MEETING AGENDA
ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

October 6-7, 2016
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, October 06, 2016 **CLOSED SESSION**		
7:00 – 8:00	• **Badging and Enrollment**	**ACMUI**
OPEN SESSION		
8:00 – 10:15	• **Opening Remarks** Mr. Bollock will formally open the meeting and Mr. Collins will provide opening comments.	**D. Bollock, NRC** **D. Collins, NRC**
	• **Old Business** Ms. Smethers will review past ACMUI recommendations and provide NRC responses.	**M. Smethers, NRC**
	• **Open Forum** The ACMUI will identify medical topics of interest for further discussion.	**ACMUI**
	• **Event Reporting Mechanisms** Multiple organizations will discuss and share information related to their event reporting databases.	**ASTRO/AAPM, CARS, CRCPD, IAEA**
10:15 – 10:30	**BREAK**	
10:30 – 11:30	• **Medical Events Subcommittee Report** Dr. Ennis will present the subcommittee's analysis of medical events for fiscal year 2015.	**R. Ennis, ACMUI**
11:30 – 1:00	**LUNCH**	
1:00 – 2:30	• **Medical Event Reporting for All Modalities Excluding Permanent Implant Brachytherapy** Dr. Suh will discuss the subcommittee's recommendations for the reporting of medical events.	**J. Suh, ACMUI**
	• **10 CFR Part 35 Rulemaking Update** Ms. Taylor will provide an update on the 10 CFR Part 35 rulemaking effort.	**T. Taylor, NRC**
	• **NRC Comments on 'Patient Intervention'** Mr. Fuller will discuss staff's comments in response to the ACMUI's Patient Intervention Subcommittee Report.	**M. Fuller, NRC**
2:30 – 3:00	**BREAK**	
CLOSED SESSION		
3:00 – 5:00	• **Ethics Training** • **INFOSEC Training** • **Allegations Training**	**M. Clark, NRC** **R. Norman, NRC** **S. Hawkins, NRC**

Friday, October 07, 2016
OPEN SESSION

	• **Yttrium-90 Microspheres Brachytherapy Licensing Guidance** Dr. Tapp will provide an overview of the revisions to the Y-90 Microspheres Brachytherapy Licensing Guidance. Dr. Metter will provide the subcommittee's comments on the proposed revisions.	**K. Tapp, NRC** **D. Metter, ACMUI**
8:00 – 10:15	• **NRC's Abnormal Occurrence Criteria Policy Statement Update** Dr. Oxenberg will provide an update on the proposed revisions to the Abnormal Occurrence Criteria Policy Statement.	**T. Oxenberg, NRC**
	• **Training and Experience for All Modalities** Dr. Palestro will discuss the subcommittee's comments on the T&E requirements for authorized individuals in 10 CFR Part 35.	**C. Palestro, ACMUI**
10:15 – 10:30	**BREAK**	
10:30 – 11:30	• **Spectrum Pharmaceuticals Proposal for Training and Experience Requirements** Representatives from Spectrum Pharmaceuticals, Inc. will discuss their proposed revisions to the T&E requirements for alpha and beta emitters.	**Spectrum Pharmaceuticals, Inc.**
11:30 – 1:00	**LUNCH**	
	• **Worldwide Supply of Molybdenum-99** Mr. Green will provide an update of the world's supply of moly-99.	**R. Green, ACMUI**
1:00 – 2:30	• **NorthStar Generator Licensing Guidance** Dr. Howe will provide an overview of the 10 CFR 35.1000 licensing guidance drafted by an NRC/OAS working group. Dr. Dilsizian will provide the subcommittee's comments on the proposed guidance.	**DB. Howe, NRC** **V. Dilsizian, ACMUI**
2:30 – 3:00	**BREAK**	
	• **Germanium-68/Gallium-68 Medical Use Generator Licensing Guidance** Dr. Tapp will provide an overview of the 10 CFR 35.1000 licensing guidance drafted by an NRC/OAS working group.	**K. Tapp, NRC**
3:00 – 4:00	• **Germanium-68/Gallium-68 Medical Use Generator Decommissioning Funding Plan Update** Dr. Daibes will provide an update on staff's efforts to address the decommissioning funding issues related to the germanium/gallium-68 medical use generator.	**S. Daibes, NRC**
	• **Enhancing Communications with the Medical Community** Dr. Alderson will provide an update on the ACMUI's efforts to improve the ACMUI and NRC's communications with	**P. Alderson, ACMUI**

various medical professional societies. **M. Smethers, NRC**

- **Administrative Closing**
  Ms. Smethers will provide a meeting summary and propose dates for the spring 2017 meeting.

4:00

ADJOURN

Badging and Enrollment

NO HANDOUT

Opening Remarks

NO HANDOUT

	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

	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*

	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		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	Accepted	Closed	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	Closed	Mattmuller/Zanzonico

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote
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	Closed	S. Holiday		

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
7	The ACMUI recommended that events reportable under 10 CFR 35.3047 that do not result in harm to the embryo/fetus/or nursing child not be captured as AO's reported to Congress.	03/20/2015	ACMUI Action	Open		Langhorst/Costello	11, 0, 1
12	The ACMUI recommended to make the following change to the Patient Intervention Subcommittee Recommendation Issue II: Unintentional Treatment outcome due to anatomic or physiologic anomaly ~~and/or imaging uncertainty~~ falls into the category "the Art of Medical Practice" provided that the standards of medical practice are met.	10/8/15	ACMUI Action	Open	M. Abogunde	Alderson/Palestro	10, 0, 1
13	The ACMUI endorsed the Patient Intervention Subcommittee Report with the modification to Issue II (listed in item 12 above).	10/8/15	ACMUI Action	Open	M. Abogunde	Costello, Alderson	10, 1, 0
14	Dr. Thomadsen requested that staff provide an update at the Spring 2016 ACMUI Meeting on staff response/action to the Patient Intervention Subcommittee Report.	10/8/15	NRC Action	Open *Delayed*	M. Abogunde		
15	The ACMUI recommended that staff issue a Generic Communication (i.e. Information Notice or Regulatory Issue Summary) to licensees to inform them of the interpretation of "patient intervention."	10/8/15	NRC Action	*Open*	M. Abogunde		
18	The ACMUI recommended that the individual who implants the source for radioactive seed localization procedures can do so under the supervision of an authorized user.	10/8/15	Accepted	Closed	S. Holiday		
22	The ACMUI endorsed the 2015 Abnormal Occurrence Criteria Subcommittee Report with the caveat that the report be amended to include an introductory paragraph that provides the rationale for the recommendations, as well as a summary paragraph to state that the Committee desires that the recommendations be incorporated into this revision of the NRC's Abnormal Occurrence Criteria Policy Statement.	10/9/15	ACMUI Action	Open			10, 1, 0

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
23	The ACMUI endorsed the NUREG-1556, Volume 9 Subcommittee Report.	10/9/15	ACMUI Action	Open			11, 0, 0

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
1	The Committee endorsed that component of the current proposed rule re-defining medical events in permanent implant brachytherapy in terms of activity (i.e. source strength) rather than radiation dose).	1/6/2016	Accepted	Open			10, 0, 0
2	The Committee endorsed, with reservation, designating the current proposed rule re-defining medical events in permanent implant brachytherapy as Compatibility Category C, with activity-based medical event metrics defined as an essential program element.	1/6/2016	Accepted	Open			10, 0, 0
3	The Committee recommended changing the language for a "wrong-location" medical event in permanent implant brachytherapy from the current proposed language, "Sealed source(s) implanted directly into a location where the radiation from the source(s) will not contribute dose to the treatment site, as defined in the written directive," to **"Sealed source(s) implanted directly into a location discontiguous from the treatment site, as defined in the written directive."**	1/6/2016	Accepted	Open			10, 0, 0
4	The Committee recommended revising the passage in lines 4182-4186 on page 167 in the Draft Final Rule as follows, thereby eliminating the dose-based criteria for a leaking source" medical event: **"3) An administration that includes the wrong radionuclide; the wrong individual or human research subject; a leaking sealed source; or a sealed source or sources implanted into a location discontiguous from the treatment site, as defined in the written directive."**	1/6/2016	Not Accepted	Open			10, 0, 0
5	The Committee endorsed the elimination of the preceptor-statement requirement for Board-certified individuals for an individual seeking regulatory authorization as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist.	1/6/2016	Accepted	Closed			10, 0, 0

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
6	With respect to the amended requirements for preceptor attestation for an individual seeking regulatory authorization as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist through the alternate pathway, the Committee endorsed changing the language for the preceptor attestation from the individual "…has achieved a level of competency to function independently…" for the authorization to **the individual can "…independently fulfill the radiation safety-related duties…" associated with the authorization being requested.**	1/6/2016	Accepted	Open			10, 0, 0
7	The Sub-Committee recommended that the date of recognition by the NRC of a certifying board should not impact individuals seeking to be named as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist through the certification pathway. During the discussion, this recommendation was modified in the final report as follows: **The Sub-Committee recommends that NRC Staff consider providing guidance in the NUREG-1556, Volume 9 update to licensees on the ways individuals with board certifications prior to NRC's board recognition date may seek authorization.**	1/6/2016	Accepted	Open			10, 0, 0
8	The Committee recommended that the NRC adopt the parent-breakthrough limits for radioisotope generators specified in the relevant Food and Drug Administration (FDA)-approved package inserts. During the discussion, the Committee recommended to eliminate this recommendation and instead, revise the general comments section of the report to suggest that NRC consider, in future rulemaking, establishing conformity with the FDA breakthrough-limit regulations.	1/6/2016	ACMUI Action	Open			9, 1, 0
9	The Committee did not endorse the new requirement in the Draft Final Rule that licensees report to the NRC as well as to the manufacturer/vendor generator elutions with out-of-tolerance parent-breakthrough but, instead, recommends a single reporting requirement to the manufacturer/vendor.	1/6/2016	Not Accepted	Open			10, 0, 0
10	The Committee endorsed allowing Associate Radiation Safety Officers (ARSO) to be named on a medical license.	1/6/2016	Accepted	Open			10, 0, 0

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
11	The Committee recommended that the designation of a board-certified authorized user, authorized medical physicist, or authorized nuclear pharmacist as the Radiation Safety Officer (RSO) or as an ARSO requires their board certification to include the designation, "RSO Eligible."	1/6/2016	Not Accepted	Open			10, 0, 0
12	The Committee did not endorse establishing a separate category of Authorized Users for parenteral administration of alpha-emitting radiopharmaceuticals but, instead, recommends deleting § 35.390(b)(1)(ii)(G)(4) in the current Draft Final Rule and revising the pertinent passage in § 35.390(b)(1)(ii)(G)(3) as follows, **"Parenteral administration of any radioactive drug for which a written directive is required."**	1/6/2016	Partially Accepted	Open			10, 0, 0
13	The Committee endorsed the elimination of the requirement to submit copies of NRC Form 313, Application for Material License, or a letter containing information required by NRC Form 313 when applying for a license, an amendment, or renewal.	1/6/2016	Accepted	Open			10, 0, 0
14	The Sub-Committee recommended changing the "medical-events" language in lines 5531-5532 (page 232) of the Draft Final Rule from, "A licensee shall report as a medical event, any administration requiring a written directive, except for an event that results from patient intervention…," back to the language in the current Draft Final Rule, "A licensee shall report any event, except for an event that results from patient intervention…" During the discussion, the recommendation was modified in the final report as follows: **The Sub-Committee recommends changing the "medical-events" language in lines 5531-5532 (page 232) of the current version of the Draft Final Rule from, "A licensee shall report any event, except for an event that results from patient intervention…" back to the language published in the Proposed Rule as presented for public comment,** **"A licensee shall report as a medical event, any administration requiring a written directive, except for an event that results from patient intervention…,"**	1/6/2016	Not Accepted	Open			10, 0, 0

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
15	The Committee endorsed the 2016 Rulemaking Subcommittee Report with modifications as listed above.	1/6/2016	NRC Action	Open			10, 0, 0
16	Dr. Alderson formed a subcommittee to review and evaluate the training and experience requirements for all modalities in 10 CFR Part 35. Subcommittee members include: Dr. Langhorst, Dr. Metter, Dr. Palestro (chair), Dr. Suh and Ms. Weil. NRC staff resource: Maryann Abogunde.	2/25/2016	ACMUI Action	Open			
17	The ACMUI recommended maintaining the current 700 training and experience hours under 10 CFR 35.390.	3/10/2016	NRC Action	Closed			11, 0, 0
18	The ACMUI recommended establishing a standing subcommittee to review the training and experience requirements for all modalities under 10 CFR Part 35.	3/10/2016	ACMUI Action	Closed			11, 0, 0
19	The ACMUI unanimously endorsed the training and experience for authorized users of alpha, beta, and gamma emitters under 10 CFR 35.390 subcommittee report.	3/10/2016	ACMUI Action	Closed			11, 0, 0
20	The NRC staff will provide data to the ACMUI for medical events reported over a five-year span for trending purposes.	3/17/2016	NRC Action	Closed		Costello/Palestro	
21	Dr. Alderson formed a subcommittee to 1) explore the impact of ME reporting and its impact on self-reporting (safety culture); 2) identify potential ways to improve effectiveness of self-reporting in support of a culture of safety; and 3) suggest ways to share ME reports and lessons-learned with the medical community to promote safety. Subcommittee members include: Mr. Costello, Dr. Dilsizian, Dr. Ennis, Dr. Langhorst (chair), and Ms. Weil. Mr. Ouhib will serve as a consultant to the subcommittee. NRC staff resource: Dr. Katie Tapp	3/18/2016	ACMUI Action	Open			
22	The NRC staff will provide the ACMUI with the draft final 35.1000 licensing guidance for the Leksell Gamma Knife Perfexion and Leksell Gamma Knife Icon. Interested members will be encouraged to provide comments to the Working Group.	3/18/2016	NRC Action	Closed			
23	Dr. Langhorst requested that NRC staff provide the ACMUI with the total number of medical use licensees within the United States (NRC and Agreement States).	3/18/2016	NRC Action	Closed			

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
24	The ACMUI will contact their respective professional organizations to request and encourage interactions between the NRC and ACMUI with their organization.	3/18/2016	ACMUI Action	Closed			
25	The ACMUI have planned to hold the fall 2016 ACMUI meeting at NRC Headquarters on October 6-7, 2016. The back-up date is September 1-2, 2016.	3/18/2016	ACMUI Action	Closed			
26	The Committee endorsed the elimination of the written directive with the understanding that there will be documentation in the medical record pre-procedure and post-procedure that would allow regulators to determine whether a medical event occurred.	6/24/2016	Accepted	Closed			
27	The Committee endorsed the third pathway in which a radiologist could become an authorized user with the listed 80-hours of training and experience. However, the Committee did not support surgeons or others without a significant background in radiation (from a residency or other similarly intense education and practical experience) becoming Authorized Users for RSL with only 80 hours of training.	6/24/2016	Accepted	Closed			9, 0, 0
28	The Committee endorsed the modified definition of medical events (MEs) with the caveat that such an outcome would not be an ME if “the physician makes the determination not to explant the seed for various patient conditions (e.g. doing so would jeopardize the patient’s wellbeing).” The Committee endorsed this change and supports exclusion from an ME under circumstances in which the physician deems removal would not be in the best interest of the patient. Additionally, the Committee endorsed the position that an ME has not occurred if the patient fails to return for the surgical removal procedure, considering this to be an instance of “patient intervention,” provided the patient has been properly counseled about the importance of returning for the procedure and the risk of radiation exposure if the sources are not removed. Documentation of this counseling should be made in the patient’s medical record.	6/24/2016	Accepted	Closed			9, 0, 0

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
29	The Committee recommended inclusion of the following in the Draft Guidance: "Patient should be advised not to breast feed from a breast into which one or more radioactive seeds been implanted and not yet removed. Breastfeeding is, of course, permissible once the seed(s) has(ve) been removed. In the event of seed rupture within the breast, the subcommittee recommends the patient be advised to never breast feed from the effected breast for this child." During the discussion, this recommendation was modified as follows: "Patient should be advised not to breast feed from a breast into which one or more radioactive seeds been implanted and not yet removed. Breast feeding is, of course, permissible once the seed(s) has(ve) been removed. In the event of seed rupture within the breast, the subcommittee recommends the patient be advised to never breast feed from either breast for this child."	6/24/2016	Not Accepted	Closed			9, 0, 0
30	The Committee endorsed the RSL Subcommittee report with the modifications above.	6/24/2016	ACMUI Action	Closed			9, 0, 0
31	The Committee recommended that the section entitled, "Licensing Guidance," be re-named, "Purpose," and re-located to the beginning of the Guidance (i.e., immediately following the Table of Contents). An explicit statement such as the following should be included, "This Guidance provides applicants with an acceptable means of satisfying the requirements for a license for the use of a column based Ge-68/Ga-68 generator for producing Ga-68 to be used in the preparation of Ga-68 radiopharmaceuticals."	8/10/2016	NRC Action	Open			

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
32	The Committee recommended to provide clarification of what is regulated under 10 CFR 35.200 and 10 CFR 35.1000. The guidance should state that the regulation of Ga-68 radiopharmaceuticals under 10 CFR 35.200 applies to patient dosages obtained from appropriately trained authorized users or authorized nuclear pharmacists within a medical facility as well as from commercial nuclear pharmacies. Accordingly, the Committee recommended revisions of the passage in lines 73-84 on page 2 of the Licensing Guidance, including the section entitled, “Commercial Nuclear Pharmacy User under 10 CFR 30.33,” as follows: Use of Ga-68 Radiopharmaceuticals Please note that licensees that use unit dosages of Ga-68 radiopharmaceuticals for medical imaging and localization studies will be regulated under 10 CFR 35.200 and authorized users (AUs) must comply with the requirements of 10 CFR 35.290. The licensee may use a Ga-68 radiopharmaceutical that is prepared from the elution of a Ge-68/Ga-68 generator for medical use for imaging and localization studies that is either: 1) Obtained in a manner described in 10 CFR 35.200 (c) or (d);	8/10/2016	NRC Action	Open			
33	The Committee recommended to modify the language in the “Use of Ge-68/Ga-68 Generators” Section to the following language: Use of Ge-68/Ga-68 Generators Recently, the FDA approved a gallium-68 (Ga-68) radiopharmaceutical for diagnostic imaging of somatostatin receptor (SSR)-positive neuroendocrine tumors. Ga-68 is a positron emitter which allows Ga-68 radiopharmaceuticals to be imaged using positron emission tomography (PET) in a manner similar to fluorine-18 (F-18) radiopharmaceuticals. Ga-68 produced in a cyclotron, like F-18, may be used to produce Ga-68 radiopharmaceuticals for use under 10 CFR 35.200. However, unlike F-18, Ga-68 can also be produced from the elution of a Ge-68/Ga-68 generator to prepare Ga-68 radiopharmaceuticals. As such, the Ge-68/Ga-68 generator eluate generally cannot be used directly in patients for imaging, but only as a precursor for the preparation of Ga-68-labeled radiopharmaceuticals.	8/10/2016	NRC Action	Open			

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
34	The Committee agreed with the recommendation to modify the language in the "Authorized Individuals" Section to the following language: 4) Meets the criteria under 10 CFR 35.290, "Training for imaging and localization studies;" 5) Has completed the following training in the use of a Ge-68/Ga-68 generator for producing Ga-68 radiopharmaceuticals for 35.200 use: a. elution and quality control procedures needed to determine Ga-68 activity and Ge-68 breakthrough levels appropriate for the preparation of radiopharmaceuticals for imaging and localization studies; b. measuring and testing the eluate for radionuclidic purity; and c. safety procedures for the use of the Ge-68/Ga-68 generator.	8/10/2016	NRC Action	Open			
35	The Committee agreed with the recommendation to modify the language in the "Training for individuals other than AUs and ANPs" Section to the following language: Training for individuals others than AUs and ANPs The applicant shall commit to provide training in the licensee's procedures to all individuals involved in Ge-68/Ga-68 generator use for the production of Ga-68 radiopharmaceuticals for 35.200 use, commensurate with the individual's duties to be performed. This training must be provided to all individuals eluting the generator or preparing, or measuring the Ga-68 unit dose.	8/10/2016	NRC Action	Open			
36	The Committee agreed with the recommendation to modify the language in the "Radiation Protection Program Changes" Section to the following language: This guidance may be revised as additional experience is gained regarding the use of a Ge-68/Ga-68 generator for preparation of Ga-68 radiopharmaceuticals for 35.200 use. An applicant initially applying for authorization for use of Ge-68/Ga-68 generator under this 35.1000 use may request to incorporate into its license a change process similar to 10 CFR 35.26. Such a change process can allow some future changes without the need to amend the license to radiation safety programs provided that the change process requires the following conditions to be met for revisions to the radiation safety program:	8/10/2016	NRC Action	Open			

	ITEM	DATE	STATUS		Assigned	1st/2nd	Vote (Y/N/A)
37	The Committee endorsed the Ge-68/Ga-68 Subcommittee report.	8/10/2016	ACMUI Action	Open			

Open Forum

NO HANDOUT

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

RO-ILS: Radiation Oncology Incident Learning System®

Adam Dicker, MD, PhD, FASTRO
Thomas Jefferson University
October 06, 2016

The New York Times | http://nyti.ms/1xy37MK

SundayReview

Why Some Teams Are Smarter Than Others

JAN. 16, 2015
Gray Matter

By ANITA WOOLLEY, THOMAS W. MALONE and CHRISTOPHER CHABRIS

29 OCTOBER 2010
VOL 330 SCIENCE

Evidence for a Collective Intelligence Factor in the Performance of Human Groups

Anita Williams Woolley,[1]* Christopher F. Chabris,[2,3] Alex Pentland,[3,4]
Nada Hashmi,[3,5] Thomas W. Malone[3,5]

Psychologists have repeatedly shown that a single statistical factor—often called "general intelligence"—emerges from the correlations among people's performance on a wide variety of cognitive tasks. But no one has systematically examined whether a similar kind of "collective intelligence" exists for groups of people. In two studies with 699 people, working in groups of two to five, we find converging evidence of a general collective intelligence factor that explains a group's performance on a wide variety of tasks. This "c factor" is not strongly correlated with the average or maximum individual intelligence of group members but is correlated with the average social sensitivity of group members, the equality in distribution of conversational turn-taking, and the proportion of females in the group.

What is RO-ILS?

- **RO-ILS: Radiation Oncology Incident Learning System®**
- **RO-ILS is the only medical-specialty sponsored incident learning system for radiation oncology.**

3

ENROLL NOW!

RO-ILS RADIATION ONCOLOGY® INCIDENT LEARNING SYSTEM

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www.astro.org/ROILS

Mission

- **The mission of RO-ILS is to facilitate safer and higher quality care in radiation oncology by providing a mechanism for shared learning in a secure and non-punitive environment.**

5

RO-ILS: Radiation Oncology Incident Learning System®

- **RO-ILS operates under the auspices of the Patient Safety and Quality Improvement Act (PSQIA) of 2005.**
- **PSQIA provides privilege and confidentiality protections to submitted data.**

6

Program Update

- **224 participating facilities***
- **2293 submitted reports***
- **2016 Year in Review**
- **7 Quarterly Reports**

***As of September 1, 2016**

7

NRC Subpart M—Reports
§ 35.3045 Report and notification of a medical event

- (1) A dose that differs from the prescribed dose or dose that would have resulted from the prescribed dosage by more than 0.05 Sv (5 rem) effective dose equivalent, 0.5 Sv (50 rem) to an organ or tissue, or 0.5 Sv (50 rem) shallow dose equivalent to the skin; and
- (i) The total dose delivered differs from the prescribed dose by 20 percent or more;
- (ii) The total dosage delivered differs from the prescribed dosage by 20 percent or more or falls outside the prescribed dosage range; or
- (iii) The fractionated dose delivered differs from the prescribed dose, for a single fraction, by 50 percent or more.

8

Cone Beam CT issues

Q3 2015: Incorrect Vertebral Body Treated

A patient was being treated with a fractionated dose of 4.0 gray (Gy) for 5 fractions for the palliation of bone metastasis in the thoracic-lumbar (T-L) spine. The incorrect vertebral body was treated for 2 of the 5 fractions. Cone-beam computed tomography (CT) was used to perform the alignment. The automatic image alignment algorithm locked onto the incorrect vertebral body, thus resulting in a large shift of the patient. The incident was discovered on the third fraction when the treating radiation therapists noted the discrepancy.

Cone Beam CT issues

Q2 2015: Incorrect Isocenter

The following event description (slightly edited for clarity) illustrates incorrect isocenter situations that can occur. A patient's thigh treatment position was off by 5 cm superior-inferior (sup-inf) for 1 fraction. This was discovered during the weekly physics review as the physicist reviewed the limitations of the CBCT for extremities. The attending physician was notified that CBCT was not valid for sup-inf positioning of the thigh treatment region, and orthogonal images were suggested for the remainder of the patient's treatments.

Recommendations from *RO-ILS*

- *Policies and procedures* should be clear regarding the actions to take when large shifts are indicated from image-guided radiation therapy (IGRT) imaging. In this case, the shift was 3 cm and was indicative of a problem. Some centers have adopted policies that require a secondary verification of patient setup when the shifts are larger than a specified amount.
- *Use a cone-beam CT setting that captures a larger extent of anatomy where appropriate.* This may aid in reducing confusion. One vendor supplies a "topogram" to specify the superior-inferior extent of the scan. Another vendor has predefined settings ranging up to 26 cm in this dimension.
- Other centers have begun using *kilovoltage (kV) or megavoltage (MV) planar images to verify alignment* in addition to cone-beam CT. These planar images can show a larger extent of anatomy and reduce the likelihood of aligning to a wrong vertebral body.

Quarterly Report Themes

Q3 2014 →

Incidents with >5% dose deviation
Incidents with possible medical impact: severe or medically severe events
Events occurring within treatment planning
Case Reviews: time-out process, treatment plan not executed as intended

Quarterly Report Themes

Q4 2014

Near miss (incorrect name, plan, prescription, calculation, treatment, labeling, missing info.)
Unsafe condition (documentation issues, scheduling issues resulting in delays, equipment malfunction/environmental safety issues, lack of handoff, lack of patient education
Staff rushed, miscommunication, incorrect spinal level lesion identified, incorrect isocenter, calculation errors, incorrect treatment area identified
Case Reviews:
multitasking/distractions/interruptions

Quarterly Report Themes

Q1 2015

Electronic communication, in-person communication, written communication
Case Reviews: used old CT sim data set for plan, SBRT target drawn on wrong side

Q2 2015

Unsafe condition, near miss, incidents: a breakdown
Case Reviews: limited field of view provided by CBCT at certain sites (thigh treatment), setup on freckle instead of tattoo

Quarterly Report Themes

Q3 2015

Importance of review: prescription errors, treatment planning calculation errors, contouring errors, previous radiation therapy not included or considered in the treatment plan
Incorrect Isocenter
Time-outs
Case Reviews: incorrect vertebral body treated, CTV used for planning instead of PTV, mouthpiece inserted incorrectly in head and neck treatment

Quarterly Report Themes

Q4 2015

Priority scale explanation
Rushed cases: incorrectly contoured boost structures, incorrect fractions delivered, error in isocenter location
Changes to the course of therapy: revision of plan without rejecting/discontinuing previous plan, plan change after start
Missed treatments and prescriptions

Quarterly Report Themes

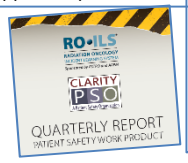
Q4 2015

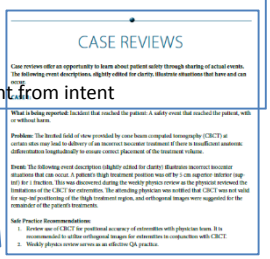
Q4 2015 Con't
MD's prescription does not match care intended/delivered: incorrect planned dose, fractions and dose inverted
Characterization of event types: approvals, breathhold, collision, contour, field, HDR, IGRT, imaging, isocenter, laterality, medical, MU, patient name, pacemaker, plan prescription, setup, treatment, and other

Quarterly Report Themes

Q1 2016

HDR with equipment from different vendors
Laterality errors
Manual data entry
Patient orientation
Approved plan different from intent





What have we observed?

- RO-HAC ranks events on a 1-5 scale, judging potential clinical significance
- Looking at 232 events ranked 4 or 5 out of 1296 (18%) through Q4, 2015

Reached the patient	**(R)**	123	53%
Near miss	**(N)**	105	45%
Unsafe condition	**(U)**	4	2%

19

Keywords	All	R	N or U
Rx, plan mismatch	44	18	26
Shifts	30	13	17
Plan quality	26	12	14
Communication	19	14	5
Human data transfer	14	14	0
Gating	12	10	2
Laterality	11	1	10
Previous treatment	10	5	5
Emergent treatment	5	3	2
Haste	2	1	1

Failure mode: *Approved* Plan ≠ Intent

Approved plan not equal to intent	**23**
MD gave incorrect instruction	4
Plan did not match Rx; unrecognized	12
Planner wrote the Rx for MD to approve	7

Examples to follow

MD gave incorrect instruction

- "SBRT" prescribed 4 Gy x 4 instead of intended 12 Gy x 4
  - Planner and checker did not question
  - Found at weekly physics check
- "SBRT" prescribed 5 Gy x 6 instead of intended 6 Gy x 5
  - Questioned by plan checker

22

Plan did not match Rx; and unappreciated at time of approval

- 12 cases; 7 reached the patient
  - Targets not planned
    - 2 not found by physics checker
  - Dose/fraction mismatch
    - 7 not found by physics checker
    - 3 found by RTT

23

Planner wrote the Rx for MD approval

- 3 cases in which this was specifically called out; 4 others in which it is implied
  - 5 involve dose/fraction
    - 6 Gy/fx intended > 2 Gy/fx
    - 2.67 > 1.8, 2.4 > 2; 2 > 2.2; 1.8 > 2
  - Supraclavicular field included in breast treatment in error

24

"12 in 2"

- The dosimetrist received a verbal order from the Radiation Oncologist for a dose of "12 in 2" to right shoulder
- The dosimetrist wrote the written directive for 6 treatments of 200 cGy each for a total of 1200 cGy.
- The written directive was approved by the Radiation Oncologist.
  - The plan should have been 2 treatments of 600 cGy for a total of 1200 cGy.
- Found at chart rounds. The patient had already received 2 fractions at 200 cGy each.
- The Radiation Oncologist decided one additional treatment of 600 cGy and finish course of treatment.

25

Wrong hepatic lesion treated

- A patient previously treated with SBRT for two liver metastases returned with a new lesion. The attending radiation oncologist and resident reviewed the imaging and made the decision to treat the new metastasis with SBRT.
- A simulation directive was completed by the resident with axial image snapshots from a diagnostic MR scan and a computed tomography (CT) scan illustrating the lesion to be treated. After simulation, the gross tumor volume (GTV) contoured by the resident covered the **wrong** liver lesion.

26

Wrong hepatic lesion treated

- Treatment planning and quality assurance (QA) were completed based on that incorrect target. The error was not detected at the time of attending approval or in peer-review rounds. Treatment was delivered to a benign liver hemangioma.
- Follow-up imaging @ four months demonstrated enlargement of the liver metastasis, prompting review and realization that the 5 SBRT fractions had been delivered to the incorrect hepatic target. Adjacent normal organs received doses within acceptable tolerances. The correct liver metastasis was treated with a treatment plan incorporating the contribution from the prior radiation.

27

Wrong hepatic lesion treated

Contributing factors in this case included:

- Failure to accurately correlate target contouring with diagnostic imaging
- Hand-offs and extended workflow with multiple people interacting with the plan
- Safety-critical issue not identified in the review by the attending physician
- Safety-critical issue not identified in peer review, despite the prospective SBRT-specific peer review being performed
- Abbreviated treatment course

28

Actions and Recommendations:

- The clinic instituted a new policy and procedure which includes the explicit review of diagnostic images by the attending physician (accompanying checklist reviewed by others in the workflow).
- The role of physician peer review (i.e. chart rounds) is well-recognized and is advocated in the ASTRO white paper.
- This case underscores the need for peer-review and suggests that for SBRT treatments it may take a special form with enhanced safety checks.
- Other suggested actions might include setting the isocenter at the time of simulation which may eliminate certain error pathways.

29

NRC Subpart M—Reports
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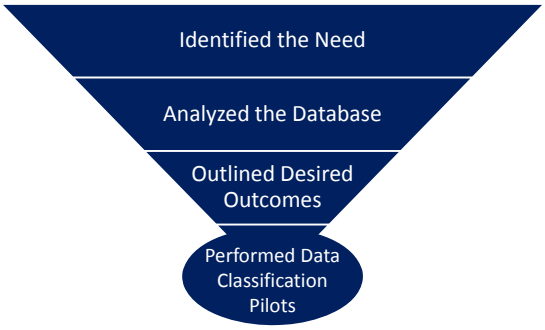
- (ii) The total dosage delivered differs from the prescribed dosage by 20 percent or more or falls outside the prescribed dosage range; or
- (iii) The fractionated dose delivered differs from the prescribed dose, for a single fraction, by 50 percent or more.

30

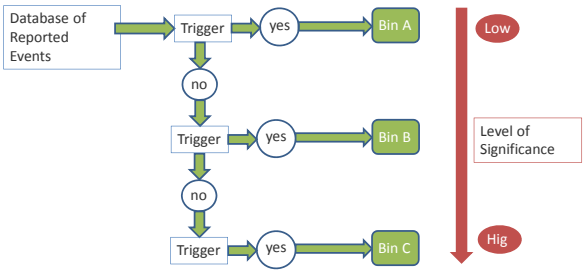
How did we get there?



31

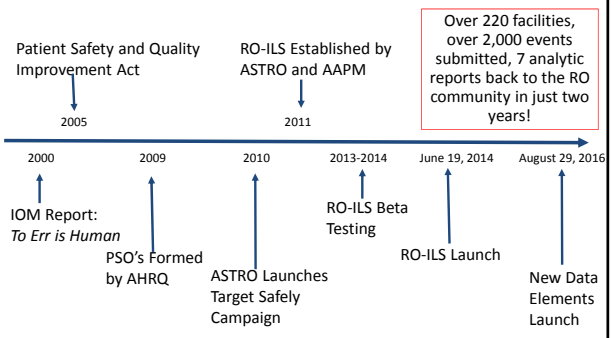
Preparing RO-ILS for big data analytics

Classification system that automatically partitions the database.



32

How far we've come!



Current Activities

- Safe Table at ASTRO/AAPM Meetings
- Educational Webinars
- Tips of the Month
- Provider Specific Reporting
- Safety Alerts
- Vendor Community Outreach

34

For more information:

www.astro.org/ROILS

ROILS@astro.org

Contact: Cindy Tomlinson, Senior Patient Safety and Regulatory Affairs Manager

Cindy.Tomlinson@astro.org

Acronyms

AAPM – American Association for Physicists in Medicine

ASTRO – American Society for Radiation Oncology

PSQIA – Patient Safety and Quality Improvement Act (PSQIA)

RO – Radiation Oncology

RO-ILS – Radiation Oncology Incident Learning System

SBRT – Stereotactic Body Radiation Therapy

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Protecting People and the Environment

CRCPD Radiation Medical Events Database

Jennifer Elee
Chair, CRCPD H-38 Committee on Medical Events

Background:

- **2011: Pilot conducted; CRCPD collected machine events for first time.**
- **2011-present: Collecting events from all states with requirements**
- **Some states have no reporting requirements, some therapy only**

2

Background:

- **In 2013, CRCPD entered into a Memorandum of Understanding with AAPM to further analyze the data (facility/state information is redacted).**
- **AAPM provides an annual report to the CRCPD and AAPM Boards and presents a summary at the CRCPD Annual Meeting**

3

Why Collect Event Information

- **Share lessons learned**
- **Prevent errors**
- **Look for trends**
- **Improve patient care and safety**

4

Event Definitions:

- Current Definitions include events resulting from the use of Therapeutic Radiation Machines and from Diagnostic Radiation Machines.
- Definition was included in latest version of CRCPD Suggested State Regulations for Diagnostic X-Ray (Part F)

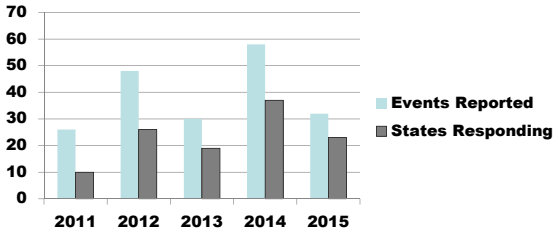
5

2011-2015 Events Reported

- Annual summary-fiscal year 10/1-9/30
- 187 Therapy Events
- 9 Diagnostic Events

6

2011-2015 Events Reported



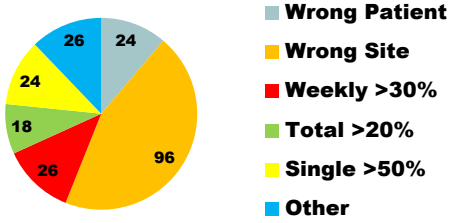
7

States Reporting

- Over the entire period, 20 states have input events
- The highest number of states responding in one year was 37 in 2013 (this included indicating that no events were reported)

8

Types of Therapy Events Reported



9

Severity of Therapy Events

- Severe Effects = 2
- Moderate Effects = 17
- Minor Effects = 130
- No Effects = 39

10

Therapy Events Discovered By:

- ~60% technologists
- ~15% physicians
- ~12% physicists
- ~13% other

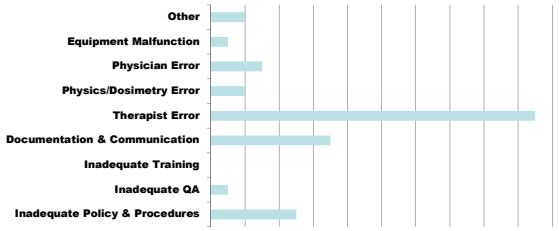
11

Events Discovered How

- Chart Check
- Portal Imaging
- Clinical Review
- ~25% indicated “other”

12

Causes and Contributing Factor



13

Diagnostic Events Summary

- 9 events
  - 4 CT Events; 3 Fluoroscopy; 1 Radiography
- 4 wrong patients
- 2 unlicensed/trained operators
- 1 0.24 Sv to lens of eye
- 1 > 2Gy unintended dose
- 1 equipment failure

14

Important Observations

- In medical use of radiation, we expose people on purpose for a potential benefit
- Unlike in other uses of Radiation
- Millions of procedures are done each year

15

What Can We Do Better?

- Better disseminate information outside of CRCPD & AAPM
- Promote reporting of events to states by facilities and states reporting to CRCPD for more complete data

16

How does "Safety Culture" apply at the facility level?

- Leadership- knowing when and who to report to
  - CRCPD is developing a list of state reporting contacts which will be posted on the CRCPD website and shared with AAPM and ASTRO

17

How does "Safety Culture" apply at the facility level?

- Problem Identification and Resolution- follow up actions
- Personal Accountability- owning up to mistakes
- Environment for Raising concerns
- Respectful work environment

18

How does "Safety Culture" apply at the regulatory level?

- All of these also apply to the inspector/regulator
- Need to be able to identify the problem
- Need to be able to communicate with the facility in a respectable manner

19

How does "Safety Culture" apply at the regulatory level?

- Continuous learning about new equipment and procedures
- Help facilities find resolutions and improve the situation rather than just cite violations
- Encourage and give credit to facilities for reporting

20

What Does CRCPD have planned?

- Topical Training at our meeting on safety culture and root cause analysis- what this looks like at a facility
- "Never Events"- looking at this with our Radiation Therapy Committee to provide information to inspectors
- Journal Article with AAPM on first 5 years of event reporting

21

H-38 Information:

- Links to reporting forms are on the CRCPD website-Completed forms need to be emailed to Bruce Hirschler at CRCPD bhirshler@crcpd.org

22

H-38 Information

- Questions regarding reporting can be sent to Jennifer Elee, Committee Chair at jennifer.elee@la.gov or by phone at 318-362-5439

23

Acronyms

- AAPM – American Association of Physicists in Medicine
- CRCPD – Conference of Radiation Control Program Director

24

2015 Summary of Medical Events Reported to CRCPD's Committee on Medical Events (H38)

CRCPD created the Committee on Radiation Medical Events (H38) in early 2010 in response to the publicity surrounding radiation events in 2009. Some of the committee's charges include, overseeing the development of a national database of radiation medical events and developing a format and mechanism for reporting of medical events. In 2010, the committee determined that the best way to begin collecting radiation medical events was to use the existing state reporting requirements. The CRCPD's H38 committee began collecting medical events that have been reported to state programs in 2011.

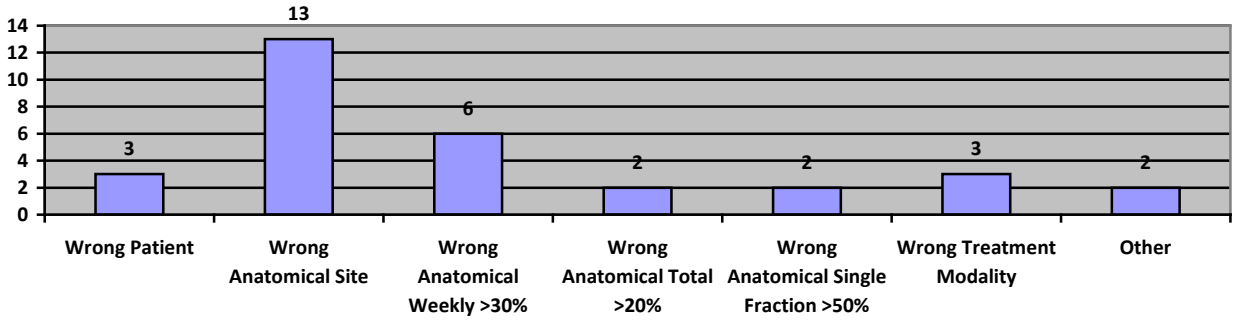
In the first year, 2011, twenty-nine therapy events were reported to CRCPD. Ten states responded to CRCPD with seven states actually inputting events. From January, 2011-September 30, 2015, CRCPD has had 187 therapy and 9 diagnostic events entered into the Medical Event Reporting Database. In the reporting year 2015 which was from October 1, 2014 through September 30, 2015, CRCPD had 31 therapy events reported and one diagnostic event. CRCPD received information from 23 states. Nine states input events, five states had events that were not input, and nine states did not have any events that met the reporting criteria. These numbers are down slightly from last year.

Of the events reported in 2015:

- 13 were treatment to the wrong anatomical site (gross alignment error),
- Six were a weekly dose greater than 30% of the prescribed dose,
- Two were total dose greater than 20% of the prescribed dose,
- Two were a single fraction greater than 50% of the prescribed dose,
- Three were the wrong treatment modality
- Three to the wrong patient

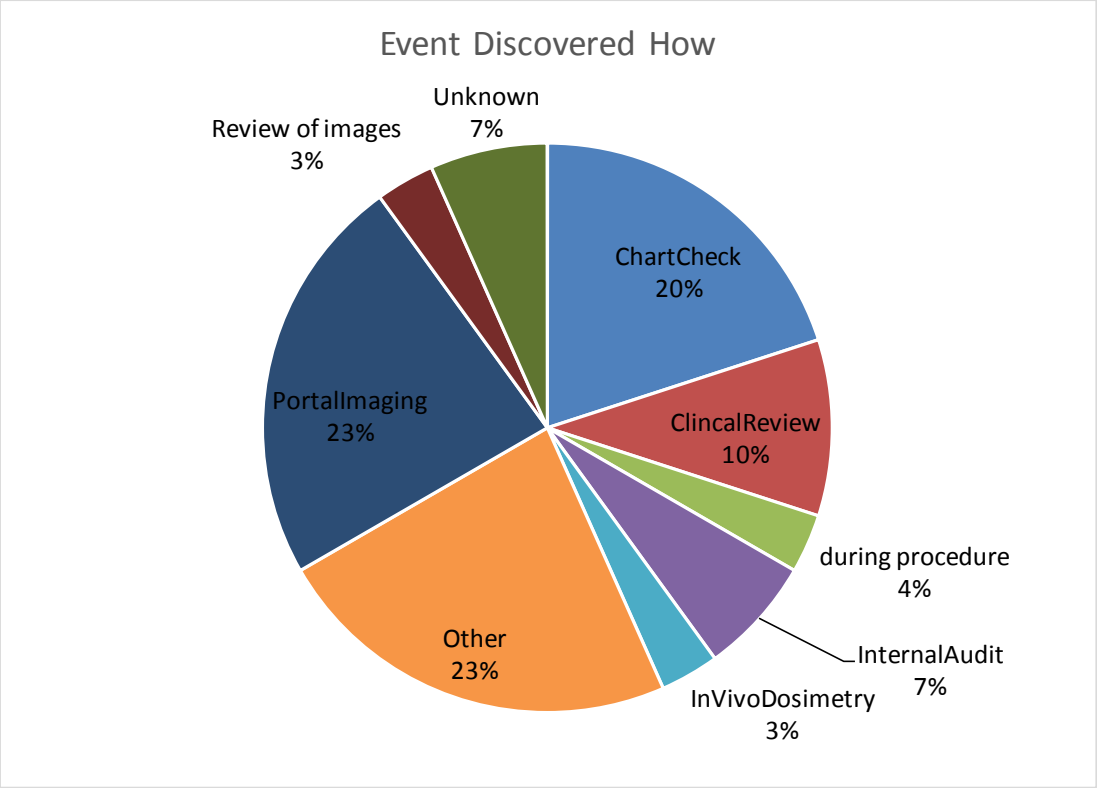
The remaining events were in the "other" category. No events indicated severe effects, six indicated moderate effects, nineteen indicated minor effects and six had no consequences.

Types of events reported:

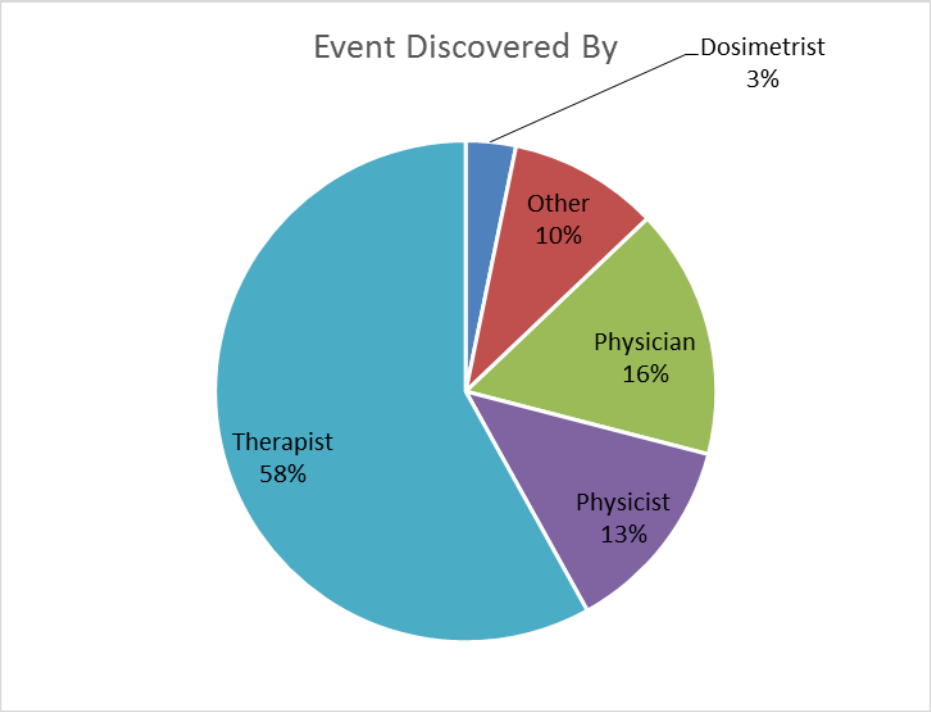


Events were discovered in a variety of ways. Portal imaging, chart check, clinical review, equipment QC, and internal audits revealed events. However, approximately a third of events indicated some other method of discovery. Most of these were by the therapist during or right after treatment. Almost 60% of the events were discovered by radiation therapists followed by physicians and physicists. All of these results are consistent with data from our past analysis.

How the event was discovered:



Event Discovered By:



Again this year, the most common cause for the events was therapist error which was listed in approximately 71% of the events. The next most common causes were documentation & communication and inadequate policy & procedures. Also noted were physician error, inadequate QA, physics/dosimetry error, and documentation/communication issues. Equipment malfunction was cited only four times. Several events had more than one cause/contributing factor noted.

Causes/Contributing Factors:

There was one diagnostic event reported to CRCPD for 2015. This incident involved the wrong patient receiving a chest CT scan. The approximate dose received by the patient was 24.3 mGy. Two patients with similar names were in the waiting room and the wrong patient was imaged. There was no verification of the patient at the time of the exam.

Once again, the most concerning issue is the number of "wrong patient" medical events. This is an area that should be considered a "never event". Another category of "never event" that should be addressed is treatment to the wrong site. The committee is recommending that the Committee on Radiation Therapy look into creating guidance on how facilities can avoid this type of event. This information could be passed along by inspectors during routine inspections to emphasize the importance of this issue.

The committee has seen consistency across all data points for the past several years. We would like to see all states inputting into the database in order to get better results. We have consistently been receiving data from about half of the 50 states, it can be assumed that the actual number of events should be larger than what we are currently receiving. The committee once again has partnered with the American Association of Physicists in Medicine (AAPM) to provide more in depth analysis of the events reported.

Center for the Assessment of Radiological Sciences

Radiotherapy Incident Reporting and Analysis System

Bruce Thomadsen

Center for the Assessment of Radiological Sciences

Disclaimer

I am the President of CARS and Director of the Reporting System.

I am also a professor at the University of Wisconsin

About CARS's System

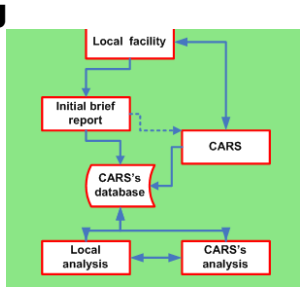
- **CARS is a 501(c)(3) non-profit Patient Safety Organization listed with AHRQ.**
- **Reporting software also used in VA.**

PSO's Charge from AHRQ

- **Help improve clients' quality and safety.**
- **Work with clients to remediate causes of reported incidents.**
- **Work with clients to develop prospective QM.**

CARS' Reporting

1. Facility files very short notice.
2. CARS calls back; fills form during call.
3. Analyzes and discusses action options.



5

Advantages of this Approach

- All incidents go into database.
- All fields completed and correct.
- Root-cause analysis done by professionals who understand both the analysis methods and radiotherapy.
- Clients are supported.

6

More about CARS

- System can serve as the local database.
- Any researcher can register and view the anonymized data.
- We accept anonymous reports. We will follow up if at a client.

7

Dissemination to Community

CARS sends information through e-mail to clients, messages to list servers and letters to professional newsletters.

8

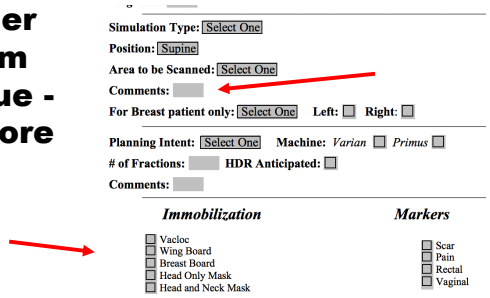
Some Findings

Following various incidents at a client facility allows identification of chronic issues:

- **Scheduling swells and lulls.**
- **Communication failures**

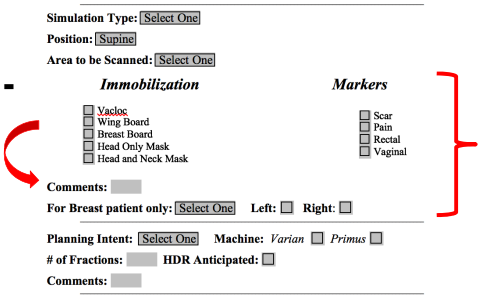
9

Order Form Issue - Before



10

Order Form Issue - After



11

Equipment Reporting

- **CARS also has reporting of equipment failures**
- **We work with vendors to improve the safety of devices and software.**
- **We take this on for clients and possibly report to FDA.**

12

Acronyms 1

- **AHRQ – Agency for Healthcare Research and Quality**
- **CARS – Center for the Assessment of Radiological Sciences**
- **FDA – U.S. Food and Drug Administration**

13

Acronyms 2

- **PSO – Patient Safety Organization**
- **VA – Veterans' Administration**

14

IAEA 60 Years Atoms for Peace and Development

Update on the Safety In Radiation Oncology Incident Learning System SAFRON

International Atomic Energy Agency
Sandy Gabriel
Debbie Gilley
6 October 2016

SAFRON

- Safety in Radiation Oncology (SAFRON) is an IAEA-developed user system for **improving the safety and quality of care in radiation therapy through the sharing of knowledge**.

SAFRON

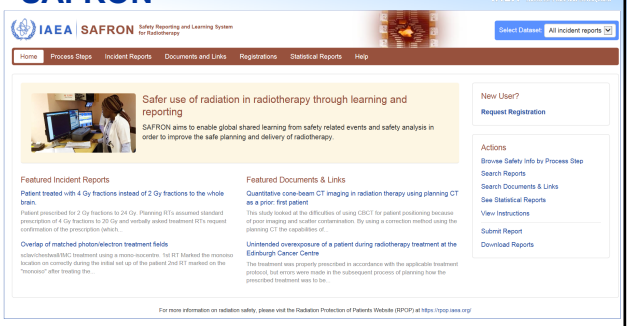
- Clearinghouse for multiple reporting systems and contains information gathered by the IAEA, ROSIS, ASN, CRCPD and individual clinics.
- Database includes 1334* incidents and near misses.
- Non-punitive, anonymous, and voluntary.

*2016-09-15

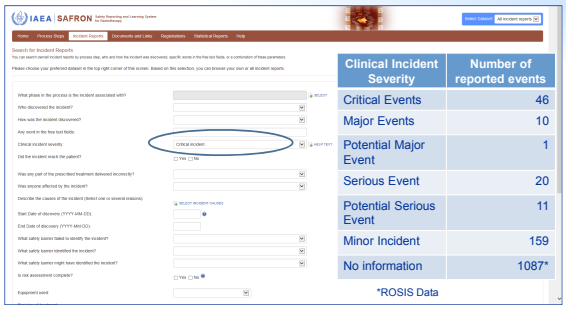
SAFRON

- Designed to:
  - provide information such as statistical data and charts to participating facilities
  - share events with other facilities to enhance their learning
  - improve safety and quality in radiotherapy as an international learning system.
- Provides additional information for improving safety in radiotherapy through detailed reports and peer reviewed publications.
- Offers direct access to information in the database to anyone who registers with the IAEA gateway NUCLEUS.

SAFRON



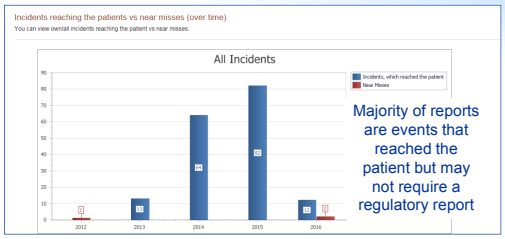
SAFRON



Clinical Incident Severity	Number of reported events
Critical Events	46
Major Events	10
Potential Major Event	1
Serious Event	20
Potential Serious Event	11
Minor Incident	159
No information	1087*

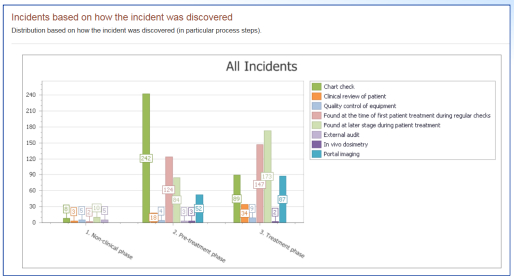
*ROSIS Data

SAFRON

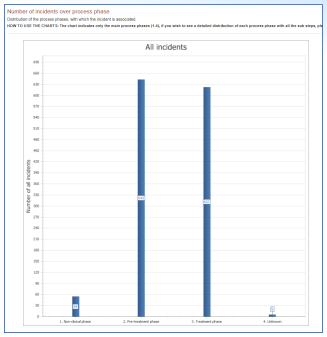


Majority of reports are events that reached the patient but may not require a regulatory report

SAFRON



SAFRON



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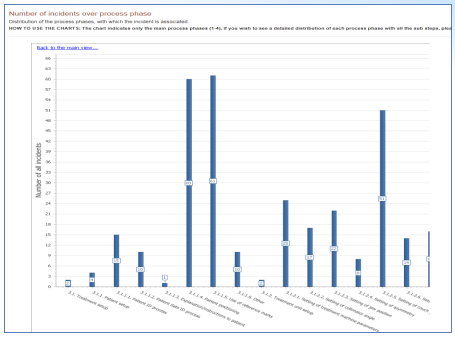
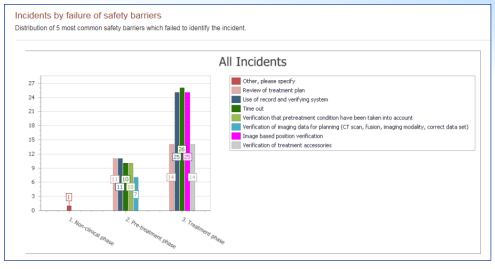


SAFRON



SAFRON

- Identify areas where safety and quality can be improved
- Support the use of safety barriers to prevent errors from reaching the patient
- Learn from events to support standardization in an effort to reduce errors from reaching the patient.

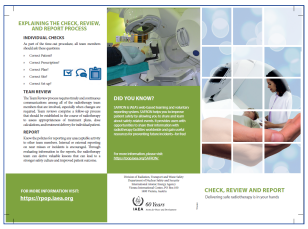
SAFRON Learning

- Presentations to interested parties
  - Numerous international presentations to medical and regulatory authorities
- Newsletters



SAFRON Learning

- Awareness




SAFRON Learning

Provides participants with an understanding of the relationship between safety and quality using illustrations from three medical errors.

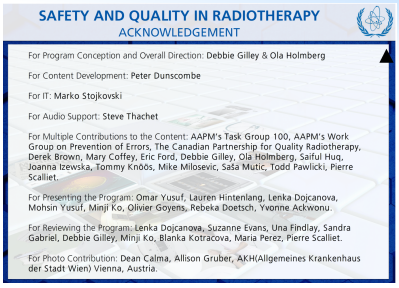
The modules cover FMEA, RCA, incident learning and Safety Culture.

SAFRON Learning

- E-Learning

Designed to allow the participant to complete over time. Each module is completed by successfully completing the quiz.

Certificate of completion is provided.



SAFRON Next Steps

- Add a prospective risk analysis feature for contributors (2017)
- Add capabilities to capture events in brachytherapy (2017/18)
- Add translation capabilities (2018)
- Add Nuclear Medicine events (2019)

International Conferences on Radiation Protection in Medicine

- Bonn, 2012
- Vienna, 2017 14-17 December 2017

60 Years
IAEA Atoms for Peace and Development

Thank you!

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Sandy Gabriel S.Gabriel@IAEA.org

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

Medical Events Report FY 2015

Ronald D. Ennis, M.D.

Advisory Committee for the Medical Uses of Isotopes

October, 2016

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

Subcommittee members

- Ronald D. Ennis, M.D. (Chair)
- Susan Langhorst, Ph.D.
- Michael O'Hara, Ph.D.
- Christopher Palestro, M.D.
- John Suh, M.D.
- Pat Zanzonico, Ph.D.

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Protecting People and the Environment

35.200 Use of Unsealed Byproduct Material for Imaging and Localization

- Time Period:10/1/2014 - 9/30/2015
- 4 events
  - ^{99m}Tc: 3 events
    - Myocardial perfusion studies:2
    - Lymphoscintigraphy: 1
  - ^{123}I: 1 event
    - Thyroid

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Protecting People and the Environment

35.200 Use of Unsealed Byproduct Material for Imaging and Localization

- ^{99m}Tc

  Myocardial perfusion studies

  (1) 4.37 GBq (118 mCi) $^{99m}TcO_4^-$ administered instead of 480 MBq (12.9 mCi) ^{99m}Tc-sestamibi. Failure to follow proper procedures

  (2) 5.92 GBq (160 mCi) $^{99m}TcO_4^-$ administered instead of 1.11 GBq (30 mCi) ^{99m}Tc-tetrofosmin. Caused by inattention to detail.

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Protecting People and the Environment

35.200 Use of Unsealed Byproduct Material for Imaging and Localization

- ^{99m}Tc

  Lymphoscintigraphy
  Patient received 1.11 GBq (30 mCi) ^{99m}Tc-MDP instead of 18.5 MBq ^{99m}Tc for sentinel node procedure. Technologist failed to verify patient ID on doseage pig prior to administration.

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Protecting People and the Environment

35.200 Use of Unsealed Byproduct Material for Imaging and Localization

- ^{123}I

  Thyroid
  136.53 MBq (3.69 mCi) ^{123}I (NaI) administered instead of 11.1 MBq (300 uCi) ^{123}I (NaI). Caused by human error

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Protecting People and the Environment

35.300 Use of Unsealed Byproduct Material, Written Directive Required

- Time Period:10/1/2014 - 9/30/2015
- 7 events
  - ^{131}I: 5
  - $^{223}RCl_2$: 1
  - ^{124}I-H89: 1

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Protecting People and the Environment

35.300 Use of Unsealed Byproduct Material, Written Directive Required

- ^{131}I

  (1) Pt. received 1.85 GBq (50 mCi) instead of 1.30 GBq (35 mCi) (42.8% overdose). Technologist failed to confirm activity and selected wrong doseage.

  (2) Pt. received 1.14 GBq (30.8.mCi) instead of 111 MBq (3 mCi) (927% overdose). Intended prescription was 1.18 GBq (32 mCi) Written directive incorrectly annotated

35.300 Use of Unsealed Byproduct Material, Written Directive Required

- ^{131}I

(3) Pt. received 5.3 GBq (143.2 mCi) instead of 1.11 GBq (30 mCi) (377% overdose). Technologist selected wrong vial & didn't confirm written directive.

(4) Pt. received 2.775 GBq (75 mCi) instead of 5.55 GBq (150 mCi) (50% underdose). Dosage supplied in 2 capsules, but only one was administered.

9

35.300 Use of Unsealed Byproduct Material, Written Directive Required

- ^{131}I

(5) Pt. received 58.09 MBq (1.57 mCi) instead of 74 MBq (2.0 mCi) (21.5% underdose). Caused by failure to follow procedures.

10

35.300 Use of Unsealed Byproduct Material, Written Directive Required

- ^{223}Ra

Pt. received 7.65 MBq (206.8.uCi) instead of 4 MBq (108 uCi) (91.48% overdose). Technologist misread prescribed dose and administered both doseages.

11

35.300 Use of Unsealed Byproduct Material, Written Directive Required

^{124}I-8H9 (monoclonal Ab)

Pt.received 64.38 MBq (1.74 mCi) instead of prescribed 120.25 MBq (3.25 mCi) (53% underdose) because of leakage at catheter connector site not obvious on visual inspection

12

35.400 Medical Events 2013-2015

35.400 Medical events	2013: 16 MEs (18 patients)	2014: 5 ME's	2015
Gynecological	2	1	0
Prostate	14 (16 patients)	4	7 (8 patients)
Head and Neck	0	0	1

35.400 Medical Events Non-Prostate Manual Brachytherapy

Head and Neck - Tongue Ir-192

- 5 strands of Ir-192 implanted.
- One strand missing when MD checked at Noon. Had been in place in AM. Found in linen which had been changed at 10AM.
- Reinserted and treatment completed.
- Not reported initially
- On site visit – possible unintended skin dose of 51.75 rem – ME
- No patient toxicity
- Cause "procedure" problem
- Corrective action – "wrote new policy"

35.400 Medical Events Prostate Manual Brachytherapy

- 7 Medical Events (8 Patients)
- Physicians mistook penile bulb as prostate
  - Licensee determined the US unit had been serviced by vendor prior the procedure. Some calibration settings were changed (i.e. gain). This led to the error in identifying correct structure.
  - No attribution to MD error
  - Corrective action – Implemented procedures to assure efficacy of US after service prior to use

35.400 Medical Events Prostate Manual Brachytherapy

- Patient received 28% more dose than intended
  - Ordered seeds based on air kerma instead of mCi. Also ordered 4 more seeds than prescribed.
  - Corrective action – new procedures, improve material labeling, handling protocols and new training
- Patient received 49% more dose than intended
  - Prescribed 13.4 mCi to deliver 10,700 cGy (boost treatment) but delivered 18.3 mCi to deliver 16,000 as full treatment
  - Corrective action modified procedures to confirm and document the implant dose.
  - Did not proceed with the planned external beam treatment

35.400 Medical Events Prostate Manual Brachytherapy

- Patient received 27% less the prescribed
  - Detected on investigation
  - No other details provided
  - Licensee sited for failure to develop written procedures, failure to perform acceptance testing of computer systems, failure to properly document post-procedure written directives, failure to conduct adequate annual review of radiation safety program
  - Licensee requested to hire medical physicist to audit safety program and recommend corrections

17

35.400 Medical Events Prostate Manual Brachytherapy

- Investigation because of "irregularities" found in a licensee's practice and therefore retrospectively reviewed prior cases
  - This may be related to prior case – different site of same corporate entity
  - Found 2 MEs of lower dose than prescribed – 37% of prescribed and 67% of prescribed. Both Pd-103.
  - No further information provided

18

35.400 Medical Events Prostate Manual Brachytherapy

- D90 34% less the prescribed dose
  - Later retracted due to further investigation by regulator
- Misplacement of seeds resulting in higher dose to rectum by 61%.
  - No cause other than "inherent difficulty in the procedure"

19

35.600 Remote Afterloaders, Teletherapy, Gamma Knife

	FY2013	FY2014	FY2015
All § 35.600	9	10	13
All HDR	8	9	13
LDR remote afterloader	0	0	0
Gamma Knife	1 (+1 Perfexion)	1 (+1 Perfexion)	(+1 Perfexion)
Teletherapy	0	0	0

HDR Brachytherapy Sites

Event Site	Number of Events
Breast	1
Gynecological (mostly vaginal cylinders)	9
Skin	1
Bronchus	2

35.600 HDR Brachytherapy Observations

- 8 Positioning problems:
  - 5 Wrong positioning,
  - 3 Wrong reference length entered,
- 2 Wrong patient's plan delivered
- 1 Deficient treatment plan
- 2 Machine problems

35.600 HDR Brachytherapy Observations

- Action plans
  - Personnel training, especially when upgrading or changing treatment units
  - Proper timeouts
  - Verification of cylinder placement before, during and after treatment
  - Manufacturer notification

35.600/35.1000 GammaKnife Medical Events

- Gamma Knife - 0 event (§ 35.600)
- Gamma Knife Perfexion – 1 event (§ 35.1000)
  - Misalignment of the patient positioning system for 8 patients. Off-target by 1.87 mm. Dose exceeded prescribed dose by 100%.
  - Action plan
    - Development of new set of tests to verify patient positioning

§ 35.1000 Medical Events

	FY2013	FY2014	FY2015
All § 35.1000	15	26	14 18 patients
All Microsphere	13	23	14 18 pts.
SIR-Spheres	10	16	6
TheraSphere	3	7	8/12
Radioactive Seed Localization	1	2	0

§ 35.1000 Medical Events Microspheres

3 - retained microspheres in catheter/tubing, hub, vial (3 Therasphere, 1 SIR) (78%, 58% and 67% of prescribed dose delivered)

5 – use of small catheters which led to microspheres retained in hub (1 institution, Therasphere) (all <80%, NOS)

1 - incorrect set-up of tubing (SIR) (79%)

1 - incorrect tightening of tubing connection leading to leak (SIR) (42%)

1 - kink in tubing (Therasphere) (35%)

§ 35.1000 Medical Events Microspheres

1 - low flow due to small arteries. 77% of dose delivered.

1 - Stomach received 57.5 rem. Detected on post-treatment scan. Infusion had been discontinued after 64% due to stasis.

1 - catheter moved, perhaps when fluoro table was moved, and infused 38% to superior mesenteric artery to small bowel. Did not re-image after moved table. Corrective action procedure modifications and additional training. Led to hospitalization of patient for pain. (SIR)

§ 35.1000 Medical Events Microspheres

2 wrong artery

1 – wrong hepatic artery, treated left lobe (segment 4) instead of right lobe (segments 1,5,6,7,8). Corrective action – have angiogram present at procedure

1 – renal artery instead of hepatic artery.

High dose (1345 Gy) to kidney. First procedure done by licensee. No kidney damage observed (yet). Corrective action – formal checklist, mapping images at procedure, review of position by second MD

28

§ 35.1000 Medical Events Microspheres

- 2 – reported underdose that were later retracted when further investigation revealed correct dose given

29

Other Medical Byproduct Material Events

- NMED event involving medical license or associated license
- NMED event associated with medical license
- Does not include § 35.3045 or 35.3047 events or other patient safety events

30

Other Medical Byproduct Material Events – identified in FY15 [FY14]

Categories

- Miscellaneous – 12 [8]
- Leaking sealed sources – 4 [4]
- Lost materials/sources (no Cat. 1 or 2) – 24 [30]
- Shipping issues – 12 [10]
- Landfill alarms – 114 [113]

31

Other Events – Miscellaneous FY15 [FY14]

- Occupational overexposure – 6 [2]
- Suspected public overexposure – 0 [1]
- Airborne constraint exceeded – 0 [1]
- Equipment failures – 3 [3]
- Contamination – 2 [0]
- Recordkeeping – 1 [0]
- Suspicious activity – 0 [1]

32

Other Events – Leaking sealed sources FY15 [FY14]

- Cs-137 source (<300 µCi) – 0 [2]
- Co-57 line source – 0 [1]
- I-125 source (localization) – 2 [1]
- I-125 source (eye plaque) – 1 [0]
- Pd-103 source (prostate seed) – 1 [0]

33

Other Events – Lost materials/sources FY15 [FY14]

- Lost after procedure (I-125) – 10 [10]
- Lost/found/lost and found – 4/1/0 [2/2/4]
- Lost during shipment – 8 [6]
- Package thrown away – 0 [1]
- Licensee out of business – 0 [1]
- Theft – 0 [3]
- Buried pacemaker – 1 [0]

34

Other Events – Shipping issues FY15 [FY14]

- Delivered wrong address/location – 4 [5]
- Stored in unsecured area – 1 [1]
- Accident/Highway Patrol delivery – 0 [1]
- Shipping package issues – 7 [2]
- No license approval for receipt – 0 [1]

35

Other Events – Landfill

Isotope	Hospital	Residence	Not identified
I-131	6 [2]	10 [23]	58 [37]
In-111	1 [1]	2 [0]	1 [2]
Tc-99m	3 [18]		10 [14]
Tl-201	0 [3]	1 [0]	1 [0]
Not identified	0 [3]	0 [3]	21 [7]

Reports from Agreement States –

18 [12]% AL 81 [85]% CA 1 [1]% FL 0 [1]% NC 1 [2]% DC

36

Conclusions

- No obvious trends or patterns this year
- Each year there are ~15,000,000 diagnostic and 150,000 therapeutic procedures performed utilizing radioactive materials
- The tiny fraction presented here today is reassuring and confirms the generally safe fashion these materials are administered to patients in the USA

Acronyms

- cm – centimeter
- Cs – Cesium
- FY – Fiscal Year
- Gy (rad) – Gray
- GYN – gynecological
- HDR – High dose-rate
- I – Iodine
- LDR – Low dose-rate
- MBq – megabequerel

Acronyms

- mCi – millicurie
- ME – Medical Event
- NMED – Nuclear Material Events Database
- Pd – Palladium
- Pt(s) – Patient(s)
- QA – Quality Assurance
- rem – roentgen equivalent in man
- Y – Yttrium

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

Medical Event Reporting for All Modalities Except Permanent Implant Brachytherapy

John H. Suh, M.D.
ACMUI

Subcommittee Members

- **Ronald Ennis, M.D.**
- **Vasken Dilsizian, M.D.**
- **Chris Palestro, M.D.**
- **John Suh, M.D. (chair)**
- **Pat Zanzonico, Ph.D.**
- ***Zoubir Ouhib, M.S.***

Subcommittee Charge

- **To propose the appropriate criteria for ME Reporting other than for permanent implant brachytherapy.***
- **On 3/17/16, the subcommittee's initial thoughts on definition of medical events reporting for all modalities except permanent implant brachytherapy were presented.**

***Permanent implant brachytherapy MEs addressed previously by the ACMUI**

Recommendations from March 2016

- **Medical events reporting should allow identification of an ME and provide a mechanism to discuss how to avoid/reduce the likelihood of such an event.**
- **The definitions of ME reporting need to be broad, simple, and consistent, so reports are easily prepared by AUs, evaluable by regulators, and process-focused in order to eliminate any ambiguity.**

Recommendations from March 2016

- The part of the definition based on "unintended permanent functional damage to an organ or a physiological system, as determined by a physician" needs reconsideration.
- The creation of a subsection within the current framework of ME reporting be considered to address the newer, highly conformal radiation oncology modalities that prescribe dose to volumes.
- Any proposed changes should not be overly prescriptive and must not encroach on the practice of medicine.

5

Subcommittee Discussions

- The Subcommittee discussed the current ME Reporting Criteria under 10 CFR 35.3045.
- The Subcommittee reviewed different scenarios in which the ME Criteria were ambiguous and therefore required possible modification(s).
- Given the spatial precision of modern therapies, a slight shift can result in significant dose to nearby tissues or parts of organs.
- Current radiation therapy plans are not prescribed to a point but usually to a treatment site.

6

Subcommittee Discussions

- Use current ME definition for radiopharmaceuticals.
- Devise definition for 2D, 3D-CRT, IMRT, SRS, SBRT, LDR/HDR brachytherapy and intraoperative modalities.
- Do not revise "unintended permanent functional damage to an organ or a physiological system, as determined by a physician" in section 3b of 35.3045.

7

ME criteria would need to cover a variety of treatment modalities

- HDR: all body sites
- Gamma Knife™
- LDR temporary implants
- Intraoperative modalities

8

§ 35.3045 Report and notification of a medical event

(1) A dose that differs from the prescribed dose or dose that would have resulted from the prescribed dosage by more than 0.05 Sv (5 rem) effective dose equivalent, 0.5 Sv (50 rem) to an organ or tissue, or 0.5 Sv (50 rem) shallow dose equivalent to the skin; and

(i) The total dose to 80% of the treatment site differs from the prescribed total dose by 20% or more;

(ii) The single fraction dose to 80% of the treatment site differs from the prescribed single fraction dose, for a single fraction, by 50% or more.

Treatment site is defined by physician and can be referenced by the signed treatment plan.

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Defining ME by Use of Treatment Site

- **Will be easier for licensee to determine if a ME occurred.**
- **Will be easier to inspect and regulate**
- **Will better protect the public**
- **Will facilitate programs, procedures and education to prevent future events.**

Since delivery systems and risks are different, a specific ME for each modality may provide some advantages, but the committee did not favor modality-specific ME, but rather classification of non-SIRT, non-Viewray™, and non-radiopharmaceuticals by use of treatment site.

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Current Recommendations

- **Use new definitions for permanent implants**
- **Use current 35.3045 definition for radiopharmaceuticals.**
- **Use treatment site definition for 2D, 3D-CRT, IMRT, SRS, SBRT, LDR/HDR brachytherapy, and intraoperative modalities.**
- **The subcommittee believes that the creation of a treatment site within the current definition of ME reporting be considered to address the newer radiation oncology modalities that prescribe dose to a volume.**

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Acronyms

- **ACMUI – Advisory Committee on the Medical Uses of Isotopes**
- **AU – Authorized User**
- **CFR – Code of Federal Regulations**
- **FY – Fiscal Year**
- **GYN – Gynecological**
- **HDR – High Dose Rate**
- **IMRT- Intensity modulated radiation therapy**
- **LDR – Low Dose Rate**
- **ME – Medical Event**

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Acronyms (Continued)

- **SBRT: Stereotactic body radiation therapy**
- **SRS: Stereotactic radiosurgery**
- **SIRT- Selective internal radiation therapy**
- **2D: Two dimensional**
- **3D-CRT- Three dimensional conformal radiation therapy**

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UPDATE ON PART 35 FINAL RULE

TORRE TAYLOR
OFFICE OF NUCLEAR MATERIAL SAFETY AND SAFEGUARDS
October 6, 2016

Outline of presentation

- Background
- Current status
- ACMUI Review
- Staff Response
- Major Changes in Final Rule
- Final Process for Publication
- Contacts
- Questions

Background

- Proposed rule noticed in Federal Register July 21, 2014
  - 79 FR 42409
- Comment Period closed November 18, 2014
- 69 comment letters
- ACMUI had early opportunities to review and provide comments on draft proposed rule and the final rule

Current Status

- SECY-16-0080
  - "Final Rule: Medical Use of Byproduct Material – Medical Event Definitions, Training and Experience, and Clarifying Amendments (RIN 3150-AI63; NRC-2008-0175), dated June 17, 2016
- ADAMS accession no. ML16123A342

ACMUI Review

- ACMUI report with its recommendations - January 6, 2016.
  - Enclosure 4 to SECY-16-0080
- ACMUI Recommendations discussed during a public teleconference on January 6, 2016.
  - 13 recommendations to the NRC

5

Staff Response

continued

- ACMUI endorsed six provisions of the final rule
- Two recommendations were accepted
- One recommendations was accepted
- One recommendation was accepted in part
- Four recommendations were not accepted

6

Major Changes in Final Rule

- ME reporting criteria for permanent implant brachytherapy
- § 35.3045 (a)(2)
  - Deleted the criteria for absorbed doses to normal tissues located outside of or within the treatment site
  - Now based on source strength
  - Clarified that it is based on post-implantation portion of the written directive

7

Major Changes

continued

- ME criteria for wrong location - § 35.3045(a)(2)(iii)(C)
  - Revised to state: "Sealed source(s) implanted directly into a location discontiguous from the treatment site as defined in the written directive."
  - Proposed rule stated "…will not contribute dose to the treatment site…"

8

Major Changes
continued

- Reporting of failed technetium and rubidium generators (§ 35.3204)
  - Requires reporting within seven calendar days
    - Proposed rule – 30 calendar days
  - Written report required in 30 days
    - Proposed rule – 45 days

9

Major Changes
continued

- Deleted separate category for training and experience for alpha-emitting radiopharmaceuticals for parenteral administration
  - Now included within § 35.390(b)(1)(ii)(G)(3)

10

Major Changes
continued

- Compatibility Category for ME – § 35.3045
  - Compatibility Category C
  - Agreement States must meet the essential objectives of the rule but can be more restrictive
  - Dose-based criteria is not considered part of the essential objective

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Major Changes
continued

- Essential Objective of § 35.3045
  - Maintain a consistent national program for reporting MEs
  - Identify trends or patterns, generic issues or concerns, recognize inadequacies or unreliability of specific equipment or procedures
  - Determine why an event occurred and any need for action

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Final Process for Publication

- **Commission SRM**
- **Review and Approval – OMB**
- **Publication**
  - **Effective date – 180 days from date of publication**
  - **Agreement States – 3 years from the effective date to adopt the final rule**

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CONTACTS

Rulemaking Process

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ACRONYMS

- **ACMUI – Advisory Committee on the Medical Uses of Isotopes**
- **ADAMS – Agencywide Documents Access and Management System**
- **ME – Medical Event**
- **OMB – Office of Management and Budget**
- **SRM – Staff Requirements Memorandum**

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Patient Intervention: How Do We Proceed?

Michael Fuller
Team Leader
Medical Radiation Safety Team
October 6, 2016

Purpose

To review the ACMUI recommendations related to the definition for "Patient Intervention" and discuss the challenges facing NRC Staff

Background/History

- **Presentation by Sandra Gabriel, Ph.D. on March 19, 2015**
- **Presentation by Frank Costello on March 19, 2015**
- **Charge by ACMUI Chairman to:**

Clarify the meaning of "Patient Intervention" to make sure that the Nuclear Regulatory Commission (NRC) and the Advisory Committee on the Medical Uses of Isotopes (ACMUI) are aligned in their interpretation of the term

Background/History

- **Presentation by Vasken Dilsizian, M.D. on October 8, 2015**
- **ACMUI Recommendation:**
  - **Issue I**
    - **Intentional/Unintentional patient action would represent a reportable medical event if it results or will result in unintended permanent functional damage to an organ or a physiological system, as determined by a physician (10 CFR 35.3045(b) – 2002 Final Rule)**
    - **Of course, the overall goal would be to prevent or mitigate patient action that may impact treatment**

Background/History

- **ACMUI Recommendation:**
  - **Issue II**
    - **Unintentional treatment outcome due to anatomic or physiologic anomaly and/or imaging uncertainty falls into the category "the Art of Medical Practice" provided that the standards of medical practice are met**
    - **Reporting such unpredictable and unavoidable patient-specific medical events will not help to prevent such events in the future, and therefore cannot be regulated**

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10 CFR Part 35 Definition

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.**

6

What Problem Needs Solving?

- **In Mr. Costello's presentation in March 2015, the concern was focused Y-90 microspheres**
  - **Specifically "…the patient's artery contracts and the spheres flow retrograde into the gastrointestinal artery…"**
  - **and, "…If the patient's lung shunt fraction was one value during the work-up and changed for the treatment…"**
- **Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance, Revision 9, issued on February 12, 2016**
  - **Exception made for shunting when shunting was evaluated prior to the treatment in accordance with the manufacturer's procedures**
  - **Exception made for emergent patient conditions that prevent administration in accordance with the written directive (e.g. artery spasm or sudden change in blood pressure) (Rev 8, June 2012)**

7

Challenges

- **NRC Staff and ACMUI are not aligned**
  - **NRC staff cannot implement ACMUI recommendations as written**
  - **What is the problem that we are trying to solve?**

8

How Do We Proceed?

- **This is more of a legal issue than a technical one**
- **According to 10 CFR 1.23 The NRC Office of General Counsel provides interpretation of laws, regulations, and other sources of authority**
- ***Patient intervention* is defined in 10 CFR 35.2**

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Questions?

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Yttrium-90 Microspheres Brachytherapy Licensing Guidance, Revision 10

Katie Tapp, Ph.D.
Medical Radiation Safety Team
October 7, 2016

Working Group Members

- Katie Tapp, co-chair, NRC NMSS
- Bob Dansereau, co-chair, NY state
- Penny Lanzisera, NRC RI
- Victor Diaz, NM
- Sara Forster, NRC RIII

Working Group Tasks

- Training and Experience:
  - Pathway 2 (Manufacture Training Pathway)
- Waste and Disposal Section
- Autopsy and Cremation Information

Training and Experience

- Two Components
  - Radiation Safety Training and Experience
  - Specific Clinical Experience for Y-90 Microsphere Therapy, including
    - Training in operation of delivery system, safety procedures, and clinical use
    - 3 supervised in-vivo cases

Training and Experience (cont.)

- Current Guidance Recommends In-Vivo Cases Supervision be from an:
  - Authorized User (pathway 1)
  - Manufacturer Representative (pathway 2)

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Pathway 2

- Pathway 2 was introduced due to limited authorized users to provide supervision
- Manufacturing supervision is unique and not found in 10 CFR 35

6

Pathway 2 Recommendation

- Two years after the Issuance of the Licensing Guidance, Remove Pathway 2
  - After 10 years of licensing AU for Y-90 microspheres, there are adequate number of AUs available to provide supervision
  - 2 year grace period

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Pathway 2 During Grace Period

- Recommending 6 month limit for completing 3 supervised in-vivo cases after AU listed on license
  - Avoid significant time between training and actual clinical experience
  - Case-by-case basis allowance

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Long-Lived Contaminants

- 2007 notification of long-lived impurities found in microspheres
- Information Notice (IN) 2007-10, "Yttrium-90 TheraSpheres® and SIRSpheres® Impurities"
- Microsphere Manufacturing Process

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Autopsy and Cremation

- Y-90 microspheres are permanent implants
- Recommendation to refer to information in NCRP Report No. 155 and NUREG-1556, Volume 9.

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Acronyms

- AU – Authorized User
- CFR – *Code of Federal Regulations*
- IN – Information Notice
- NCRP – National Council on Radiation Protection & Measurements
- Y-90 – yttrium-90

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ACMUI Sub-committee on the Draft Y-90 Microspheres Brachytherapy Licensing Guidance, Rev. 10

Darlene Metter, M.D.
ACMUI
October 7, 2016

Sub-Committee Members

- **Frank Costello, CHP**
- **Sue Langhorst, PhD**
- **Darlene Metter, MD (Chair)**
- **Chris Palestro, MD**

Background

- **Manual intra-arterial brachytherapy implants with unique properties for 1° and 2° hepatic malignancies**
- **Regulated under 10 CFR 35.1000 "Other Medical Uses of Byproduct Material or Radiation from Byproduct Material"**

NRC/OAS Working Group Recommendations for ACMUI Review

- **NRC licensing guidance on Y-90 Microsphere Brachytherapy Sources and Devices draft Revision 10 is near complete.**
- **ACMUI was tasked to comment on 3 draft guidance issues.**

NRC/OAS Working Group Recommendations for ACMUI Review

1. Consider the elimination of Pathway 2 (manufacturer AU training)

1. Update the waste and disposal section

2. Review Y-90 radiation safety issues in autopsy and cremation

ISSUE 1: Authorized User - Training and Experience

The draft guidance delineates:

1. AU qualifications

2. Training and clinical experience (3 hands-on cases)

   a. AU supervised (Pathway 1)

   b. Manufacturer supervised (Pathway 2)

AU Training (Pathway 1)

- A physician AU for a specific Y-90 microsphere therapy supervises the training and clinical experience of 3 patient hands-on cases for which the specific Y-90 microsphere therapy is being sought.

- After the 3rd supervised hands-on Y-90 microsphere therapy, the training is complete. The individual is then listed as an AU on their site's radioactive license for this specific therapy.

Manufacturer Training (Pathway 2)

- A Y-90 microsphere manufacturer supervises 3 in-vitro simulated Y-90 therapies for the specific AU therapy being sought.
- The individual is then listed as an AU on their site's radioactive license for this therapy.
- The 1st 3 in-vivo specific Y-90 therapy cases, for which approval is being sought, must be supervised by the manufacturer proctor and completed within 6 months after the date of license amendment.

History of Pathway 2

- 2004 NRC licensed AUs for Y-90 brachytherapy under 10 CFR 35.1000
- 2004: Few AUs available to provide supervision
- 2008 Pathway 2 created to allow manufacturer provided clinical training to attain AU status for Y-90 microsphere therapy

Pros: Rationale for Eliminating Pathway 2

- After > 10 years, there are sufficient AU's to meet the clinical demand and provide the required clinical experience for new AUs.
- Licensees AU listing does not differentiate AU's who have completed the 3 clinical cases (AU or manufacturer proctored) from AU's in Pathway 2 who have not.

Pros: Rationale for Eliminating Pathway 2

- Tracking AU's in Pathway 2 who have or have not met the clinical experience is difficult and at times impossible.
- NRC state regulatory authority:
  - NRC 13%
  - Agreement 87%

Pros: Rationale for Eliminating Pathway 2

LS1

- Manufacture AU proctors are not physicians.
- Pathway 1 AU training will be:
  1) more clinical, based on the AU physician proctor's direct patient experience, and
  2) complete when the physician seeking AU is listed on a radioactive license.

Slide 12

LS1 Do we know whether this is always the case? Could we say, "... proctors are not required to be physicians."
Langhorst, Susan, 09/11/2016

Eliminating Pathway 2

- NRC is proposing a multi-year delayed removal of Pathway 2 with a subsequent deadline date.
- Individuals may enter Pathway 2 up until the deadline.

Cons: For Eliminating Pathway 2

- Limit rural community access without AUs
- Negative effect on patient safety & access to care
- No uniform standardized training with potential training gaps
- Patients may not receive timely care
- Potential lack of co-operation between networks/institutions to train AUs
- AU's "too busy" to supervise clinical cases

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Eliminating Pathway 2

PROs

- Over 10 years of implementation with many Y-90 microsphere AUs
- Pathway no longer deemed necessary, sufficient AUs to meet the clinical demand and supervise potential AUs
- Tracking difficulties in AU license listing for those who have from those who have not completed the 3 required hands-on AU manufacturer –proctored supervised cases versus those who have not.

CONs

- Limit access to rural communities without AUs
- Negative effect on patient safety and access to care
- lack of uniform training and potential training gaps
- May delay patient care
- Potential of no AU co-operation between networks/institutions
- AUs "too busy" to supervise clinical cases

Subcommittee comments on eliminating Pathway 2

- If there is a sufficient need for Y-90 microsphere training, sites performing large number of therapies may offer "mini fellowships."
- If a current AU for Y-90 microsphere joins a new site, their prior training and experience will apply to the new site.
- The subcommittee encourages AUs for Y-90 microsphere therapy to drive the proctoring experience in their community.

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ISSUE 2: Waste & Disposal Issues

- **Y-90 production varies* resulting in a mixture of impurities with varying half lives ($t_{1/2}$): current guidelines**
- **Disposal:**
  - **Decay in storage with $t_{1/2}$ < 120 days or short-lived (allowed)**
  - **Concern would be for $t_{1/2}$ > 120 days** or long-lived, which cannot be decayed in storage.**

*Generator or reactor produced

**Europium-152, europium154, cobalt-60

ISSUE 2: Waste & Disposal Issues

- **Licensees need to be aware of long-lived impurities which can increase with partially used or unused vials.**
- **Long-lived impurities present disposal issues.**
- **Subcommittee supports: "Although impurities need not be listed on an NRC license; licensees are responsible to ensure the microspheres are handled and disposed of in accordance with 10 CFR Part 20 and 35 requirements."**

ISSUE 2: Waste & Disposal Options

- **Short-lived: Decay in storage (10 CFR 35.92); or**
- **Long-lived: Return used/unused vials to the manufacturer if the manufacturer is authorized to receive them; or**
- **Transfer remaining Y-90 to an authorized recipient (10 CFR Part 20 and 30)**

ISSUE 2: Waste & Disposal Issues

- **Measurable long-lived impurities need to be returned or transferred to an authorized recipient.**
- **Most licensees are not detecting these impurities, and measurable long-lived impurities is uncommon, thus the material may be decayed in storage.**
- **The subcommittee supports the NRC draft and this additional guidance on waste disposal.**

ISSUE 3: Autopsy & Cremation

- Y-90 microspheres: millions of permanent implants; not biodegradable
- $T_{1/2}$ = 64 hours
- Pure beta emitter
- Max energy: 2.27 MeV
- Range (tissue): 11 mm (max)
- Size: 20 to 60 microns

ISSUE 3: Autopsy & Cremation

- Autopsy related personnel: current guidelines
  - Radiation exposure can be increased with the handling of radioactive autopsy tissue
  - Notify RSO & patient's AU about death
  - RSO must approve autopsy
  - ALARA principles adhered to as assessed and directed by the RSO

ISSUE 3: Autopsy & Cremation

- Subcommittee comments:
- Deceased Y-90 microsphere patients do not generally present a radiation hazard when handling the deceased's body.
- Autopsy performed within 2-4 weeks after Y-90 therapy may call for precautions to manage worker's radiation exposure
- Cremation within 2-4 weeks of Y-90 therapy may also require precautions, and potentially beyond that date due to long-lived contaminants.

Summary of ACMUI Sub-Committee Recommendations

1. Consider the elimination of Pathway 2 (manufacturer AU training): support
2. Update the waste disposal section: adequate, support
3. Review Y-90 radiation safety issues in autopsy and cremation: support with suggested edit on autopsy timing

Acronyms

ACMUI	Advisory Committee on the Medical Uses of Isotopes
ALARA	As low as (is) reasonably achievable
AU	Authorized user
CFR	Code of Federal Regulations
MeV	Mega (million) electron-volts
NRC	Nuclear Regulatory Commission
OAS	Organization of Agreement States
RSO	Radiation Safety Officer
$T_{1/2}$	Half-life
T&E	Training and experience
Y-90	Yttrium-90

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Nuclear Regulatory Commission (NRC)

Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Sub-Committee on

Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSpheres

and SIR-Spheres Licensing Guidance

Draft Report

September 13, 2016

Sub-Committee Members:

Mr Frank Costello
Dr. Susan M. Langhorst
Dr. Darlene Metter (Chair)
Dr. Christopher Palestro

Introduction

The liver is a common site for primary and secondary malignancies. The traditional management of these diseases has been either surgical and/or by chemotherapy, the latter by oral, intravenous or intra-arterial. Over the last several years, the introduction of transarterial radioembolization with yttrium-90 (Y-90) impregnated microspheres has emerged as an important therapy in the management of hepatic malignancies[1].

Y-90 microspheres are manual permanent brachytherapy implants which are small, with a diameter of 20-60 microns for resin microspheres and 20-30 microns for the glass microspheres. These radiolabeled microspheres are delivered intra-arterially, usually by an interventional radiologist. Y-90 microspheres are regulated under 10 CFR 35.1000 “Other Medical uses of Byproduct material or Radiation from Byproduct material.”

[1] Kallini JR, Gabr A, Salem R, et al. Transarterial Radioembolization with Yttrium-90 for the Treatment of Hepatocellular Carcinoma. Adv Ther. 2016;33:699-714

Background

The draft Revision 10 of the NRC licensing guidance on Y-90 Microsphere Brachytherapy Sources and Devices is near complete. This ACMUI subcommittee was tasked to provide comments on the following:

1) the removal of the authorized user (AU) manufacturer training Pathway 2;
2) update of the waste and disposal section on long-lived impurities; and
3) addition of a section on autopsy and cremation of Y-90 microsphere patients.

The removal of AU Pathway 2

The draft NRC "Yttrium-90 Microsphere Brachytherapy Sources and Devices: TheraSpheres and SIR-Spheres Licensing Guidance, Revision 10" outlines the updated qualifications of an AU for Y-90 microspheres as well as the required training and experience. The required clinical experience of 3 supervised hands-on patient cases continues to be allowed through either of two pathways.

Pathway 1: A physician seeking AU status for Y-90 microsphere therapy has work experience with the specific microsphere therapy for which approval is being sought by performing 3 hands-on supervised cases under the direct supervision of one or more qualified physician AUs for that specific Y-90 microsphere therapy; or

Pathway 2: A Y-90 microsphere manufacturer supervises 3 in-vitro simulated Y-90 microsphere cases for the type of therapy for which approval is being sought, after which the individual is listed on the institutional license and commits to completing the first 3 patients as hands-on supervised cases under the direct supervision of the manufacturer's representative within 6 months of being listed on the license.

However, the draft guidance document proposed the elimination of Pathway 2, which was established in 2004, with a 2-year deadline date. AU candidates will be able to initiate Pathway 2 up to the deadline date. The NRC/OAS Working Group provided the following rationale for eliminating Pathway 2:

1. After more than a decade of AU and manufacturer training, the current number of AUs is sufficient to meet the clinical demand and provide the required clinical use experience for training new AUs.
2. Tracking the AUs listed on a license who have or have not completed the required 3 hands-on manufacturer-supervised therapies is difficult and at times impossible. Consequently, there potentially could be individuals listed as AUs who have not completed the required supervised clinical cases before performing these therapies on their own.
3. The use of non-physician proctors providing clinical experience for radionuclide therapy by physicians is less than optimal.

The proposed elimination of Pathway 2 raises concern whether there are sufficient training and experience opportunities for new AUs, especially in those cases where the therapy use is new for a medical licensee. The subcommittee considered whether the Pathway 2 elimination could have a negative effect on patient safety or cause potential delay or limited access for patient care, particularly in rural communities. The subcommittee also considered that manufacturer training provides a uniform standard of didactic and in-vitro clinical training which may not be provided by physician AUs who may also be unable to supervise cases due to time constraints (i.e., "too busy') or co-operation issues between institutions or networks.

With the elimination of Pathway 2, it is the subcommittee's opinion that if there is a sufficient need for Y-90 AU microsphere training, institutions that perform large numbers of these treatments will likely offer "mini fellowships" to satisfy training or experience needs, and could be done in coordination with the manufacturer's didactic and in-vitro clinical training program. Furthermore, an AU approved for a specific type of Y-90 microsphere therapy can be named as an AU at another institution which performs or will perform that Y-90 microsphere therapy without need to do additional training or experience. The subcommittee also encourages current AUs for Y-90 microsphere therapy to support the proctoring experience for AU Y-90 microsphere therapy within their communities.

The subcommittee supports the phase out of the Pathway 2 option following their review of the subcommittee's considerations and suggestions on addressing training and experience needs after elimination of the Pathway 2 option.

Y-90 waste and disposal

Y-90 microspheres can be generator- or reactor- produced, resulting in a range of impurities with widely varied half-lives. According to 10 CFR 35.92, byproduct material with a physical half-life of 120 days or less (short-lived) may be held for decay-in-storage before disposal. Y-90 microspheres contain both short-lived (Y-88 and Y-91) and long-lived impurities (i.e., europium-152, europium-154, cobalt-60, strontium-90) from reactor production. Licensees need to be aware of these long-lived impurities as they may present disposal issues. Y-90 vials, in which no measurable impurity activity is detected, may be held for decay- in-storage. Y-90 vials with measurable long-lived impurity activity, however, need to be returned to an authorized manufacturer or transferred to an authorized recipient.

The section of the Rev. 10 draft license guidance entitled "Waste Disposal Issues" was updated to provide additional information on the potential longer-lived contaminants that may be found in Y-90 microspheres, and continues to refer the reader to NRC Information Notice 2007-10, along with updated journal references for additional information. Specifically, the draft guidance states, "Although impurities need not be listed on an NRC license; licensees are responsible to ensure the microspheres are handled and disposed of in accordance with 10 CFR Part 20 and Part 35 requirements." The reader is provided the same routes of disposal to consider as have been listed since the September 2007 (Rev. 3) update. In addition, the reader is referred to Regulatory Information Summary 2004-17, Revision 1 for more information regarding requirements for holding waste for decay-in-storage.

The subcommittee supports inclusion of this additional guidance information on Y-90 waste and disposal in the NRC Rev. 10 draft guidance. One minor suggestion is to remove the two uses of the word, "recently," in the first paragraph of this section. Use of that word would eventually need to be changed in subsequent updates, and is not necessary for this update.

Autopsy and cremation

A section of the Rev. 10 draft license guidance entitled "Autopsy and Cremation" is added to note that handling the body of a deceased Y-90 microspheres patient may require additional radiation precautions. A healthcare worker's radiation exposure can be increased by handling Y-90 microsphere impregnated autopsy tissue. Y-90 microsphere therapy involves millions of permanent brachytherapy particles that are not biodegradable. As a pure beta emitter, Y-90 has a physical half-life of 64 hours and a tissue range of 11 mm. The draft guidance refers the

reader to NCRP Report No. 155 and to NUREG-1556, Volume 9, Appendix N for additional information and guidance.

The subcommittee supports inclusion of this section on autopsy and cremation in the NRC Rev. 10 draft guidance. One suggestion is to include a description as to the timing of the autopsy as it relates to the Y-90 microsphere therapy and why additional radiation precautions may need to be considered. The subcommittee recommends the following edit:

> "Patients treated with Y-90 microspheres will not usually present an external radiation hazard to persons handling the deceased's body. However, if the autopsy is performed within two to four weeks after the Y-90 microsphere therapy, an autopsy healthcare worker's radiation exposure may increase due to the handling of Y-90 impregnated tissue, which could still contain a significant number of the high energy, beta-emitting Y-90 microspheres. Cremation occurring within this same timeframe may also necessitate additional precautions due to the remaining Y-90 microspheres, and potentially beyond four weeks due to long-lived contaminants[2]."

Respectfully submitted, September 13, 2016.

Sub-Committee on Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSpheres and SIR-Spheres Licensing Guidance, Revision 10
Advisory Committee on the Medical Use of Isotopes (ACMUI),
Nuclear Regulatory Commission (NRC)

[2] Nelson K, Vause PE, Koropova P. Post-mortem considerations of Yttrium-90 90Y microsphere therapy procedures. Health Phys. 2008 Nov; 95(5 Suppl):S156-61.

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NRC's Abnormal Occurrence Criteria Policy Statement Update

Advisory Committee on the Medical Uses of Isotopes
October 7, 2016

Tanya Palmateer Oxenberg, Ph.D.
Abnormal Occurrence Coordinator
Office of Nuclear Regulatory Research

Background

- Abnormal Occurrence (AO) defined as "unscheduled incident or event which the Commission determines is significant from the standpoint of public health or safety"
- Required by Section 208 of the Energy Reorganization Act of 1974
- Initial criteria in 1977 and updated periodically
- Last revision in 2006
- NRC submitted proposed AO criteria to the Commission in 2015 for review and vote
- NRC briefed ACMUI on the proposed changes in March 2015

Background (cont.)

- Commission approved proposed changes with edits
- Commission directed staff to seek public comment on screening all reports for exposures to an embryo/fetus or nursing child as AOs
  - under Criterion I.A.2, related to the unintended radiation exposure of minors, vs
  - under Criterion III.C, resulting from treatment to a patient, that are required by 10 CFR 35.3047, "Report and Notification of a Dose to an Embryo/Fetus or a Nursing Child"
- Published in the Federal Register in August 17, 2015
- Comments received from ACMUI, Organization of Agreement States (OAS), VA, and WA

Criterion I – All Licensees

Footnote added to title

Medical patients and human research subjects are excluded from consideration under these criteria, and these criteria do not apply to medical events defined in Title 10 of the Code of Federal Regulations (10 CFR) 35.3045, "Report and notification of a medical event," which are considered in AO Criteria III.C.

Criteria I.A and III.C

- The staff is not recommending changing the embryo/fetus criterion in I.A.2
  - Embryo/fetus dose of 50 mSv (5 rem) or more is 50 times the public dose limit of 1 mSv (100 mrem)
  - Intended for all licensees, not just medical facilities
- The staff is not recommending a new criterion in I.C.III regarding accidental embryo/fetus criterion
- The staff is not recommending establishing two different thresholds for reporting an AO involving an embryo/fetus
  - One for an unintentional exposure to an embryo/fetus due to an administration to a pregnant individual
  - One for an embryo/fetus exposed from all other sources of licensed material

5

Criteria III.A.

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

A. Events Involving Design, Analysis, Construction, Testing, or Operation, Transport, Use, or Disposal – **Commission deleted *of Licensed Facilities or Regulated Materials* from title**

1. An accidental criticality.
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.

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Criteria III.B. Fuel Cycle Facilities

The Commission modified footnote

- added “High-consequence events for facilities licensed under 10 CFR Part 70 are those that could seriously harm the worker or a member of the public in accordance with 10 CFR 70.61.”
- deleted “Safety controls may include items relied on for safety designated in accordance with 10 CFR 70.61 (e) as well as other controls available to prevent or mitigate the consequences of an event. High-consequence events should be considered as those that could seriously harm the worker or a member of the public in accordance with 10 CFR 70.61.”

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Criteria III.C.

C. Events Involving the Medical Use of Radioactive Materials in Patients or Human Research Subjects

1. A medical event, as defined in 10 CFR 35.3045, which results in a dose that:
   a) is equal to or greater than 1 Gray (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
   b) exceeds, by 10 Gy (1,000 rad), the expected dose to any other organ or tissue from the administration defined in the written directive; and

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Criteria III.C.

2. A medical event, as defined in 10 CFR 35.3045, which involves:
   a) a dose or dosage that is at least 50 percent greater than that prescribed, or
   b) a prescribed dose or dosage that
      (i) uses the wrong radiopharmaceutical or unsealed byproduct material; or
      (ii) is delivered by the wrong route of administration; or
      (iii) is delivered to the wrong treatment site; or
      (iv) is delivered by the wrong treatment mode; or
      (v) is from a leaking source or sources; or
      (vi) is delivered to the wrong individual or human research subject.

9

Current and Future Actions

- Commission review final revision and vote
- Publication of revised AO Reporting Criteria in the *Federal Register*
- Incorporate revised criteria in the FY 2016 report to Congress

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Discussion

11

ACMUI Subcommittee on the Training and Experience for All Modalities

Christopher Palestro, M.D.
ACMUI

October 7, 2016

Nuclear Regulatory Commission (NRC)

Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Standing Subcommittee on Training and Experience Requirements

Subcommittee Status Report

September 16, 2016

SubCommittee Members:

Dr. Susan M. Langhorst

Dr. Darlene F. Metter

Dr. Christopher J. Palestro (Chair)

Ms Laura Weil

Charge

To periodically review training and experience (T&E) requirements currently in effect making recommendations for changes as warranted.

Background

Beginning in 2014, stakeholders expressed concerns that the 10 CFR 35.396 T&E requirements currently in effect, 700 hours in total, adversely affects patient care by limiting use of parenterally administered alpha and beta emitting radiopharmaceuticals to physicians who complete the requisite 10 CFR 35.390 T&E requirements, thus resulting in a shortage of authorized users (AUs). A subcommittee of the ACMUI, charged with looking into this situation, provided their report on March 10, 2016 and did not find evidence to support these concerns. The subcommittee recommended against changing the T&E requirements currently in effect. The subcommittee also noted that over the nearly fifteen years since these requirements went into effect new radiopharmaceuticals, both diagnostic and therapeutic, have been developed. Furthermore, the educational paradigm has evolved from “experience-based” to “competency-based”. Therefore, the subcommittee recommended, and the ACMUI approved, the creation of a standing subcommittee to periodically review and, when warranted, recommend changes to the T&E requirements.

Standing Subcommittee Focus

Part 35 of the Code of Federal Regulations (CFR) pertains to the medical use of byproduct material. The specific parts of part 35 that will be the initial focus of the subcommittee include:

Subpart D-Unsealed Byproduct Material Written Directive Not Required

35.190 Training for uptake, dilution, and excretion studies.

35.290 Training for imaging and localization studies.

Subpart E- Unsealed Byproduct Material Written Directive Required

35.390 Training for use of unsealed byproduct material for which a written directive is required.

35.392 Training for the oral administration of sodium iodide I-131 requiring a written directive in quantities less than or equal to 1.22 gigabecquerels (33 millicuries).

35.394 Training for the oral administration of sodium iodide I-131 requiring a written directive in quantities greater than 1.22 gigabecquerels (33 millicuries).

35.396 Training for the parenteral administration of unsealed byproduct material requiring a written directive.

Standing Subcommittee Considerations

The standing subcommittee is charged with the responsibility to "periodically review" the T&E requirements. However, what constitutes a reasonable periodic review? Fifteen years is too long an interval, while at the other extreme one year probably is neither a practical nor a useful interval. The subcommittee believes that the T&E requirements should be reviewed at least once every five years, and more frequently if warranted. The subcommittee is not certain how T&E changes in one section of Part 35 will affect T&E requirements in other sections. The subcommittee is also uncertain, given the time needed to make changes to Part 35 and the status of the most recent change to Part 35, how quickly any proposed changes to Part 35 T&E requirements can be considered and instituted.

An important issue that the subcommittee will need to address is "competency". In other words, what constitutes satisfactory completion of T&E requirements? Can merely completing a predetermined number of hours of T&E be equated with competency? This is not an issue now because the vast majority of physicians seeking AU status satisfy the T&E requirements by obtaining certification through a Medical Specialty Board whose certification process is recognized by the NRC or an Agreement State. The situation is different, however, for physicians seeking AU status through an alternate pathway. For example, it has been suggested that 80 hours of T&E is sufficient for hematologists/oncologists to

administer one or perhaps two different parenterally administered therapeutic radiopharmaceuticals to patients with malignant diseases. The number of hours aside, how will the consistency and quality of the T&E be assured and how will competency be determined? Would a Medical Specialty Board, or Boards, assume the responsibility for establishing a "curriculum" and administering a "certification examination"? If so, what criteria would the NRC use to recognize the board? How many different categories of therapeutic radiopharmaceuticals can the NRC and Agreement States manage for medical licenses?

Standing Subcommittee Plan

First and foremost, the subcommittee recognizes that any recommendations for or against changes in T&E should be made to ensure that the requirements and provisions in part 35, which "provide for the radiation safety of workers, the general public, patients, and human research subjects" are satisfied, while simultaneously ensuring that patient access to these procedures is not unnecessarily compromised.

The subcommittee intends to begin:

A thorough review of T&E requirements in CFR sub parts D (35.190, 35.290), and E (35.390, 35.392, 35.394, 35.396);

To make recommendations for/against changes in these T&E requirements for presentation at the Spring 2017 ACMUI meeting.

The subcommittee

Welcomes stake holder and NRC input throughout the process;

Asks the full ACMUI for suggestions on how to improve the subcommittee's considerations and plan.

Requests that the Medical Team appoint an NRC contact to assist the subcommittee in its work.

UAMS
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UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES

OFFICE OF THE DEAN

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501-686-6390
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800-245-3256 (toll free)
501-526-6872 (fax)

Arkansas Poison Control
501-686-5540
800-3POISON (toll free)
501-296-1451 (fax)

Drug Information
501-686-5072
888-228-1233 (toll free)

Continuing Education Program
501-686-5396

September 16, 2016

Ms. Sophie Holiday
Health Physicist / ACMUI Coordinator
U.S. Nuclear Regulatory Commission (NRC)
Washington, DC 20555-0001

Re: NRC Training and Experience Requirements for Alpha and Beta Emitters

Dear Members of the Advisory Committee on the Medical Use of Isotopes,

Thank you for taking into consideration updated educational requirements for authorized user training. The education and training should be commensurate with the responsibilities and assess the competencies required to safely handle radioactive materials.

As experienced nuclear pharmacists and experts in the field of radiation safety education and training, we appreciate the opportunity to submit our comments on the training and experience requirements for authorized users of alpha and beta emitters.

It is discouraging to see radiopharmaceuticals with documented clinical impact not used because they are not readily available in physician treatment regimens. For example, Zevalin (Ibritumomab tiuxetan) has been approved for first line therapy against Non-Hodgkin's lymphoma, the seventh most common type of cancer. Xofigo (Radium-223 dichloride) was fast-tracked by the FDA after demonstrating an increased patient life span and pain control in prostate cancer patients. However, the regulatory restrictions on access drive oncologists to use less effective chemotherapy regimens associated with significant side effects and diminished patient outcomes. With expanded physician access to radiopharmaceuticals, the standard of care will be improved for patients.

These current alpha and beta emitting radiopharmaceuticals, and others under development, would be delivered to licensed healthcare sites as patient-ready doses with no additional manipulations needed before patient administration. The needed training and experience for safe handling of these specific drugs does not warrant the full 200 hours of didactic training and 500 hours handling experience. In addition, it does not require three

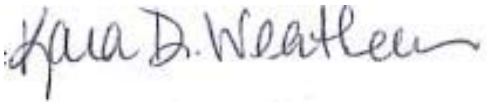
months of experience to learn how to inject and monitor a patient-ready dose that does not require any preparation or imaging expertise.

We recommend that NRC, as part of expedited rulemaking, modify the training & experience requirements for authorized users for patient ready alpha and beta emitters to a didactic program which consists of competency based training with regards to the limited scope of practice. This will provide a strong foundation for practitioners who wish to become involved in the administration of alpha and beta emitting radiopharmaceuticals. A program such as this would also include enhancements to the distance based didactic education, including specific requirements for experiential radiation safety hands-on exercises as well as supplemental handling experience for each specific radiopharmaceutical. An updated representative outline of our consensus for a competency based training program is included as an addendum to this letter.

An addition to the user training requirements, each facility is mandated to have a radioactive materials license and radiation safety officer. With adequate training, radiation safety procedures and guidance documents in place, the risks should be minimal while providing the maximum benefit in patient care.

Sincerely,

Nicki L. Hilliard, Pharm.D, MHSA, BCNP, FAPhA
Professor of Nuclear Pharmacy
University of Arkansas for Medical Sciences
NLHilliard@uams.edu



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Director of Continuing Pharmacy Education
University of New Mexico
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Limited Patient-Specific Radiotherapy Education & Training Program

Program Restrictions:

- Limited to patient-specific, ready to administer unit doses
- No radiopharmaceutical preparation
- RAML line item restriction(s) to specific radionuclide and radiopharmaceutical
- No imaging or quantification of radiopharmaceutical distribution

Goal: Provide licensed medical specialists (urologist, oncologist, hematology-oncologists) with competency in cognitive and psychomotor skills necessary to effectively and safely prescribe and administer patient-specific radiopharmaceuticals.

Competency	**Assessment**
PHYSICS	
1. Explain radioactivity, radiation and radioactivity	Written exam
2. Define characteristics of radioactivity including mode(s) of decay, half-life, and energy.	Written exam
3. Discuss interaction of radiation with matter including direct and indirect ionization emphasizing interaction on living matter.	Written exam
4. Calculate radioactive decay and activity remaining	Written exam
INSTRUMENTATION	
1. Explain the operation and use of gas-filled detectors (survey meters & dose calibrators) used to detect and measure radiation	Written exam
2. Explain the operation and use of sodium iodide detectors (well counters) used to measure radioactivity.	Written exam
3. Explain operation and use of personnel monitoring devices.	Written exam & laboratory exercise
4. Demonstrate appropriate use of: a. Survey meter b. Dose calibrator c. Well counter	Laboratory exercises
5. Define routine quality assurance parameters (including calculations) for detection & measurement instruments.	Written exam & laboratory exercises
RADIATION BIOLOGY	
1. Explain the chemical and physical effects of ionizing radiation on biological systems.	Written exam
2. List the types of molecular and cellular damage to living tissue resulting from ionizing radiation.	Written exam
3. Compare the relative risks of low level radiation with other health risks.	Written exam
4. Discuss the therapeutic use of radionuclides in treating metastatic disease.	Written exam
5. Explain the mechanism of action of particulate radiation in treating metastatic disease.	Written exam

RADIATION SAFETY AND REGULATIONS	
1. Discuss principles and applications of personnel radiation protection (dose limits, dosimeters, protective equipment, training, monitoring).	Written exam
2. List regulatory requirements for personnel radiation protection (training, monitoring, postings, standard operating procedures, record-keeping, declared pregnant worker).	Written exam Written exam
3. List and define scope of oversight compliance for federal agencies regulating human use of radiopharmaceuticals.	Written exam
4. List record-keeping requirements for regulatory compliance.	Written exam Written exam
5. Discuss radioactive waste management requirements.	
6. .Discuss requirements for management oversight of radiation safety program.	Written exam & laboratory exercises
7. Demonstrate technique(s) and record-keeping for receiving incoming packages containing radioactive materials	Written exam & laboratory exercises
8. Demonstrate technique(s) and record-keeping for preparing outgoing packages containing radioactive materials including limited quantity shipments.	Written exam & laboratory exercises
9. Demonstrate technique(s) and record-keeping for conducting area contamination wipes and surveys.	Written exam & laboratory exercises
10. Demonstrate technique(s) and record-keeping for quality assurance of detection and measurement equipment (calibration, daily checks, functionality tests).	

Training and Experience Requirements For Patient Ready Alpha- and Beta-Emitter Therapies

ACMUI Meeting

October 7, 2016

Jennifer L. Cultrera, M.D.; Joseph R. Mace, M.D.

Introduction

Jennifer L. Cultrera, MD

Board Certified: Medical Oncology, Hematology, and Internal Medicine

Joseph R. Mace, MD

Director of the Radioimmunotherapy Program

Board Certified: Medical Oncology, Hematology, and Internal Medicine

2

Key Points

- Safe and effective alpha- and beta-emitter therapies are underutilized due to limited access to Authorized Users (AUs)
- Oncologists have significant training and experience in administering highly toxic chemotherapy
- Practicing oncologists cannot become AUs because 700 hours of T & E places unrealistic burden on their practices
- Patient-ready doses are prepared by licensed radiopharmacies and administered without manipulation, presenting little safety risk
- Targeted, competency-based T & E framework would allow oncologists to demonstrate competencies needed to administer therapeutic patient-ready doses safely

Regulatory Barriers to Alpha- and Beta-Emitter Patient Access

- Patients in community oncology setting face disruptions in continuity of care due to need to find an AU who can administer alpha- and beta-emitters
- Physicians are discouraged from recommending treatment due to difficulty of finding AU geographically accessible to patient
- Patients in need are often debilitated due to cancer or treatment and/or elderly with limited mobility, making travelling great distances for treatment infeasible

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Oncologist Experience with Toxic Therapies

- Oncologists want **limited authorization** to administer therapeutic patient-ready doses of alpha- and beta-emitters
- Oncologists have training and experience in handling and intravenous administration of dangerous materials in provision of chemotherapy
- Oncologists are trained in safe handling and waste management measures applicable to highly toxic therapies
- Limited and targeted additional training is needed to learn precautions and practices specific to safe administration of therapeutic patient-ready doses of alpha- and beta-emitters

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Dr. Cultrera: Training and Experience

- Moffit Cancer Center: Lymphoma specialist for 3 years, utilizing Zevalin for patients several times per year achieving longstanding remissions while maintaining patients' quality of life
- Florida Cancer Specialists (The Villages, FL): No AU available to partner with to administer radiopharmaceuticals to patients
- Over 10 years practicing in hematology and medical oncology, working with chemotherapeutics and highly toxic agents

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Dr. Cultrera: No Feasible Pathway to Become AU

- Currently not authorized to administer patient-ready doses of alpha- and beta-emitters to patients in need
- In rural areas throughout the US, there are no local AUs providing therapeutic alpha- and beta-emitter administration to whom patients can be referred
- Limited authorization would be beneficial, but impractical to spend 700 hours for T & E and would impact current patient care

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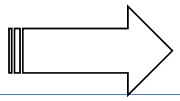
Dr. Mace: Limited Authorized User

- Obtained AU status before the current 700-hour T & E requirement was put into place
- Administering Zevalin for 10 years and Xofigo for nearly 3 years with no safety incidents
- Role of AU in ordering and receiving the patient-ready dose, preparation and injection of the dose, and post-administration steps



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Ordering and Receiving Patient-Ready Dose

- Patient-ready dose prepared and compounded at licensed radiopharmacy and delivered in patient-ready dose on day of treatment
- Facility confirms specifications and places product in treatment area
- AU's role:
  - Prescription and order placement
  - No mixing, handling, manipulation, or long-term storage

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Patient Administration Protocol

- AU's role:
  - Confirmation of patient preparation and order specifications
  - Confirmation of dose calibration
  - Documentation
  - Administration:
    - Syringe shield, connects syringe to tubing
    - 10 minute administration
    - Saline flush of line to clear product residue

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Post-Administration Protocol

- Administration material storage/disposal
  - Syringe cap, syringe, and personal protective equipment placed in acrylic receptacle for decay, then disposed of
  - Used/emptied pig (syringe container) placed in transport package for retrieval by nuclear pharmacy
- Survey meter readings taken:
  - Patient, AU, preparation/treatment areas, equipment, and decaying disposal materials
- Wipe test

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Treatment Area, Storage and Handling Precautions

- AU conducts limited storage and handling activities:
  - Material stored temporarily in designated treatment area
  - Treatment area / documentation audits
  - Treatment area locked when not in active use
  - Access to treatment area limited
  - Door signs clearly warn of radioactive substances within and list contact numbers for emergencies
- Spill handling and decontamination
  - Handled in accordance with NRC's Model Spill/Contamination Procedures (NUREG-1556 Vol. 9 Rev. 2, Appendix N)

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Conclusion

- Dr. Cultrera is equally competent to obtain limited AU license, but no current feasible pathway
- 700 hours of T & E includes material not relevant to the qualification of an oncologist or hematologist to administer a therapeutic patient-ready dose prepared by a licensed radiopharmacy
- **Limited authorization** to administer therapeutic patient-ready doses of alpha- and beta-emitters should be available through a targeted, competency-based training program

13

DR. STEVEN FEIN
MIAMI CANCER INSTITUTE

Member of
American Society of Hematology
Foundation and Development Committee
Lymphoma Specialist

ACMUI Meeting
October 7, 2016

Follicular lymphoma treatment

- Subtype of Non-Hodgkins Lymphoma
- 14000 new pts per year, 100k living with FL
- Most eventually need anti-tumor therapy
- Zevalin prolongs time off chemotherapy
- No other treatment compares for duration of benefit or quality of life

Zevalin is not used enough

- Hematologists rarely prescribe Zevalin even though it is so safe and effective
- Requires referral to another doctor because very few medical oncologists are trained
  - In some places Zevalin is impossible to obtain
- Each medical oncologist has anecdotes about successes with Zevalin, but it remains so uncommon that it stays off our radar

Zevalin is not used enough (Cont.)

- Newer anti-tumor therapy like idelalisib has been shown to be challenging and toxic to some follicular lymphoma patients
- At one time it was too expensive, but now it is covered better, and newer agents cost more
- Because we are not using Zevalin enough, patients are suffering and maybe dying earlier
- Zevalin is known to be a safe medication to administer

ASH letter to NRC 12/2015

"Since the implementation of the 700-hour requirement, it has become more difficult for patients in certain parts of the country to locate Authorized Users who are licensed to administer alpha- and beta-emitters outside of the academic medical center setting."

"With this current rulemaking, the NRC has the opportunity to improve access to these potentially life-saving anti-cancer treatments by addressing the shortage of Authorized Users able to administer them"

"This could significantly improve patient access to lifesaving treatments in the community hematology/oncology setting"

Zevalin needs to be used more

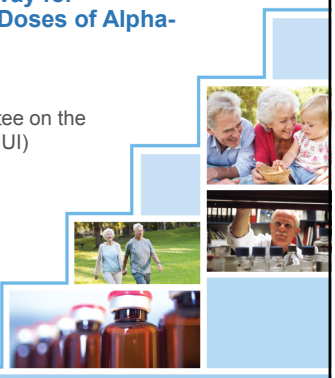
- I support the development of a limited authorization for hematologists who seek to administer therapeutic patient-ready doses of alpha- and beta-emitters.
- By enabling hematologists to train to become authorized users, more patients will have access to Zevalin, an important treatment for follicular lymphoma.

Limited Authorization Pathway for Therapeutic Patient-Ready Doses of Alpha- and Beta-Emitter Therapies

Presented to: Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Rajesh C. Shrotriya, MD
CEO, Chairman of the Board

October 7, 2016



SPECTRUM PHARMACEUTICALS
Redefining Cancer Care

Key Points

- NRC should initiate a standalone expedited rulemaking on therapeutic patient-ready doses of alpha- and beta-emitters; there are no safety reasons why cancer patients should have to wait for 2021 rulemaking
- Current 700-hour training and experience requirement is over-inclusive for limited administration of patient-ready doses
- Regulations create patient access issues in rural and socioeconomically disadvantaged areas; no hematologists have become authorized under 700-hour pathway
- Zevalin is a safe and effective cancer treatment option
- Hematologists and oncologists should be able to obtain limited authorization to administer patient-ready dose of alpha- and beta-emitters after completing a targeted, competency-based training program

Training and Experience Requirements Overbroad for Patient-Ready Doses

- To safely administer therapeutic patient ready-doses of alpha- and beta-emitters, clinicians must be competent in ordering, receiving, injecting, and proper handling and disposal of waste
- The 700-hour T & E requirement imposed in the 2002 rulemaking includes training on many competencies not required to administer therapeutic patient-ready doses of alpha- and beta-emitters
  - The 700-hour training regimen includes instruction on radiochemistry and imaging and the administration of other modalities

Cancer Patient Access Restrictions

- Regulations have restricted patient access in the community oncology setting, particularly in rural / socioeconomically disadvantaged areas far from academic institutions and large hospitals / clinics
  - 80% of fNHL patients are treated in this setting, managed by Medical Oncologist or Hematologist/Oncologist
  - Elderly and infirm patients unable to travel long distances most impacted
- Hematologists / Oncologists in community oncology setting have shown interest in limited AU status for administration of patient-ready doses
  - Not aware of any hematologists or medical oncologists certified to date under 700-hour pathway and Zevalin treatments have declined
- Regulations have constrained doctor / patient choices about care
- More difficult for Spectrum to support Zevalin due to decreased availability
- Patients would benefit if experienced physicians like Dr. Cultrera had a more viable pathway to authorization

Competency-Based Limited Authorization

- Community-based hematologists/oncologists routinely compound, prepare, and administer non-radioactive highly toxic and volatile substances during chemotherapy administration
- A limited authorization pathway to administer therapeutic patient-ready doses of alpha- and beta-emitters through targeted, competency-based T & E needs be established on expedited basis
- Competencies:
  - (1) physics; (2) instrumentation; (3) radiation biology; and (4) radiation safety and regulations
  - Assessment by written examination and laboratory exercises
  - Three proctored cases

5

Safety of Zevalin Administration

- More than 10,000 administrations, no known radiation safety events
- More than 30 published studies of radiation safety with Y-90 Zevalin – all concluded risks are minimal to negligible
- Zevalin® (Y-90 ibritumomab) approved by the FDA in 2002 and remains one of the most safe and effective treatments for follicular non-Hodgkin's lymphoma
- Zevalin prepared at licensed radiopharmacy and delivered to clinician in patient-ready dose
- Administration of patient-ready doses of Zevalin requires no manipulation, reducing likelihood of accident
- Zevalin may only be administered at a facility that has a radioactive materials license from NRC

6

Support for Changing Alpha- and Beta-Emitter Requirements

- **Patients**

- **Patient Advocacy Groups**

LYMPHOMA RESEARCH FOUNDATION

LEUKEMIA & LYMPHOMA SOCIETY

Patients Against Lymphoma www.Lymphoma.org

- **Physician & Industry Associations**

American Society of Hematology
Helping hematologists conquer blood diseases worldwide

Community Oncology Alliance
Dedicated to high quality, affordable, and accessible cancer care

CORAR Council on Radionuclides and Radiopharmaceuticals, Inc.

Florida Cancer Specialists & Research Institute
World Class Medicine. Hometown Care.

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Conclusion and Recommendations

- The NRC should establish on an expedited basis targeted, competency-based training pathway to become licensed as an AU for the limited administration of ***therapeutic patient-ready doses of alpha- and beta-emitters***
- The NRC should enact these training requirements now or through an expedited standalone rulemaking
- There are no safety reasons why cancer patients in underserved areas should have to wait for next NRC rulemaking in 2021

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Thank You

Rajesh C. Shrotriya, MD
CEO, Chairman of the Board

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

Worldwide Supply of Molybdenum-99 (^{99}Mo)

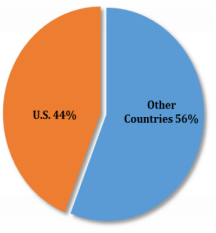
Richard L. Green, R.Ph, BCNP
Nuclear Pharmacist
October 07, 2016

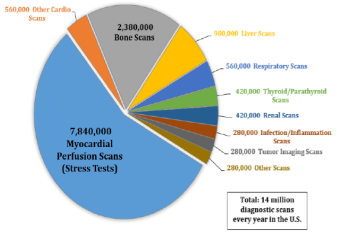
Today's Objectives

- **Explain the current ^{99}Mo / ^{99m}Tc Global Supply Chain**
- **Explain how the impending closure of the NRU reactor may affect supply**
- **Identify issues with HEU to non-HEU to support GTRI**
- **Discuss new non-HEU, domestic sources of ^{99}Mo**

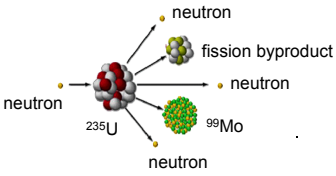
Problem: Fragility of the Domestic Supply of ^{99}Mo

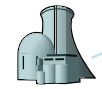
Several factors undermine the future availability of Mo-99 in the U.S., which consumes approximately half of the world's supply of the medical isotope Mo-99.





Current ^{99}Mo Product Supply Chain





Reactors

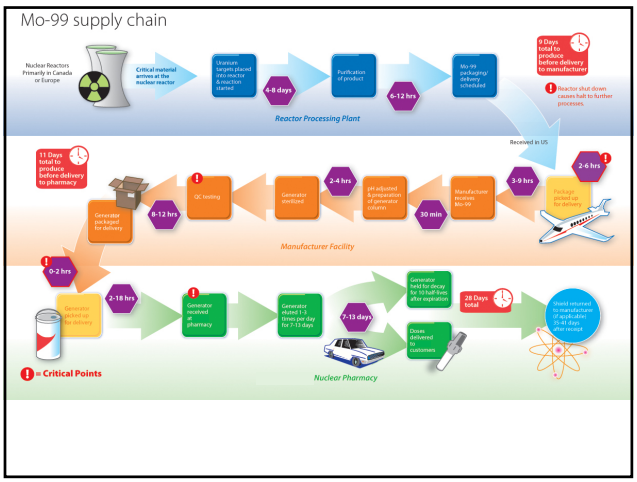
Processors

^{99}Mo Generators

Reactors and ^{235}U

- **Fission of enriched ^{235}U**
  - **Abundance in nature = 0.7%**
- **Enrichment level trigger point**
  - **Low enriched uranium (LEU)**
    - **<20%**
  - **High enriched uranium (HEU)**
    - **>20%**
- **<u>Current</u> ^{99}Mo production involves**
  - **Reactor fuel (LEU or HEU)**
  - **Targets (LEU or HEU)**

5

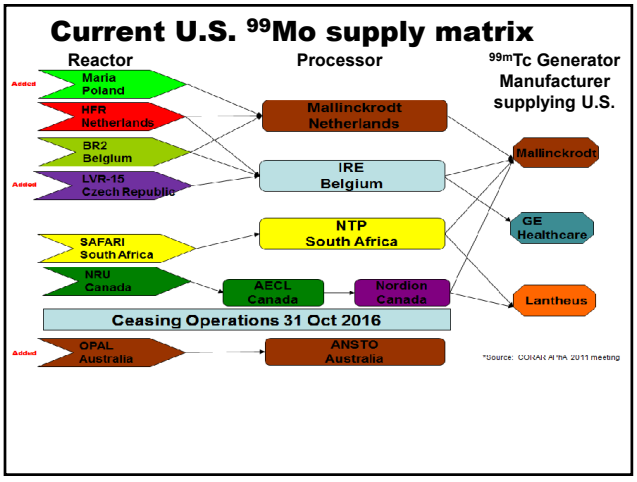


Reactors and type

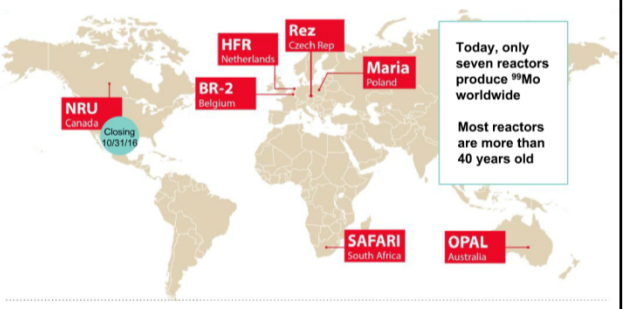
Reactor	Location	Commissioning Date	Fuel Type	Target Type	Global Mo-99 Processor
NRU	Chalk River, Canada	1957	HEU	HEU	Nordion
HFR	Petten, Netherlands	1961	LEU	HEU*	Covidien/IRE
BR2	Mol, Belgium	1961	HEU	HEU*	Covidien/IRE
OSIRIS	Saclay, France	1966	HEU	HEU	Covidien/IRE
SAFARI	Pelindaba, South Africa	1965	LEU	HEU/LEU	NTP
MARIA	Otwock-Swierk, Poland	1974 1993 (rebuilt)	HEU**	HEU*	IAE-Polatom/ Covidien
LVR-15	Rez, Czech Republic	Mid 1950's	LEU	HEU	Czech Nuclear Research Institute/IRE
OPAL	Lucas Hts, Australia	2007	LEU	LEU	ANSTO

Closing 2016

Closed 2015



World ^{99}Mo Supply Under Pressure



9

American Medical Isotopes Production Act of 2009

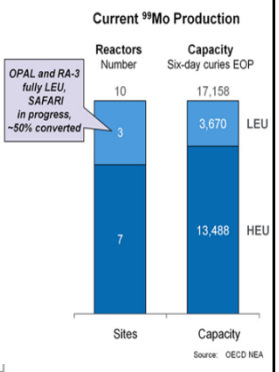
- **Provides $163 million to DOE to support Mo-99 production with LEU**
- **Prohibits export of HEU for medical isotopes from US after 7 years (provision to extend 3 yrs)**
- **Requires NRC to report disposition of previous exports of HEU**
- **Allows NRC to license HEU production under certain conditions**
- **Requires annual reports from DOE on support of US ^{99}Mo production**
- **Requires a NAS study 5 years after enactment**

HEU to LEU Conversion

- **2005 Energy Act had an Amendment that calls for the elimination of HEU as a source of medical isotopes**
- **Global Threat Reduction Initiative (GTRI) has HEU elimination as part of their mission within the National Nuclear Security Administration (NNSA) of the DOE**

Uranium Policy Imperatives

- American Medical Isotopes Production Act was passed in 2013, which restricts the export of HEU for medical isotope production by **2020**
- All major ^{99}Mo producing countries have agreed to convert to the use of LEU targets
  - Proliferation concerns
  - Other safety/security issues
- Currently HEU is sourced only from the United States and Russia, with the majority coming from the US
- Global Threat Reduction Initiative (GTRI) formed by NNSA to reduce usage of HEU around the world



^{99m}Tc Supply Chain Challenges

Irradiator disruptions

- Extended unplanned shutdowns frequent with aging reactors
- Permanent shutdown are imminent at NRU and OSIRIS
- Permanent shutdown at HFR on horizon

Rising prices

- Governments taper subsidies and prices come to cover costs more fully
- Switch to LEU
- Potential supply squeeze

Industry Response

- Renovation of existing reactor/processing facilities
- New conventional reactor capacity
- New ^{99}Mo production technologies
- Improved supply chain efficiency
- Increased globalization of supply chain

Source: OECD NEA

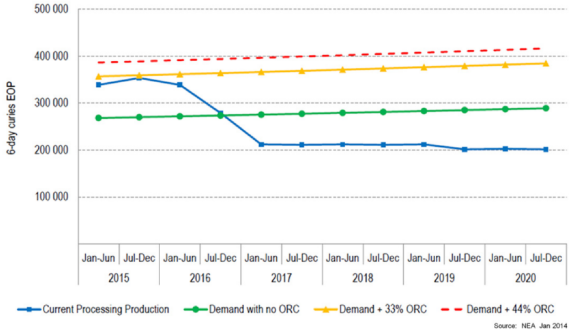
New U.S. Producers?

- **NorthStar Medical Radioisotopes, LLC**
  - **Beloit, WI**
    - **Short term – MURR**
      ^{98}Mo(n,γ)^{99}Mo
    - **Long term - linear accelerator**
      ^{100}Mo(p,2n)^{99}Mo
- **Shine Medical Technologies**
  - **Monona, WI**

Neutrons from accelerator **U salts** **^{99}Mo**

RadioGenix™

Current Processing Production & Projected Future Demand, Global, 2015 -



Acronyms

ACMUI – Advisory Committee on the Medical Uses of Isotopes
DOE – Department of Energy
EOP – end of production
^{99}Mo – nuclide of molybdenum with 66 hour half-life, precursor of ^{99m}Tc
GTRI – Global Threat Reduction Initiative
HEU – highly enriched uranium (>20%)
LEU – low enriched uranium (<20%)
LSA– low specific activity

Acronyms

MURR – Missouri University Research Reactor
non-HEU ^{99}Mo – molybdenum 99 manufactured without the use of highly enriched uranium
NRU – National Research Reactor in Canada
NNSA – National Nuclear Security Administration
^{99m}Tc – nuclide of technetium with 6 hour half-life, used in ~85% of diagnostic nuclear medicine imaging
^{235}U – radioactive form of uranium used to fuel reactors

17

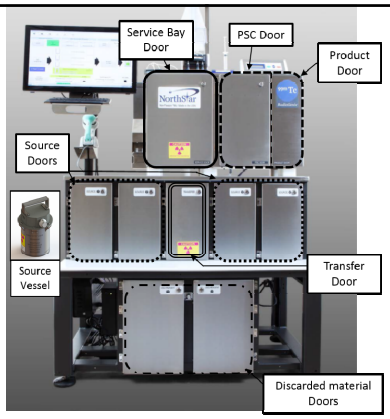
U.S.NRC
United States Nuclear Regulatory Commission
Protecting People and the Environment

NorthStar Medical Radioisotopes LLC. RadioGenix™ Molybdenum-99/ Technetium-99m Generator System

Licensing Guidance for Medical Use Licensees, Medical Use Permittees and Commercial Nuclear Pharmacies

Donna-Beth Howe, Ph.D.

October 7, 2016



2

Design

- **A closed system that contains, moves, and shields all Mo-99 (as a mixture of radioactive Mo-99 and nonradioactive Mo-98 or Mo-100).**
- **Computer driven process that isolates Tc-99m from molybdenum before delivering Tc-99m into an elution vial.**
- **Materials and components engineered that maintain the device's integrity as a closed system, withstand high radiation fields for extended periods, and maintain adequate shielding of the radioactive material with all doors closed and supplemental shielding in place.**

3

Medical and Commercial Nuclear Pharmacies 10 CFR 35.1000 and 30.33

- **Designed and constructed with components and operations that differ significantly from conventional Mo-99/Tc-99m generators using fission produced Mo-99.**
- **Needs additional information and commitments not required to safely use a conventional fission Mo-99/Tc-99m generator.**
- **Additional training and experience for individuals, and commitments to address specific training and safety provisions.**

4

Licensing Guidance

- Radionuclides, Form, Possession Limits, and Purpose of Use
- Posting Requirements
- Training and Experience
  - Authorized Individuals
  - Radiation Safety Officer
  - Supervised Individuals Operating the RadioGenix™ System
  - RadioGenix™ System Administrator and RadioGenix™ System Administrator Designee

5

Licensing Commitments

- Molybdenum-99 concentrations
- Training in licensee's procedures
- Training as a result of changes to the RadioGenix™ System that affect the safety and operation of the generator
- Annual Emergency Procedures Refresher Training
- Revision to NRC's Training and Experience Criteria Guidance
- Specific Information on Radiation Safety Precautions and Instructions

6

Notes to Licensees

- Alterations to RadioGenix™ System
- Use of Other Mo-99/Tc-99m Solutions or Other Generator Systems
- Change in Physical Conditions of Use
- Notification for Authorized Users and Authorized Nuclear Pharmacists
- Revisions to existing RadioGenix™ System Radiation Safety Programs to conform to future changes in Licensing Guidance and additional safety recommendations from the manufacturer

7

Abbreviations

Mo - Molybdenum

Tc - Technetium

8

Questions?

9

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

Comments on the NorthStar Molybdenum-99 / Technetium-99m Generator (RadioGenix™) Licensing Guidance

Vasken Dilsizian, M.D.
ACMUI Nuclear Cardiologist
October 7, 2016

Subcommittee Members

- Francis Costello, CHP
- Vasken Dilsizian, M.D. (chair)
- Christopher Palestro, M.D.
- Pat Zanzonico, Ph.D.

2

Subcommittee Charge

- To review the guidance and provide comments, with a particular focus on

I. Training and Experience –

All individuals interacting with the generator

II. Safety Precautions –

To minimize the potential radiation exposure for individuals running the protocols and others in the room.

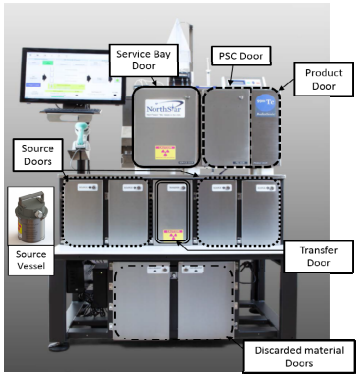
3

Background

- The conventional column-based generator utilizes exclusively fission (i.e., reactor)-produced Mo-99.
- Since foreign reactors which produce Mo-99 are aging and increasingly unreliable, there is an urgent need for a reliable, domestic supply of Mo-99 to avoid potential shortages of Tc-99m for clinical studies.
- The RadioGenix™ generator system utilizes non-fission produced Mo-99 produced either by photons from a linear-accelerator or neutrons from a reactor, and thus should address this important unmet need for non-HEU Mo-99.

4

RadioGenix™ Generator



5

Annotated Figure and/or a Video Clip of the Generator System

Subcommittee recommendation:

- ***The use of labeled arrows to identify each component by name directly on the photograph. For the training module, the subcommittee recommends that NorthStar provide a video clip of how the system operates.***

6

Authorized User and Training Requirements

There are specific training and experience and administrative requirements that are unique to the system. These include:

1) Training individuals to perform the individual protocols,

2) Identifying a system administrator and designee

3) Naming the radiation safety officer responsible for radiation safety oversight of the system

4) Designating an authorized medical-use licensee or nuclear pharmacist responsible for the system.

7

1 Software Production Package with 6 Protocols

1) **Initialize system**
2) **Add/change reagent kit**
3) **Produce (i.e., separate) Tc-99m**
4) **Remove source vessel**
5) **Sterilization**
6) **Exchange used reagent container**

8

I. Training and Experience

- **The RadioGenix™ System protocols will generally be performed by individuals who are working under the supervision of AUs or ANPs.**
- **Since there may be a large number of such individuals, arranging for the manufacturer to train all of them may be impractical.**
- **On the other hand, given the gradual shift of nuclear medicine imaging centers from on-site Mo-99/Tc-99m generators to unit doses, the subcommittee estimates that perhaps < 10% of all clinical imaging programs in the US may have one of these generators on site.**
- **Moreover, given the complexity of the System, it is more likely that this generator will be used almost exclusively by commercial radiopharmacies.**

9

I. Training and Experience

Subcommittee recommendation:

- ***The subject of whether the NorthStar training course should be reviewed and approved by the NRC was considered. Given the unique design and operation of the NorthStar system, the subcommittee agreed that NorthStar should have sole responsibility for the content of the training course and certification.***

10

"System Administrator" and "System Administrator Designee

Subcommittee recommendations:

- ***It is important to clarify that a System Administrator can be any individual assigned by the AU without a specifically defined educational or training background.***
- ***Given the unique role of the System Administrator, perhaps that individual should be named on the license.***
- ***Regarding System Administrator Designee, although it may not have been intended, one could infer from the description of the system administrator designee that there can be only one designee. Presumably, there can, and should, be multiple System Administrator designees. This should be stated explicitly.***

11

Additional Training as a Result of Changes to the RadioGenix™ System

Subcommittee recommendations:

1) ***The appropriate time period allotted for training on the "changes" and the responsibility of the vendor/manufacturer to inform and train the applicants on changes in a timely manner should be specified.***
2) ***Will the generator be "non-operational" until ALL individuals handling the generator are trained in the changes, including the AU, RSO, system administrator, etc. or does it require only the AU to be trained on the "changes"? This needs clarification in the Guidance.***
3) ***If the latter, once the AU is trained on the "changes", is the AU then solely responsible for training all others on these changes? This should be stated.***

12

Clarifications for the Use of "Protocol" and "Software" Applications

Subcommittee recommendation:

- ***The subcommittee recommends using the term, "individual tasks" throughout the document for consistency and to clarify that there is only one protocol and software program with this system.***

13

II. Safety Precautions

The Draft Licensing Guidance is largely silent on emergency response other than to defer to the procedures of the manufacturer.

Subcommittee recommendation:

- ***While the subcommittee appreciates that NRC endeavors to be non-prescriptive, given the potential severity of a spill with such large quantities of radioactivity in liquid form, perhaps the manufacturer's procedures should be reviewed and incorporated into the Licensing Guidance itself.***

14

II. Safety Precautions

Regarding the Surveys/Survey meters/monitors:

The Draft Guidance states that "it is necessary for the licensee to routinely perform additional surveys to identify higher than expected radiation fields and system failures".

Subcommittee recommendation:

- ***The term "higher than expected" should be defined in terms of a maximum specific exposure or exposure-rate limit which a survey meter should be capable of measuring.***

15

Concluding Remarks

The subcommittee agrees with the remainder of the Draft Licensing Guidance.

The subcommittee felt that the draft Licensing Guidance is, overall, reasonable and not particularly onerous for prospective users and, given the new and novel features of the NorthStar generator system, licensing under 10 CFR 35.1000 is reasonable.

16

Acronyms

- **ACMUI – Advisory Committee on the Medical Uses of Isotopes**
- **ANP - Authorized Nuclear Pharmacist**
- **AU – Authorized User**
- **Mo – Molybdenum**
- **NRC – Nuclear Regulatory Commission**
- **RSO – Radiation Safety Officer**
- **Tc – Technetium**

17

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

Subcommittee on

NorthStar Molybdenum-99 / Technetium-99m Generator (RadioGenix™) Licensing Guidance

***Draft* Report**
September 08, 2016

Subcommittee Members:
Dr. Vasken Dilsizian (Chair)
Mr. Frank Costello
Dr. Christopher Palestro
Dr. Pat Zanzonico

I. Introduction

There were multiple presentations to the ACMUI over the past several years on a new molybdenum-99 (Mo-99)/technetium-99m (Tc-99m) generator system, the RadioGenix™, developed by NorthStar Medical Radioisotopes, LLC. This novel generator system provides a practical alternative to the conventional and widely used column-based Mo-99/Tc-99m generator. Since the column-based generator utilizes exclusively fission (i.e., reactor)-produced Mo-99 and since the foreign reactors which produce Mo-99 are aging and increasingly unreliable, there is an urgent need for a reliable, domestic supply of Mo-99 to avoid potential shortages of Tc-99m for clinical studies, such as those which occurred several years ago. The RadioGenix™ generator system utilizes linear-accelerator rather than fission-produced Mo-99 and thus should address this important unmet need[1]. A joint NRC/Agreement States working group was formed to review, evaluate, and determine how this generator should be licensed. Through their evaluations, it was decided that this particular generator needs to be licensed under 10 CFR 35.1000 and is intended for both 1) medical-use licensees and 2) commercial radiopharmacies (nuclear pharmacies).

Unlike the conventional Mo-99/Tc-99m generator using fission-produced Mo-99, the NorthStar device is designed as a closed system to contain, move, and shield all Mo-99 (as a solution of a mixture of radioactive Mo-99 and Mo-98 or Mo-100) during the computer-driven process of isolating Tc-99m from molybdenum before delivering Tc-99m for injection into a patient. However, individual users of the system do interact with several shielded doors, by opening and closing them, in order to insert new and remove used source vessels from the system. As a result,

[1] According to the NorthStar Medical Radioisotopes, LLC web site, it is projected that when fully operational its manufacturing facility in Benot, WI will be able to supply 50% of the Mo-99 needs required by the US market, http://www.northstarnm.com/advanced-production, Accessed 9/7/2016.

there are specific training and experience and administrative requirements that are unique to the system. These include 1) training individuals to perform the individual tasks within the protocol, 2) identifying a system administrator and designee, 3) identifying the radiation safety officer responsible for radiation safety oversight of the system, and 4) identifying an authorized medical-use licensee or nuclear pharmacist responsible for the system. In addition, there is specific vendor training for changes to hardware and software related to the operation and safety of the RadioGenix™. Design specifications of the components are necessary to maintain the device's integrity as a closed system and to ensure that the radioactive material is adequately shielded with all doors closed and with supplemental shielding in place and that safety features are designed so that the device fails in a shielded (or fail-safe) manner.

II. Authorized User and Training Requirements

The RadioGenix™ System protocols will generally be performed by individuals who are working under the supervision of Authorized Users (AUs) or Authorized Nuclear Pharmacists (ANPs). Since there may be a large number of such individuals at a medical facility or a commercial nuclear pharmacy, arranging for the manufacturer to train all of them in the protocols may be impractical. On the other hand, given the gradual shift of nuclear medicine imaging centers from on-site Mo-99/Tc-99m generators to unit doses, the subcommittee estimates that perhaps less than 10% of all clinical imaging programs in the United States may have one of these generators on site. Moreover, given the complexity of use of the RadioGenix™ System, it is more likely that this generator will be used almost exclusively by commercial radiopharmacies.

The training will initially be provided by a NorthStar representative (or an individual certified by NorthStar to provide the training) and the AU, the System Administrator or the System Administrator designee who have successfully fulfilled the requisite NorthStar training and experience and who will subsequently train other individuals responsible for performing the specific tasks within the protocol. The subject of whether the NorthStar training course should be reviewed and approved by the NRC was considered. *Given the unique design and operation of the NorthStar system, the subcommittee agreed that NorthStar should have sole responsibility for the content of the training course and certification.*

The requirement for three (3) proctored "cases" in all aspects of the operation of the NorthStar generator system is reasonable and consistent with other "35.1000" agents. However, the Draft Guidance (page 10, lines 29-32) states that the training for users of the NorthStar system must include the following, "Perform each of the protocol tasks (i.e., initialize system, produce Tc-99m, add/change reagent kit, exchange used reagent container, add source vessel, remove source vessel, and sterilization) at least three times in the physical presence of a NorthStar representative or an individual certified by NorthStar to proctor all the protocol tasks." The subcommittee questions if this requirement is practically compatible with the "lifespan" of the Mo-99/Tc-99m source vessel. Specifically, if the lifespan is of the order of several days or longer, the foregoing requirement would require the trainer to return to or otherwise be present at the applicant facility on three separate occasions that are days apart in order to satisfy the "add-source-vessel" training requirement. On the other hand, if there are multiple RadioGenix™ Systems at the NorthStar training site, and each of the generators are at various operational stages (including the several days

lifespan of the Mo-99/Tc-99m source vessel), then the training can be expedited and accomplished during that same training period. *This part of the training requires further clarification. Alternatively, could training be performed and therefore expedited using a "dummy" (ie non-radioactive) source vessel?*

Further Clarifications for the Use of "Protocol" and "Software" Applications: It is stated in the document (bottom of page 7) that "The RadioGenix™ System is fully computer-driven with specific protocols that must be performed in a set sequence and by individuals with specific radiation safety training and experience for each protocol". Similarly, on page 8, item 1, the applicant must commit to the following: "To use the accounts and roles structure of the RadioGenix™ System's software to limit what protocol can be initiated by an individual." The use of the term "protocol" in these sentences is a bit confusing. A protocol usually connotes a series of tasks and not an individual task. The most common meaning of protocol is "a system of rules that explain the correct conduct and procedures to be followed in formal situations." This was made clear under the subheading of "Protocol tasks" which was placed before the body of the narrative of the Licensing Guidance, where all the individual "tasks" were listed: 1) initialize system, 2) add/change reagent kit, 3) produce (i.e., separate) Tc-99m, 4) remove source vessel, 5) sterilization, and 6) exchange used reagent container. However, within the body of the narrative the terms "protocol" and "software" are used rather than the term "individual tasks." It is confusing because the reader may be left with the (unintended) impression that there may in fact be several protocols and software programs that could be applied with the RadioGenix™ System, with each protocol and program having a unique set of individual tasks. *Accordingly, the subcommittee recommends using the term, "individual tasks," throughout the document for consistency and to clarify that there is only one protocol and software program with this system.*

The System Administrator (or administrator designee) is responsible for ensuring that an individual initiating a protocol task meets the training and experience for that protocol outlined in this Guidance. The sequence of tasks and training was felt to be more analogous to chemistry modules for preparing cyclotron-produced radiopharmaceuticals rather than generator-produced radiopharmaceuticals. The applicant's name is apparently added to the "software" after the training of individual "protocol tasks" is completed. *This entire sequence of training for individual tasks within a "protocol" and then adding the applicant's name to the "software" should be clarified in the document.*

Additional Training as a Result of Changes to the RadioGenix™ System: The Guidance states that if there are software, hardware or procedure changes to the RadioGenix™ System, the applicant shall commit to successful completion of the training on the "changes" prior to first operation of any component or first handling of licensed material associated with the system. The subcommittee felt that this section was rather vague. For example, what is the responsibility of the vendor/manufacturer to inform and train the applicants on changes in a timely manner? What is the appropriate time period allotted for training on the "changes"? Will the generator be "non-operational" until ALL individuals handling the generator are trained in the changes, including the AU, RSO, system administrator, etc. or does it require only the AU to be trained on the "changes"? If the latter, once the AU is trained on the "changes", is the AU then solely responsible for training all others on these changes?

III. Safety Precautions

The subcommittee understands that the NorthStar system utilizes a Mo-99/Tc-99m solution in a source vessel and that the activity in this vessel (which is on the order of Curies) can be very high relative to typical "nuclear medicine" clinical activities. Such a large quantity of activity in liquid form raises the possibility, at least in theory, of a very significant spill (more so than for a conventional Mo-99/Tc-99m generator in which the activity is bound to a column). The Draft Licensing Guidance is largely silent on emergency response other than to defer to the procedures of the manufacturer. *While the subcommittee appreciates that NRC endeavors to be non-prescriptive, given the potential severity of a spill with such large quantities of radioactivity in liquid form, perhaps the manufacturer's procedures should be reviewed and incorporated into the Licensing Guidance itself.*

Surveys/Survey meters/monitors: Given the complexity of the entire system with the potential for increased exposure of the workers to radiation fields higher than those associated with conventional fission Mo-99/Tc-99 generators, "it is necessary for the licensee to routinely perform additional surveys to identify higher than expected radiation fields and system failures". *The term "higher than expected" should be defined in terms of a maximum specific exposure or exposure-rate limit which a survey meter should be capable of measuring.*

IV. Other Recommendations and Specific Comments

Annotated figure and/or video clip of the generator system: The inclusion of an annotated figure of the NorthStar generator system and a summary of its operation is very helpful but the subcommittee felt that it is confusing to insert it before the body of the narrative of the Draft Licensing Guidance, that is, without some introductory description of what the figure depicts. The use of color-coded contours to identify the various components of the generator system was also felt to be confusing. *The subcommittee recommends the use of labeled arrows to identify each component by name directly on the photograph. For the training module, the subcommittee recommends that NorthStar provide a video clip of how the system operates.*

"System Administrator": Given the unique role of the "System Administrator", will that individual be named on the license? It is also important to clarify that a system administrator can be any individual assigned by the AU without a specifically defined educational or training background.

"System Administrator Designee": Regarding "System Administrator Designee", although it may not have been intended, one could infer from the description of the System Administrator designee that there can be only one designee (as the term, "designee," is used exclusively in the singular). Presumably, there can, and should, be multiple System Administrator designees. This should be stated explicitly.

"Sensitive Security Related Information": The section on "Sensitive Security Related Information" may be unnecessary as Mo-99 and Tc-99m are not covered by the guidance for sensitive security-related information.

Specific Comments (page numbers refer to the file page numbers)

Pg 2 Line 14 The phrase, "…for the…," is repeated.

Pg 3 Lines 19-20 The phrase, "…opening shielded door, handling and disposal of radioactive materials and potentially contaminated components," should be changed to, "…opening the shielded door and handling and disposal of radioactive materials and potentially contaminated components."

Pg 16 Lines 18-19 The Draft Guidance states that applicants must commit, "Having radiation monitor(s)/meter(s) (in addition to the radiation monitor in the RadioGenix™ System) with the ability to monitor and detect expected transients." As noted above, this seems ambiguous; the maximum exposure or dose rate value measurable for a compliant radiation monitor, for example, should be specified.

Pg 17 Lines 17-18 The Draft Guidance states that the licensee will commit to the following, "To confirm that individuals will not stand near the system during the protocol due to elevated dose rates that will occur during portions of the protocol." This, too, seems ambiguous, as the term, "near," is not precisely defined. Should a minimum specific distance away from the generator be used instead? Further, should the system operator visually monitor the system during the elution procedures and would that require the operator being near the system?

V. Concluding Remarks

The subcommittee agrees with the remainder of the Licensing Guidance. The subcommittee felt that the draft Licensing Guidance is, overall, reasonable and not particularly onerous for prospective users and, given the new and novel features of the NorthStar generator system, licensing under 10CFR 35.1000 is reasonable.

Respectfully submitted, September 08, 2016
***Subcommittee on* Draft NorthStar Molybdenum-99 / Technetium-99m Generator (RadioGenix™) Licensing Guidance,**
Advisory Committee on the Medical Use of Isotopes (ACMUI),
Nuclear Regulatory Commission (NRC)

Eckert and Ziegler GalliaPharm Ge-68/Ga-68 Generator Licensing Guidance

Katie Tapp, Ph.D.
Medical Radiation Safety Team
October 7, 2016

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

Germanium/Gallium-68 Medical Use Generator Decommissioning Funding Plan Update

Said Daibes, PhD
Medical Radiation Safety Team
October 7, 2016

Overview

- **Background**
- **Current Status**
- **Regulatory Options**

Ga-68 PET Imaging Background

- **Instrumental for patients with neuroendocrine disease.**
  - **Use expanding in clinical research.**
- **Demonstrated advantages over clinical agents.**
  - **greater sensitivity and specificity.**

Current Status

- **A DFP must be developed by the licensee before it can possess the Ge-68/Ga-68 generator.**
  - **parent radionuclide long half-life**
  - **unsealed radioactive material**

Regulatory Options

- **License Specific Exemption**
  - **Exempting the DFP requirement**
    - **Provided to Regions (July 29, 2016)**
    - **STC letter to AS (August 18, 2016)**
- **Direct Final Rule**
  - **Amend Appendix B (10 CFR 30.35) to include the Ge-68 limit changes.**
  - **This new limit will allow a licensee to use a Ge-68/Ga-68 generator and not trigger the DFP requirement.**

5

Financial Assurance

- **Licensees possessing 1 or 2 medical Ge-68/Ga-68 generators (50 to 100 mCi) would be subject to a $225,000 minimum in financial assurance.**
- **Licensees possessing more than 2 and up to 20 medical Ge-68/Ga-68 generators (>100 to 1000 mCi) would then be subject to the existing requirement in § 30.35(d) for a minimum $1,125,000 in financial assurance.**

6

Acronyms

AS – Agreement States
DFP – Decommissioning Funding Plan
FDA – Federal Drug Administration
Ga-68 – Gallium-68
Ge-68 – Germanium-68
PET – Positron Emission Tomography
STC – State and Tribal Communications

QUESTIONS?

8

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

Enhancing Communications with the Medical Community

Philip Alderson, M.D.
ACMUI Chairman
October 07, 2016

Background

- **ACMUI members along with NRC staff should speak at relevant annual societal meetings to enhance communications with the medical community**
- **Various ACMUI members were charged with speaking to their respective organizations concerning such interactions.**

Professional Society Outreach Proposals

- **A regularly scheduled presentation by an NRC rep at the annual society meeting**
- **An NRC booth in the exhibit area**
- **A regular NRC column in the society newsletter**
- **An NRC-sponsored "travel fellowship"**
- **A "reverse outreach"**

Professional Society Feedback

- **Overall, the majority of the professional societies responded and were amenable to holding "Ask the Regulator"-type sessions during their meetings**
- **Many organizations believe they have open communications and exchange with the NRC.**

Path Forward

- ACR will consider holding an "Ask the Regulator Session" (CME) – May 2017.
- SNMMI is very interested in hosting an "ACMUI Session" (CME) – June 2017.
- ASTRO feels that they have an open and productive communication with NRC. A formal session is anticipated for the September 2017 meeting.
- ARRO is supportive of incorporating a session in the September 2017 meeting for residents.

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Path Forward

- AAPM and ABS are interested in maintaining already existing efforts in communication and exchange of ideas between organizations.
- HPS was very receptive to the proposed NRC outreach program. The midyear is scheduled for January 2017 (North Bethesda), where HPS plans to invite NRC representatives as speakers.

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Acronyms

AAPM – American Association of Physicists in Medicine

ABS – American Brachytherapy Society

ACR – American College of Radiology

ARRO – American Association of Resident in Radiation Oncology

ASTRO – American Society of Radiation Oncologists

HPS – Health Physics Society

SNNMI – Society of Nuclear Medicine and Molecular Imaging

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March 2017

Monday	Tuesday	Wednesday	Thursday	Friday
		1 X	2 X	3 X
6 X	7 X	8 X	9 X	10 X
13 X	14 X	15 X	16 X	17 X
20	21	22 X	23 X	24 X
27 X	28 X	29 X	30 X	31 X

April 2017

Monday	Tuesday	Wednesday	Thursday	Friday
3 X	4 X	5 X	6 X	7 X
10 X	11 X	12 X	13 X	14 X
17 X	18 X	19 X	20	21
24 X	25	26	27	28