}I] @ 130 m: 0.0045 μCi/m^3 ← *~1000-fold dilution*
Reference Man respiratory volume: 20,000 ml /min = 0.02 m^3/min
Over 3 h: 0.03 μCi ^{125}I inhaled → **ED = 0.75 mrem**

Que. J Appl Clin Med Phys, 2001

∴ **The body of ^{125}I prostate-implant patients can be cremated safely at any time**

Cremation - ^{90}Y Microspheres

- **Long-lived radiocontaminants**
  - **^{152}Eu: $T_{1/2}$ = 13.3 y, 39-keV - 1.4-MeV photons**
    ^{154}Eu: $T_{1/2}$ = 8.8 y, 43-keV - 1.3-MeV photons
  - **~10x more ^{152}Eu than ^{152}Eu - (n,γ) cross-sections**
  - **~10 μCi ^{152}Eu+^{154}Eu per ^{90}Y-microsphere dose**
- **Maximum ED from crematorium effluent: 220 - 2,200 mrem?**

Nelson et al. Health Physics 95 (Supplement 5): S156–S161; 2008
NRC Information Notice 2007-10, 2007

Cremation - ^{90}Y Microspheres cont

- **Re-calculated ED from crematorium effluent**
  assuming all radioeuropium inhaled by single individual

Europium Isotope	Inhalation Dose Conversion Factor * (Sv/Bq)	(mrem/μCi)	Cadaver Activity (μCi)	Effective Dose (rem)
^{152}Eu	4.20E-08	155	10	1,554
^{154}Eu	5.30E-08	196	1	196
			Total:	1,750

* ICRP Publication 98. Ann ICRP 41 (Suppl 1), 2012

- **Options**
  - **Prohibit cremation of ^{90}Y microsphere patients**
  - **Remove liver prior to cremation**
  - **More realistic dose analysis (Plume model)**

Guidance and Standards: US

- **NBS Handbook 65, 1958: If the body contains**
  - **> 5 mCi of any isotope - Autopsy should be done only with advice of RSO**
  - **< 30 mCi of any isotope - Embalming does not require any special precautions**
- **NRC, 10CFR35: "...notify the RSO and an AU as soon as possible if the patient...dies"**
- **CDC, Guidelines for Handling Decedents Contaminated with Radioactive Material, 2007: "Do not cremate a decedent whose body contains man-made radioactive material"**
- **NCRP No 155, 2007: RSO guidance for projected dose-based precautions**

Guidance and Standards: IAEA, 2007*

Isotope	Maximum Permissible Activity per Cadaver (mCi) Autopsy / Embalming	Burial	Cremation
^{131}I	0.27	11	11
^{90}Y	5.4	54	1.9
^{32}P	27	54	0.81
^{89}Sr	1.4	54	0.54

* **Subsequent IAEA publication (2014) did not specify any such MPAs, consistent with NCRP No 155**

Guidance and Standards: Cremation

- **Restriction period post-implantation**
  - **^{125}I: 1-y (Japan)* to 3-y (France)**
    - *** Implant must be removed prior to cremation**
- **Restriction activity**
  - **^{32}P: 11 mCi (Sweden, Australia)**
  - **^{90}Y: 27 mCi (Australia) to 32 mCi (Sweden)**
  - **^{125}I: 27 mCi (Australia)**
  - **^{131}I: 27 mCi (Australia) to 32 mCi (Sweden)**
- **Scattering of ashes: After 10 $T_{1/2}$s**

AAPM TG-56, 1997; ICRP Publication 98. Ann ICRP 35 (3), 2005; Singleton et al. Histopathology, 2007; Satoh et al. Brachytherapy, 2011

Concluding Remarks

- **Available guidance is sparse and somewhat outdated and contradictory**
- **Restrictions and other precautions should be based on measurement-derived projected doses - RSO guidance critical**
- **Cremation problematic, but any restrictions should be based on realistic dose models**

Abbreviations and Acronyms

cfm	cubic feet per minute
ED	Effective Dose
hr	hour
IAEA	International Atomic Energy Agency
min	minute
MPA	Maximum Permissible Activity
MPD	Maximum Permissible Dose
NCRP	National Council on Radiation Protection and Measurement
No	Number
PPE	Personal Protective Equipment
RSO	Radiation Safety Officer
$T_{1/2}$	Half-life
Tx	Therapy
y	year

Compatibility For Medical Event Reporting

Frank Costello, CHP

ACMUI Meeting
March 19, 2015

Short History Lesson

- March 28, 2013: ACMUI comments on proposed Part 35 amendments:
  - ✓ "The ACMUI and its Rulemaking Sub-Committee recommend that the draft rule re-defining medical events in permanent implant brachytherapy be designated as Compatibility Category B. This recommendation was approved by the ACMUI with one dissenting vote".

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Short History Lesson

- August 8, 2013: SECY 2013-84 proposes amendments to 10 CFR Part 35:
  - ✓ This rule proposed amendments to the reporting and notification requirements for a medical event (ME) for permanent implant brachytherapy.
  - ✓ NRC staff recommended that the Compatibility Category for reporting medical events remain as "C".

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Short History Lesson

- January 6, 2014: Commission issues SRM on amendments to 10 CFR Part 35
  - ✓ The Commission votes 4-1 to change the compatibility category for reportable medical events from "C" to "B".
  - ✓ Chairman MacFarlane, in her vote sheet, states, "I agree with the staffs recommendation to set the medical event definition as Compatibility Category C and to invite comment on this issue. While I understand the medical community's preference to set this at Compatibility B, I am not convinced that the medical event definition is a true trans-boundary issue where nationwide standards are needed for uniformity in the regulation of agreement material".

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

ACMUI AS Representative Role

Provides advice to NRC on regulatory issues associated with medical applications of byproduct material:

- NRC proposed rules and guidance documents
- Providing recommendations on training and experience requirements
- Evaluating non-routine uses of byproduct material
- Bringing key issues from the Agreement States to the attention of NRC
- Evaluating the compatibility of federal and state regulations
- Issues as they relate to radiation safety and NRC medical-use policy

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

NRC Proposed Rules/Guidance

- Process already exists for Agreement State participation in NRC Working Groups and Steering Committees, including the Standing Committee on Compatibility
- However, ACMUI comments on NRC proposed rules and guidance; Agreement State representative (AS rep) can provide input
- Important for OAS and individual states to submit views to AS rep
- Compatibility designation for recent Part 35 changes

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Compatibility Categories

Compatibility Category	Definition
A	Basic radiation protection standard or related definitions, signs, labels or terms necessary for a common understanding of radiation protection principles. The State program element should be essentially identical to that of NRC.
B	Program element with significant direct trans-boundary implications. The State program element should be essentially identical to that of the NRC.
C	Program element, the essential objectives of which should be adopted by the State to avoid conflicts, duplications or gaps. The manner in which the essential objectives are addressed need not be the same as NRC, provided the essential objectives are met.
D	Not required for purposes of compatibility.
NRC	These are NRC program elements that address areas of regulation that cannot be relinquished to Agreement States pursuant to the Atomic Energy Act or provisions of 10 CFR regulations. The State should not adopt these program elements.
H&S	Program elements identified by H&S are not required for purposes of compatibility; however, they do have particular health and safety significance. The State should adopt the essential objectives of such program elements in order to maintain an adequate program.

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Compatibility of Reporting

Compatibility: Regulation	Topic	Compatibility
20.2201(a)-(e)	Theft or loss of material	C/D
20.2202(a)-(d)	Dose exceeds limits	C
20.2203(a)-(b)	30-day written report	C
20.2203(d)	Address for submitting	D
20.2205	Exposure data to individuals	D
20.2207	NSTS reporting	B
30.50(a)(b)(c1)(c2)	Fires, explosions, gas releases, contamination, equipment fails to function as designed	C
35.3045	Report and notification of a medical event	C
35.3047	Report and notification of a dose to an embryo/fetus or a nursing child	C
37.81(a)-(f)	Loss of Category 1 and 2 sources during shipment	B
37.81(g)-(h)	30-day written report	C

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Compatibility of Reporting

- With the exception of reporting events that have National Security implications, no NRC reporting requirements are currently designated as Compatibility Category B.
- This includes the report and notification of a medical event (10 CFR 35.3045) and the report and notification of a dose to an embryo/fetus or a nursing child (10 CFR 35.3047).

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Compatibility of Reporting

- The previous NRC event reporting rule (Quality Management Program and Misadministrations-Part 35) promulgated in 1992 also specified that the compatibility level for reporting was C.
- For almost a quarter century, the NRC specified that the reporting of misadministrations or medical events was to be Compatibility C for the Agreement States.

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Compatibility of Reporting

- With a compatibility "C", Agreement States must meet the essential objective of the NRC's medical event definition and report to the NRC any medical events meeting NRC's criteria.
- With maintaining compatibility "C", the Agreement States have the flexibility to add additional reporting terms, e.g., shorter timelines for reporting or a state requirement to report diagnostic events.

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Compatibility of Reporting

- The ACMUI recommendation for Compatibility Category B applied only to the reporting of permanent brachytherapy events.
- The current proposed rule would make the reporting of all medical events, Compatibility Category B.

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Recommendation

- Form sub-committee to investigate changing the ACMUI recommendation for the Compatibility Category for reporting medical events to either:
  1. Compatibility C for all reporting all medical events;
     or
  2. Compatibility C for reporting medical events other than permanent brachytherapy; and
     Compatibility B for reporting permanent brachytherapy events

My preference is for option 1.

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Questions?

- Who has the first question???

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

Bureau of Radiation Protection

Frank Costello, CHP
DEP Radiation Health Physicist

fcostello@pa.gov
www.dep.state.pa.us
484-250-5833

Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- AS – Agreement States
- OAS – Organization of the Agreement States
- SECY – Office of the Secretary
- SRM – Staff Requirements Memorandum

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

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

Proposed Abnormal Occurrence Criteria for Medical Events

Advisory Committee on the Medical Uses of Isotopes
March 20, 2015

Katie Tapp, Ph.D.
Abnormal Occurrence Coordinator
Office of Nuclear Regulatory Research

Background

- Abnormal Occurrence (AO) defined as "unscheduled incident or event that the NRC determines to be significant from the standpoint of public health and safety"
- AOs are required by Section 208 of the Energy Reorganization Act of 1974
- Criteria initially created in 1977 but is updated periodically

2

History

- NRC established a working group in 2011 to evaluate the changes to the AO Criteria
- NRC presented staff's proposed AO criteria to ACMUI September 2012
- ACMUI provided recommendation for medical event AO criteria on April 15, 2013
- Agreement States provided proposed AO criteria in October 2013 for review and comment

3

Medical Event Criteria III.C

Current Title	Staff's Proposed Title
For Medical Licensees	**Events Involving the Medical Use of Radioactive Materials in Patients or Human Research Subjects Criteria[12]** **Footnote 12: Criteria III.A.2, III.A.3, and III.A.4 also apply to medical licensees.**

Note: Blue font highlights NRC's proposed changes

4

Generic Trend Criteria III.A

III. Events at Facilities Other Than Nuclear Power Plants and All Transportation Events

A. Events Involving Design, Analysis, Construction, Testing, Operation, Transport, Use, or Disposal of Licensed Facilities or Regulated Materials
   1. An accidental criticality [10 CFR 70.52(a)].
   2. **A major deficiency in design, construction, control, or operation having significant safety implications that require immediate remedial action.**
   3. **A serious safety-significant deficiency in management or procedural controls.**
   4. **A series of events (in which the individual events are not of major importance), recurring incidents, or incidents with implications for similar facilities (generic incidents) that raise a major safety concern.**

5

NRC Proposed Criteria III.C

1. A medical event **as defined in 10 CFR 35.3045 and results in a dose that**:
   - is equal to or greater than 1 Gy (100 rad) to a major portion of the bone marrow or to the lens of the eye; or equal or greater than 2.5 Gy (250 rad) to the gonads; or
   - **exceeds,** by 10 Gy (1000 rad), **the expected dose** to any other organ or **tissue from the administration defined in the written directive;** and

6

NRC Proposed Criteria III.C (cont.)

2. Represents either:
   - a dose or dosage that is at least 50 percent greater than that prescribed, or
   - a prescribed dose or dosage that
     - uses the wrong radiopharmaceutical or unsealed byproduct material; or
     - is delivered by the wrong route of administration; or
     - is delivered to the wrong treatment site; or
     - is delivered by the wrong treatment mode; or
     - is from a leaking source or sources; or
     - is delivered to the wrong individual or human research subject; **and**

7

NRC Proposed Criteria III.C (cont.)

3. **Results in one or more of the following, as determined by an independent physician(s) deemed qualified by NRC or an Agreement State:**
   - **unintended or unexpected permanent functional damage to an organ or physiological system;**
   - **a significant unexpected adverse health effect; or**
   - **death**

- **Independent physician is defined to be a physician not on the licensee's staff and who was not involved in the care of the patient involved.**

8

NRC Proposed Criteria I.A

- New Criterion : **These criteria [in section I.A] do not apply to medical events defined in 10 CFR 35.3045 and included in AO Criteria III.C. "Events Involving the Medical Use of Radioactive Materials in Patients or Human Research Subjects."**
- New Footnote : **Medical patients are excluded from consideration under this criterion.**

9

NRC Proposed Criteria I.A (cont.)

- The staff is not recommending changing the embryo/fetus criterion (I.A.2)
  - Any unintended radiation exposure … to an embryo/fetus resulting in a dose equivalent of 50 mSv (5 rem) or more.
- The staff is not recommending a new criterion in I.C.III regarding accidental embryo/fetus criterion

10

Next Steps

- Commission Review and Vote
- Publish in *Federal Register* for Public Comment Period (90 days)
- Staff Incorporation of Comments
- Commission Review and Final Approval
- Final AO Criteria published in *Federal Register*

11

Discussion

12

Concerning Requirements for Physical Presence during Leksell Gamma Knife® Treatments

Per Kjäll

March 19-20, 2015

ELEKTA

1

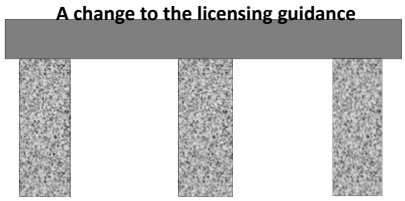
Why we are here

We are here to ask for ACMUI's support of a change in the Leksell Gamma Knife® Perfexion™ - Licensing Guidance

The suggested change concerns the requirement on the Physical Presence of the AU and AMP throughout the treatment.

2 ELEKTA

The support for the arguments



- How Patient Safety is managed outside US -

3 ELEKTA

Agenda

- Who is Elekta?
- Leksell Gamma Knife Overview
- Patient Safety
  - Statistics on incidents
  - Presence at the console outside US
- Guidance change recommendations

4 ELEKTA

ELEKTA

Elekta

ELEKTA

5

Elekta is a pioneer in modern cancer care

Every year…

- Close to 1,000,000 patients receive treatment with radiation therapy and radiosurgery equipment from Elekta
- Whereof 70,000 patients undergo Gamma Knife® radiosurgery

Every day…

- 100,000 patients receive diagnosis, treatment or follow-up facilitated by software systems from Elekta

6 ELEKTA

Leksell Gamma Knife®

ELEKTA

7

Leksell Gamma Knife® Perfexion™

ELEKTA

ELEKTA

Evolution of Gamma Knife technology 1968 - ….

The establishment of the field of Stereotactic Radiosurgery

1968 - Prototype
1 Collimator
helmet
Slit beams
Max 1 isocentre

1987 - Model U
201 sources
4 collimators
7 mins per isocentre

1988 - Model B
Easy reloading
201 sources
4 collimators
7 mins per isocentre

1999 – Model C
201 sources
2 mins per isocentre

2007 – Leksell Gamma Knife Perfexion
192 sources
3 collimators
4 seconds per isocenter
Automated planning

Still the intra-cranial system that all other solutions measure themselves against.

9 ELEKTA

The treatment procedure

1. Frame fixation

2. Diagnostic imaging

3. Treatment planning

4. Treatment

10 ELEKTA

Gamma Knife® radiosurgery - principles

Protective shielding
Collimator channels
Leksell® Coordinate Frame
Isocenter/Target in the brain
Patient positioning system
Radiation sources

The only modality that can cross-fire a large number beams simultaneously to a point in space

Fixed beam geometry is most reliable and reduces QA burden

11 ELEKTA

Gamma Knife® radiosurgery - principles

Sources

Axis for moving sectors

5 different sector positions:

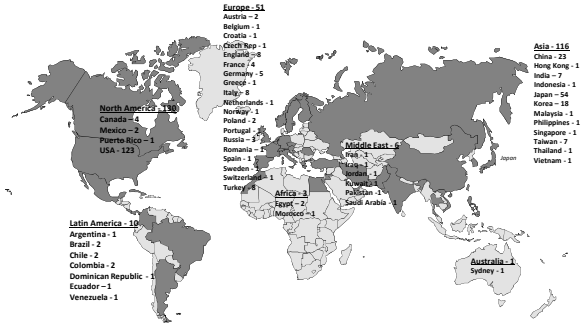
- **Home (closest to back)**
- **8 mm**
- **Off**
- **4 mm**
- **16 mm (closest to front)**

Radiological Focus Point

ELEKTA

Leksell Gamma Knife®

317 Units in clinical use worldwide – September, 2014



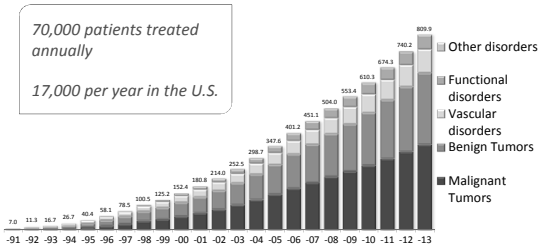
ELEKTA

Leksell Gamma Knife®

810,000 patients treated worldwide through 2013

70,000 patients treated annually

17,000 per year in the U.S.



Source: Leksell Gamma Knife Society

ELEKTA

Patient Safety

ELEKTA

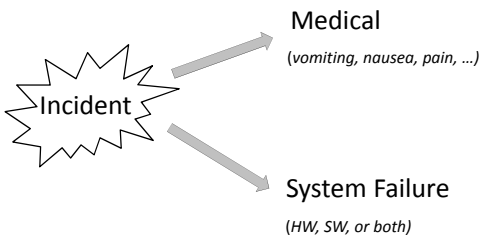
Leksell Gamma Knife®

Treatment Workflow	Risk Mitigation Workflow
Diagnosis	Competence, experience, colleagues
Diagnostic information	Service, QA, design
Transfer diagnostic information	Service, QA, procedures
Treatment planning	Competence, experience, QA, design, procedures
Transfer plan to treatment unit	QA, procedures
Patient set-up	Design, QA, procedures, competence, experience, service
Treatment	Design, procedures, competence, experience, service

ELEKTA

ELEKTA

Incident



17 ELEKTA

Competencies required during incidents

Event	Required Action	Competencies/knowledge required
Medical	Recognize	Medical
	Respond	System, Medical
System failure	Recognize	System
	Respond	System

System competence = to be able to handle the system during normal operation as well as during malfunction, including knowing the risks and characteristics of radiation.

18 ELEKTA

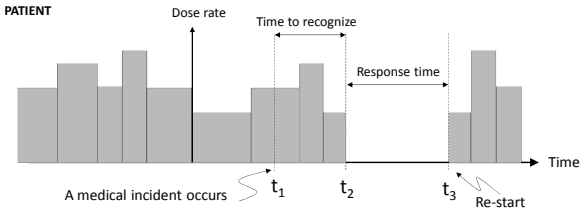
Reaction times

Reaction time = time to recognize + time to respond

	Time to [s]		
Incident	Recognize	Respond	Result
Medical	0 – 30	< 15	Depends on medical incident and not on treatment unit. No dose to patient. No dose to operator(s)
System Failure	0 - 15	0 - 30	Potentially unwanted dose to patient and operator(s)

19 ELEKTA

Medical incidents



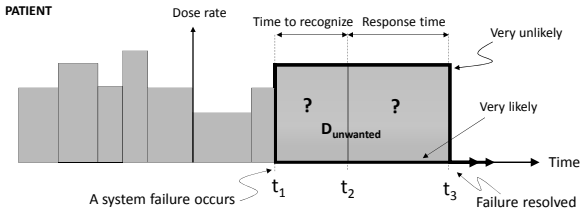
- **Mitigation objectives**: Minimize time to recognize and time to respond
- **Mitigated by**: System design, human-machine interface, operator attention / experience, work environment aspects, room layout, doors, etc.
- **Competencies needed**: Medical, e.g. a Nurse.

Acute, medical emergencies during Leksell Gamma Knife® treatments are very, very rare!

20 ELEKTA

ELEKTA

System Failure



Total dose received by the patient during a single session treatment or during one fraction is NOT the factor that determines the maximum level of risk – the maximum dose rate does!

- **Mitigation objectives**: Minimize probability of occurence, minimize time to recognize and time to respond , minimize $D_{unwanted}$,
- **Mitigated by**: System design, human-machine interface, operator attention/ experience, work environment aspects, room layout, doors, etc.
- **Competencies needed**: Technical/radiation safety, e.g. a radiation therapist

21 ELEKTA

Safety comparison with other systems

Unit	Reaction time [s]	Maximum dose rate [Gy/min]	Dose during reaction time [Gy]	Max field size [mm x mm]
Linac (FFF)	45	24	0 – 18	400 x 400
Cyber Knife®	45	10	0 – 7.5	60 (circular)
View Ray®	45	6	0 – 4.5	273 x 273
LGK	45	4	0 – 3	25 (spherical)

Reaction time = time to recognize + time to respond

22 ELEKTA

Statistics on incidents

23 ELEKTA

Statistics

- During the period 1999 – 2011 a total of approximately 2500 Customer Feedback Reports were logged by Elekta Q&RA staff,
- Of these, a total of 33 reports describe incidents where manual undocking of the patient was required (9 for PFX but always when sectors were in the home position, i.e. Beam Off)
- Assuming that the reporting rate is only 30% of the total incident rate, i.e. it is assumed that 100 incidents required manual undocking of patient during this period (30 for PFX),
- During the period 1999 – 2011, a total of approximately 700 000 patients were treated with Leksell Gamma Knife® (~ 300 000 for PFX),

In conclusion, it is estimated that a situation where staff is required to enter the treatment room to undock a patient, other than when treatment is paused or when the treatment ends, occurs approximately 1 time per 5000 (B/C) – 10 000 (PFX) patients treated.

24 ELEKTA

ELEKTA

Presence at the console outside US

25

Leksell Gamma Knife® Perfexion™ - patient safety outside US

- A short survey was sent out asking users to state who must be present at the console and who must be in the department (but not at the console) during treatment and what competencies are needed.
- The survey was answered by Leksell Gamma Knife® users representing the following 12 countries:

  Sweden, Norway, Republic of Korea, China, France, Japan, India, Morocco, Italy, Canada, Spain, (UK)

- The total (cumulative) number of patients treated by the sites responding to the survey is > 200 000.

26

Leksell Gamma Knife® Perfexion™ - patient safety outside US

The two main questions asked were:

"*At your site, who must be present at the console for the duration of the treatment – and why? (By asking the question "Why?" we want to understand what specific competence each person has that is considered important to have at the console, e.g. in case of emergency.)*"

And

"*What additional personnel must be reasonably close to the console i.e., "in the department" during the procedure, and why*? "

27

Who is present at the console during treatment?

"*At your site, who must be present at the console for the duration of the treatment – and why? (By asking the question "Why?" we want to understand what specific competence each person has that is considered important to have at the console, e.g. in case of emergency.)*"

Nurse	Technologist	Neurosurgeon	Physicist	Radiation Oncologist
57 %	51 %	49 %	29 %	9 %

Nurse: Competence and ability to tend to patient in the event of a medical incidence (vomiting, nausea, pain, anxiousness most prevalent).
Technologist: Technical system issues, emergency management.

Canada: (Radiation therapist trained for LGK emergencies)
UK: (Physicist and radiographer(s))

28

What additional personnel are available in the department?

"What additional personnel must be reasonably close to the console i.e., "in the department" during the procedure, and why? "

Nurse	Technologist	Neurosurgeon	Radiation Oncologist	Physicist
14 %	37 %	54 %	26 %	26 %

MD: Close to the control room in case deeper clinical knowledge is needed. Distances from the control room stated ranges from 10 feet to "in the hospital". Most replys were close "but not necessarily in the department".
Physicist/Tech.: Close to the control room, but not necessarily in the Leksell Gamma Knife® department: needed for technical competence.

Canada: (Radiation Oncologist and Nurse)

29 ELEKTA

Guidance Change Recommendation

30 ELEKTA

Leksell Gamma Knife® Perfexion™ - Licensing Guidance

The present wording

According to 10 CFR 35.615(f) (3)

…a licensee shall

For gamma stereotactic radiosurgery units, require an authorized user and an authorized medical physicist to be physically present throughout all patient treatments involving the unit.

Where "physically present" is defined as within hearing distance of normal voice."

31 ELEKTA

Physical Presence requirements of other treatment units

	Linear Accelerator	ViewRay	Gamma Knife
Total Activity	N/A	45 000 Ci	6600 Ci
Physical presence requirements	NO	Yes, AU **or** AMP in the department	Yes, AU **and** AMP within hearing distance of normal voice

32 ELEKTA

ELEKTA

The reasons why the requirement of physical presence of an AU and an AMP should be relaxed

- The safety of Leksell Gamma Knife® treatments has evolved significantly over the years. Emergency situations occur very infrequently during Leksell Gamma Knife® Perfexion™ treatments: < 1 time per 10 000 patients,
- Anyone of the existing team can be trained to respond,
- Requiring the physical presence of an AU and an AMP ties up two scarce resources in the clinic without improving patient safety. Besides having the AU and AMP helping other patients increases their access to medical care and increases patient safety for these other patients,
- One cannot motivate the strict rules of physical presence required for Leksell Gamma Knife® based on the comparative risk for different treatment units,

33 ELEKTA

A suggestion how the requirement of physical presence of an AU and an AMP can be worded

"We will have either an Authorized User or Authorized Medical Physicist physically present in the department during patient treatment and immediately available to come to the treatment room to respond to an emergency."

34 ELEKTA

Thank you!

ELEKTA

35

ELEKTA

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

10 CFR Part 35 Rulemaking Update

Neelam Bhalla/Jim Danna
Office of Nuclear Material Safety and Safeguards

Status

- Amends Part 35 regulations related to the medical use of byproduct material
- Proposed rule published for comment July 21 through November 18, 2014
  - Approximately 47 comment letters received; parsed into several hundred individual comments
- Staff is currently preparing the final rule
- Due to the Commission for vote in December 2015

Commenters Include:

- Professional societies
- The Organization of the Agreement States
- Conference of Radiation Control Program Directors
- Individual States
- Practicing physicians, medical physicists, radiation safety officers, nuclear pharmacists
- Individual members of the public

Commenters' Key Areas

- Associate Radiation Safety Officer
- Medical Event Definitions for Permanent Implant Brachytherapy
- Agreement State Compatibility for Medical Event Definition
- Training for alpha and beta emitters
- Reporting of failed generators
- Attestation requirements

Questions?

Contact: neelam.bhalla@nrc.gov

5

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

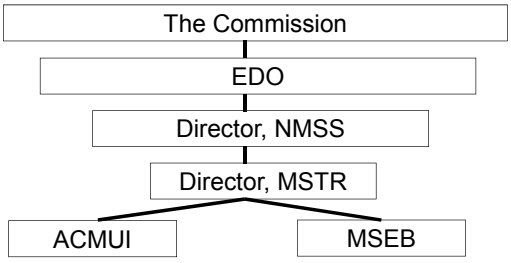
ACMUI
Reporting Structure

Sophie Holiday, ACMUI Coordinator
Medical Radiation Safety Team
Office of Nuclear Material Safety and Safeguards

Outline

- **Current Reporting Structure**
- **Annual Review**
- **Meetings**
- **Discussion**

Current Reporting Structure



Current Reporting Structure

January 5, 2011 Teleconference

- **Recommendation to maintain current reporting structure**

Reaffirmed in May 2014

Annual Review

Jan. 12, 2011 Teleconference and Sept. 20, 2012 Meeting

- **Recommendation by ACMUI to have an annual review of reporting structure**

May 08, 2014 – ACMUI Bylaws Report

5

Meetings

Two meetings at Headquarters each year

- **March/April**
- **September/October**

Approximately 2-3 teleconferences (as needed)

6

Discussion

7

Points of Contact

- **Laura Dudes – MSTR Director**
  - **301-415-3340; Laura.Dudes@nrc.gov**
- **Douglas Bollock – Designated Federal Officer**
  - **301-415-6609; Douglas.Bollock@nrc.gov**
- **Michael Fuller – Leader, MRST**
  - **301-415-0520; Michael.Fuller@nrc.gov**
- **Sophie Holiday – ACMUI Coordinator**
  - **301-415-7865; Sophie.Holiday@nrc.gov**

8

Acronyms

- **EDO – Executive Director for Operations**
- **NMSS – Office of Nuclear Material Safety and Safeguards**
- **MSTR – Division of Material Safety, States, Tribal and Rulemaking**
- **MSEB – Medical Safety and Event Assessment Branch**

9

Open Forum

NO HANDOUT

September 2015

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		1 X	2 X	3 X	4 X	5 X
6	7 LABOR DAY	8	9 X	10 X	11 X	12 X
13 ASTRO Annual Meeting	14 Rosh Hashana	15 Rosh Hashana	16	17	18 X	19 X
20 X	21 X	22 Yom Kippur	23 Yom Kippur	24	25	26 X
27 X	28 Sukkot	29 Sukkot	30			

October 2015

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
				1 Sukkot	2 Sukkot	3 Sukkot
4 Sukkot	5 Shmini Atzeret	6 Simchat Torah	7	8	9	10
11 X	12	13	14 X	15 X	16 X	17 X
18 X	19 X	20 X	21 X	22 X	23 X	24 X
25 X	26 X	27 X	28 X	29 X	30 X	31 X