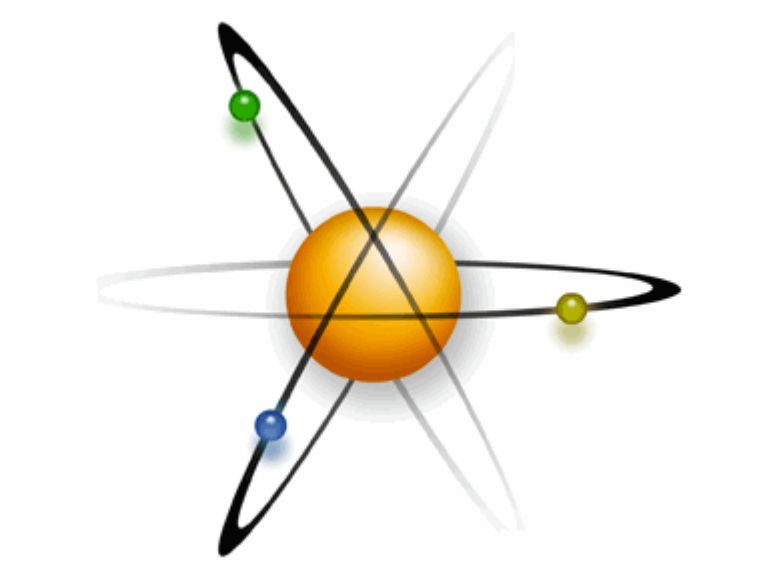
ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES

SPRING 2024 MEETING
APRIL 8 - 9, 2024

Meeting Handout



MEETING AGENDA
ADVISORY COMMITTEE ON THE MEDICAL USES OF ISOTOPES
April 8 – 9 2024
One White Flint North Building, 11555 Rockville Pike, Commissioner's Hearing Room
North Bethesda, Maryland 20852

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.

Monday, April 8, 2024 OPEN SESSION		
8:30 – 8:45	**1. Opening Remarks** Mr. Einberg will formally open the meeting and Mr. Williams will provide opening remarks.	**C. Einberg, NRC K. Williams, NRC**
8:45 – 9:00	**2. Old Business** Ms. Armstead will review past ACMUI recommendations and provide NRC responses.	**L. Armstead, NRC**
9:00 – 9:15	**3. Open Forum** The ACMUI will identify medical topics of interest for further discussion.	**ACMUI**
9:15 – 10:45	**4. Medical Related Events** Mr. Dimarco will provide an update on recent medical events.	**D. Dimarco, NRC**
10:45 – 11:15	**5. Akesis Galaxy RTi Unit Subcommittee Report** Dr. Wolkov will discuss the subcommittee's comments and recommendations on the NRC's draft licensing guidance for the Akesis Galaxy RTi unit.	**H. Wolkov, ACMUI**
11:15 – 11:45	**6. A Review of Prescription Error Reduction Methods** Mr. Green will review seven published articles on error reduction methodologies and their relative success and value.	**R. Green, ACMUI**
11:45 – 1:00	**LUNCH**	
1:00 – 1:45	**7. Eye90 Microsphere Device Subcommittee Report** Dr. Folkert will discuss the subcommittee's comments and recommendations on the NRC's draft licensing guidance for the Eye90 microsphere device.	**M. Folkert, ACMUI**
1:45 - 2:30	**8. Medical Events Subcommittee Report** Dr. Harvey will review medical events reported to the NRC from fiscal years 2021-2023.	**R. Harvey, ACMUI**
2:30 - 3:15	**9. Medical Team Updates** Dr. Valentin-Rodriguez will provide an update on the Medical Radiation Safety Team's activities.	**C.Valentin-Rodriguez, NRC**
3:15 – 3:30	**BREAK**	

3:30 – 4:00	**10. Liberty Vision Y-90 Episcleral Brachytherapy Source Subcommittee Report** Mr. Ouhib will discuss the subcommittee's comments and recommendations on the NRC's draft licensing guidance for the LV Liberty Vision Y-90 Episcleral Brachytherapy Source.	**Z. Ouhib, ACMUI**
4:00– 4:15	**11. ACMUI Reporting Structure** Ms. Armstead will provide an overview of the current reporting structure. Members will discuss the reporting structure of the Committee and provide feedback to the NRC.	**L. Armstead, NRC**
4:15 – 4:30	**12. Open Forum** The ACMUI will discuss medical topics of interest previously identified.	**ACMUI**
4:30 – 4:45	**13. Administrative Closing** Ms. Armstead will provide a meeting summary and propose dates for the fall 2024 meeting.	**L. Armstead, NRC**
4:45	**BREAK** (public portion ends)	
Tuesday, April 9, 2024 Open Session		
10:00 – 12:00	**14. Commission Meeting with the ACMUI** The ACMUI will brief the Commission on various topics in a public meeting.	**ACMUI**
	15. Group Photo The ACMUI will take a group photo with and without the Commission.	**ACMUI**
12:00	**ADJOURN**	

2020 ACMUI Recommendations and Action Items

	ITEM	DATE	STATUS		Target Completion Date for NRC Action
11	As part of the Non-Medical Events report, the ACMUI recommended to the NRC staff and/or NMP to evaluate the issue of detection of short-lived medical isotopes in municipal waste (waste from nuclear medicine patients that might be triggering the landfill alarms) and provide some level of guidance, best practices, or additional instructions.	9/21/2020	*Accepted*	Open	Fall 2024

2021 ACMUI Recommendations and Action Items

	ITEM	DATE	STATUS		Target Completion Date for NRC Action
7	The ACMUI formed a new subcommittee on the Liberty Vision Y-90 Manual Brachytherapy source. The subcommittee is expected to provide a draft report and any recommendations at the spring 2022 ACMUI meeting.	10/04/2021	*Accepted*	Propose to close	Spring 2024
10	The ACMUI endorsed the Radionuclide Generator Knowledge and Practice Requirements Subcommittee Report and the recommendations provided therein.	10/04/2021	*Accepted*	Open	March 2026

2022 ACMUI Recommendations and Action Items

	ITEM	DATE	STATUS		Target Completion Date for NRC Action
4	The ACMUI endorsed the Y-90 microsphere ME Subcommittee report and the recommendations therein.	12/5/2022	*Accepted*	Open	Fall 2024
6	The ACMUI established two subcommittees: one to create generic process checklists to be used during medical administrations and one to review the DFA draft proposed rule. The ACMUI also reestablished the Nursing Mothers guidelines to update the 2019 guidelines.	12/5/2022	*Accepted*	Open	Fall 2023

2023 ACMUI Recommendations and Action Items

	ITEM	DATE	STATUS		Target Completion Date for NRC Action
1	The ACMUI tentatively scheduled the Spring meeting for April 8-9, 2024. The alternate meeting date is XXX.	10/23/2024	*Accepted*	Propose to close	Spring 2024
2	The ACMUI recommended that NRC obtain the number of annual Y-90 microsphere administrations from the manufacturers.	10/23/2024	*Accepted*	Propose to close	Spring 2024

OPEN FORUM

(No Handout)

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

Status of Medical Events FY 2023

Daniel DiMarco
Medical Radiation Safety Team
April 8, 2024

Medical Events FY 2018 - 2023

	FY18	FY19	FY20	FY21	FY22	FY23
35.200	0	1 (8*)	0	4	0	1
35.300	2	9	2	10	10	11
35.400	11 (13*)	5	6	4	1	3
35.600	10	9 (10*)	13	5	11 (40*)	8
35.1000	25 (26*)	32	27	41	34	36
Total	48	56	48	64	56	59

* The total number of patients involved if greater than the number of reports

Medical Events 2023

35.200 Medical events	**1**
I-123	1

35.200 I-123

- Wrong Drug [230114]
  - Patient prescribed I-123 scan, received 162.8 MBq (4.4 mCi) I-131 TBI scan
  - Scheduled in electronic medical system for TBI scan with Thyrogen
  - Patient was administered the first dose of Thyrogen, however the technologist realized that the patient had their thyroid before the second injection of Thyrogen
  - Administered the I-131 injection and the radiologist discovered that the patient had been administered the wrong drug when reviewing the images
  - The dose to the thyroid was estimated to be 150 Gy (15,000 rad)

35.200 I-123

- Wrong Drug [230114] (cont.)
  - Patient followup reported no adverse effects to the patient
  - Root cause was determined to be human error; protocol to have all patient records and lab work completed before administration was not followed
  - Additionally, the written directive did not specify the radioisotope, only that a total body iodine scan had been prescribed
  - Corrective actions included the creation of a new form requiring the inclusion of all relevant patient labs to be completed before signing the written directive

Medical Events 2023

35.300 Medical events	**11**
Lutetium-177	9
I-131	2

35.300 Lu-177

- Wrong Drug [230424]
  - One patient was prescribed commercially available Lu-177 Dotatate, another prescribed Lu-177 dotatate under a new investigational new drug label
  - Patient prescribed the commercially available Lu-177 was instead administered the investigational drug
  - The patient was given the correct activity, chemical form, and route of administration
  - Root cause was determined to be human error
  - No adverse effects are expected
  - Additional notifications were made to the Institutional Review Board, considering the involvement of an investigational drug product

35.300 Lu-177

- Patient overdose [230370]
  - Prescribed 5.92 GBq (160 mCi), administered 7.65 GBq (206.7 mCi)
  - RSO indicated that the technologist did not follow the written directive to verify activity before injection
  - Typical injection uses 7.4 GBq (200 mCi), technologist did not recognize the updated dose
  - Corrective actions included updated procedures

35.300 Lu-177

- Patient underdose [230360]
  - Patient prescribed 7.4 GBq (25 mCi), received 70-75% of the dose
  - Administering Lu-177 via syringe pump
  - 20 minutes into the injection, patient reported a wet feeling on their hand
  - Leak was traced to the connection between the syringe pump and the patient's IV site
  - Bedding and materials had absorbed a majority of the leak and spill response protocols were initiated
  - Estimates of the material remaining in the vial, the contamination on the bedding, and patient dose rate measurements post-treatment suggested an underdose of 25-30%
  - Skin exposure was estimated to be under 10 cSv (rem)
  - Corrective actions included updated procedures and training, and clarification that all future therapy administrations will be through secured connections

35.300 Lu-177

- Patient underdose [230102]
  - Prescribed 7.4 GBq (100 mCi), administered 5.83 GBq (157.57 mCi)
  - During the administration, the technologist noticed drips from the tubing
  - Investigation indicated the patient had received 21.22% less dose than prescribed
  - Root cause was determined to be leaky tubing, additionally tubing from the same lot was also found to be leaky
  - Corrective actions included removing that lot from use and notifying the vendor of the defect
  - Additionally, the licensee updated procedures to visibly check for leaks

35.300 Lu-177

- Patient underdose [230023]
  - Patient prescribed 7.4 GBq (200 mCi), received 4.48 GBq (121 mCi)
  - The normal apparatus used for administering Pluvicto was not available due to supply chain issues
  - A similar, pressurized apparatus was used instead
  - Leak was identified at the rubber septum of the vial in the shielded storage container
  - Root cause was determined to be pressurization of the vial, manufacturer does not recommend pressurizing the vial
  - Another dose of Pluvicto was administered to replace the underdosed administration and was administered without incident

35.300 Lu-177

- Patient underdose [230023]
  - Patient prescribed 7.4 GBq (200 mCi), received 4.77 GBq (129 mCi)
  - The normal apparatus used for administering Pluvicto was not available due to supply chain issues
  - A similar, pressurized apparatus was used instead
  - Leak was identified at the rubber septum of the vial in the shielded storage container
  - Root cause was determined to be pressurization of the vial, manufacturer does not recommend pressurizing the vial
  - Patient will be monitored during the rest of their treatment regimin and appropriate equipment will be used for following treatments

35.300 Lu-177

- Wrong drug [220531]
  - 2 patients, one prescribed 7. Gbq (200 mCi) of Lu-177 dotatate, another prescribed 7.4 GBq (200 mCi) of Lu-177 vipivotide tetraxetan
  - Vials were switched and each patient was administered the incorrect drug
  - Root causes were determined to be complacency and lack of training
  - Additionally, both doses were identical and the shipping containers were similarly colored
  - Corrective actions included implementing a new scheduling process so Lutathera and Pluvicto treatments are not scheduled on the same day and institution of a dual verification process
  - Additionally, the licensee provided reeducation on package checks and patient verification

35.300 Lu-177

- Patient underdose [220448]
  - Patient prescribed 7.4 GBq (200 mCi), received 3.92 GBq (106 μCi)
  - Injection occurred without incident
  - Post-treatment investigation discovered residual radiopharmaceutical in the injection tubing giving an estimate of the underdose
  - Root cause was determined to be human error
  - Corrective actions included increasing the mandatory saline flush from 25 mL to 250 mL, staff training, and strict vetting of technologists for therapy administrations

35.300 Lu-177

- Patient underdose [220432]
  - Patient prescribed 7.4 GBq (200 mCi), received 5.11 GBq (138 mCi)
  - Injection occurred without incident
  - Post-treatment investigation discovered residual radiopharmaceutical in the injection tubing giving an estimate of the underdose
  - Root cause was determined to be human error
  - Corrective actions included increasing the mandatory saline flush from 25 mL to 250 mL, staff training, and strict vetting of technologists for therapy administrations

35.300 I-131

- Patient overdose [230279]
  - Prescribed 2.78 GBq (75 mCi), administered 3.7 GBq (100 mCi)
  - 2 dose of I-131 were prepared for 2 separate patients
  - While preparing the dose for the first patient, the technologist mistakenly assayed the second dose
  - The first patient was inadvertently administered the dose intended for the second patient
  - The mistake was discovered prior to treating the second patient
  - Root cause was determined to be human error
  - Corrective actions included staff training on time-out procedures and posting a physical copy of the time-out procedures on the wall in the therapy room

35.300 I-131

- Patient overdose [220338]
  - Patient prescribed 740 MBq (20 μCi), received 780.7 MBq (21.1 μCi)
  - Patient received the intended dose but the written directive incorrectly specified “20 μCI” instead of “20 mCi”
  - No adverse effects are expected
  - Corrective actions included combining WD checklist and WD prescription into one form
  - AU also now is required circle the word millicurie or microcurie on the form, and the technologist has to sign off on dose verification

Medical Events 2023

35.400 Medical events	**3**
Eye Plaque	1
Cs-131 Brachytherapy	2

35.400 I-125 Eye Plaque

- Patient underdose [230335]
  - Prescribed 8,500 cGy (rad), received 5,700 cGy (rad)
  - Licensee believes the eye plaque may have shifted over the seven day treatment
  - Update required

35.400 Cs-131

- Patient underdose [230354]
  - Prescribed 11,500 cGy (rad), received 5,750 cGy (rad)
  - Planned to implant a total of 98 C-131 seeds with a total of 10.46 GBq (282.6 mCi)
  - 37 seeds unused after the treatment, 70 total were implanted
  - Root cause was determined to be swelling and excessive bleeding causing coagulated blood in the Mick applicator
  - Corrective actions included revising procedures

35.400 Cs-131

- Patient underdose [230219]
  - Prescribed 6,000 cGy (rad), received 3,700 cGy (rad)
  - Patient was implanted with seeds totaling 1.42 GBq (39.5 mCi)
  - Following implantation, the patient was diagnosed with a medical condition that necessitated the immediate removal of the seeds
  - All seeds were accounted for, and actual dose was calculated
  - Incident was discovered during a routine safety inspection
  - No corrective actions were taken

Medical Events 2023

35.600 Medical events	**8**
HDR	8

35.600 HDR

- Wrong Site [230417]
  - 185 GBq (5 Ci) I-192 HDR Unit
  - Cylinder inadvertently shifted during a vaginal treatment by 3.5 cm
  - Update required

35.600 HDR

- Wrong site [230365]
  - 192.4 GBq (5.2 Ci) Ir-192 HDR unit
  - Patient prescribed 1,800 cGy (rad) in three fractions
  - CT planning, plan review, time-out, and device insertion (including depth verification) were all completed without incident
  - During the first fraction the patient notified the AU that the cylinder was in the wrong place
  - The administration was stopped 111 seconds into the treatment and it was discovered that the cylinder had been placed into the rectum instead of the vagina.

35.600 HDR

- Wrong site [230365](cont.)
  - After removal of the device and discussion with the team, treatment resumed with the correct placement of the device
  - The remaining fractions were adjusted and the dose to the rectum was estimated at 239 cGy (rad)
  - No adverse effects are expected
  - Corrective actions included additional training, including verification the the device is in the correct anatomy

35.600 HDR

- Patient overdose [230255]
  - Patient was prescribed 500 cGy (rad) in three fractions for a total of 1500 cGy (rad) to the keloid skin surface
  - Mistakenly administered the full 1500 cGy (rad) in one fraction
  - Update required

35.600 HDR

- Patient underdose [230166]
  - Patient prescribed four treatments of 500 cGy, received 156 cGy on the fourth treatment
  - HDR unit gave an error during the fourth treatment indicating a source retraction issue
  - The right and left partial ring treatments were administered but not the tandem
  - Root cause was determined to be failure of the HDR motors
  - Additionally, the licensee used an applicator that was not approved for use with the Flexitron system, which resulted in the source capsule becoming stuck
  - Corrective actions included equipment testing, a hold on the program pending root cause analysis, evaluation of policies and procedures, and additional training

35.600 HDR

- Patient underdose [230104]
  - 251.6 GBq (6.8 Ci) Ir-192 HDR unit
  - Prescribed 5 fractions of 600 cGy (rad), received less than 50% of the fraction for the first two fractions
  - Planning had mapped the channels to specific catheters, but post-treatment review discovered that during the administration the channels had been incorrectly mapped
  - Adjustments were made in the following fractions to ensure appropriate tumor coverage and tissue sparing
  - No adverse effects are expected
  - Corrective actions included updated procedures and checklists

35.600 HDR

- Patient Underdose [230062]
  - 275.28 GBq (7.44 Ci) HDR unit
  - Prescribed 1,350 cGy (rad), administered 326.56 cGy (rad)
  - During treatment the AU observed that the transfer stretcher was pitched towards the patient's head and interrupted the treatment
  - 15 of 17 needles had been extracted approximately 2 centimeters
  - Patient was monitored for any adverse effects, but none were expected

35.600 HDR

- Patient Underdose [230062](cont.)
  - Root cause was determined to be an issue with the hydraulics in the patient transfer stretcher, with lack of attention to the patient as a contributing factor
  - Corrective actions included amending the procedures to maximally lower the stretcher during treatment
  - The state also recommended evaluing the roles of individuals present during treatment to ensure continuous patient monitoring

35.600 HDR

- Patient Underdose [220508]
  - 329.3 GBq (8.9 Ci) Ir-192 HDR unit
  - Prescribed 750 cGy (rad) per fraction, administered 12.7 cGy (rad) in the third fraction
  - During treatment, the HDR unit was unable to detect one of the transfer tubes connecting it to the applicator, resulting in a partial delivery of the fraction
  - The field service engineer determined that the HDR's unit selector should be recalibrated, after which the unit functioned correctly
  - The patient was then successfully treated the following day

35.600 HDR

- Patient Overdose [220495]
  - 327.5 GBq (8.85 Ci) I-192 HDR unit
  - Prescribed five fractions of 600 cGy (rad), received the full 3000 cGy (rad) in a single fraction
  - During the treatment the MP misread the written directive and delivered the full 300 cGy
  - Patient was monitored following the treatment and no adverse effects were observed

35.600 HDR

- Patient Overdose [220495](cont.)
  - Root cause was determined to be human error, the licensee uses two treatment planning systems and the MP read the secondary plan instead of the primary plan
  - Corrective actions included having one person perform the planning and another perform the verification, with each signing off before the treatment.
  - Additionally, a generic table of expected treatment times based on dose was developed
  - The state reported that the corrective actions taken were suitable

Medical Events 2023

35.1000 Medical events	**36**
Seed localization	1
Intravascular Brachytherapy	1
GSR	1
Y-90 Microspheres	
– TheraSphere™	22
– SIR-Spheres®	9
– Unknown	2

35.1000 Radioactive Seed Localization

- Failure to Explant [230348]
  - Patient went into surgery to have localization seed explanted the day after it had been implanted
  - 10 months later, it was discovered that the seed remained in the patient
  - The previous surgery had removed a clip, instead of the seed
  - The calculated dose to the tissue was 74 cGy (rad)
  - The seed will be removed in a future planned surgery

35.1000 IVB

- Wrong site [230291]
  - Patient prescribed 2,300 cGy (rad), delivered to the wrong treatment site
  - 3.62 GBq (97.84 mCi) Sr-90 source
  - During treatment, the cardiologist used fluoroscopy to determine the treatment site
  - Post-treatment review of the images could not accurately assess the location of the source
  - Prescribing physician determined that the dose had been delivered to another part of the vasculature proximal to the intended location

35.1000 IVB

- Wrong site [230291](cont.)
  - No permanent damage is expected
  - Root cause was determined to be human error; the cardiologist misread the images due to poor quality and obscuration of the images by medical equipment
  - Corrective actions included additional training, procedure modifications, and an agreement for an independent assessment of the dose by a medical physics consultant

35.1000 Gamma Knife

- Patient Underdose [230108]
  - Patient prescribed 1,500 cGy (rad), delivered 44.11 cGy (rad)
  - Planned for 13 shots, unit malfunctioned after completing 3 shots
  - Error could not be resolved by licensee and required service
  - Technician identified and repaired a worn sector drive assembly
  - Patient was rescheduled for successful treatment

35.1000 Y-90 Microspheres

- Y-90 underdose [220492]
  - Patient prescribed 15,000 cGy (rad), received 7.905 cGy (rad)
  - Update required

35.1000 Y-90 Microspheres

- Y-90 underdose [230361]
  - Patient prescribed 2.11 GBq (57.03 mCi), received 0.927 GBq (25.05 mCi)
  - Update required

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230425]
  - Patient prescribed 1.7 GBq (45.92 mCi) ,administered 1.3 GBq (35.15 mCi)
  - Administration occurred without incident and the delivered dose was determined to be clinically effective
  - Post-treatment calculations revealed the underdose, imaging of the waste determined the majority of the remaining dose was in the vial
  - Inspectors concluded that the practitioner did not tap the vial sharp enough against a hard surface prior to administration (i.e. inadequate agitation of the vial)
  - Corrective actions included checklist revision to better describe dose vial preparation and additional training

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230395]
  - Patient prescribed 40,700 cGy (rad), received 31,320 cGy (rad)
  - AU discovered that a significant amount of residual dose was in the vial post-treatment
  - Update required

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230392]
  - Patient prescribed 6.7 GBq (181.08 mCi), received 5.02 GBq (135.81 mCi)
  - Root cause was suspected to be due to air in the tubing during the administration
  - No adverse impacts to the patient are expected, the dose was determined to be medically sufficient

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230363]
  - Patient prescribed 1.24 GBq (33.51 mCi), received 0.715 GBq (19.32 mCi)
  - During treatment, the microspheres required higher pressure to deliver and the spillover vial had a high volume of microspheres
  - Post-treatment surveys confirmed that a large portion of microspheres had not been delivered
  - Root cause was suspected to be failure of the needle or equipment, since no other operating steps showed signs of failure
  - The patient was scheduled for a follow-up treatment
  - The equipment will be returned to the manufacturer when sufficiently decayed

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230357]
  - Patient prescribed 17,500 cGy (rad), received 3,170 cGy (rad)
  - Physician noted resistance during administration and the pressure vial was noticed to be filling with saline
  - Treatment was stopped and a plug of microspheres was discovered in the line
  - The plug was dislodged, and saline was flushed eight times, but the procedure was terminated since it was clear the administration was not successful
  - A follow-up procedure was scheduled for the patient
  - The treating equipment was returned to the manufacturer for investigation

35.1000 TheraSphere™

- Y-90 TheraSphere™ wrong site [230341]
  - Patient prescribed 3.07 GBq (83 mCi) to the right lobe of the liver, received the dose to the left lobe of the liver
  - Tc-99m planning study indicated primary deposition in the right lobe of the liver with some deposition in the left lobe
  - However, primary distribution was to the right lobe of the liver
  - Treatment had been planned to the right lobe under a different written directive, so no adverse effects to the patient are expected

35.1000 TheraSphere™

- Y-90 TheraSphere™ wrong site [230341](cont.)
  - Corrective actions included a new process where nuclear medicine to contact interventional radiology when images indicate any activity in an unintended area
  - Additionally, all AUs have been directed to consider all distribution pathways discovered during the planning study
  - The state inspectors determined that all procedures were followed and the corrective actions implemented were acceptable

35.1000 TheraSphere™

- Y-90 TheraSphere™ wrong site [230329]
  - Patient prescribed 1.41 GBq (38 mCi), received 63 Gy (6300 rad)
  - Post-treatment imaging determined that some activity was taken up by unintended segments of the liver
  - The procedure was determined to be performed correctly but the activity was transferred due to the complex hepatic flow
  - No adverse effects are expected
  - The licensee indicated that the procedure was performed successfully and that this is an expected risk of the procedure, therefore no corrective actions can be taken
  - This event is still under review

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230326]
  - Patient prescribed 0.98 GBq (26.4 mCi), received 0.77 GBq (20.7 mCi)
  - Treatment was performed without incident
  - Post-treatment surveys discovered a significant number of microspheres remaining in the source vial
  - The dose administered was determined to be clinically sufficient
  - Root cause was unable to be determined, the licensee plans to return the device to the manufacturer for examination

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230322]
  - Patient prescribed 1.08 GBq (29.18 mCi), received 0.784 GBq (21.18 mCi)
  - Treatment occurred without incident, but post-treatment surveys revealed microspheres in the waste vial
  - Imaging revealed that microspheres were stuck at the juncture of the outflow tube and the microcatheter
  - No adverse effects are expected
  - Reactive inspection did not identify a clear cause, increase pressure may have been caused by tortuous anatomy or microcatheter issues
  - Procedure was followed correctly, and no problems were indicated during the administration
  - The licensee plans to return the device to the manufacturer for investigation

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230305]
  - Patient prescribed 12,000 cGy (rad), received 9,140 cGy (rad).
  - No indication that anything was wrong during the administration, four saline flushes went into the patient with no problem
  - The treatment was observed by the RSO and a manufacturer representative, and all procedures were followed
  - Post-treatment, microspheres were discovered attached to the bottom portion of the septum, and clumped in the microcatheter that did not cause clogging
  - The licensee plans to send the device to the manufacturer for investigation following decay

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230281]
  - Patient prescribed 539.46 MBq (14.58 mCi), received 36.74 MBq (0.993 mCi)
  - Physician stated that the procedure proceeded normally aside from a little more resistance than usual
  - Subsequent imaging showed little to no activity in the patient, surveys of the waste revealed that the majority of the activity remained in the tubing
  - A specialized catheter for Y-90 administrations (Trinav 130 cm) was used with a 20 cm extension catheter

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230281](cont.)
  - Root cause was determined to be the use of the extension catheter
    - The larger internal diameter of the extension reduced the saline velocity, causing the microspheres to fall out of suspension
  - The patient underwent a repeat procedure without issue
  - Corrective actions included training, no longer using extension tubing, and ordering longer Trinav catheters

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230275]
  - Patient prescribed 753 MBq (20.35 mCi), received 215 MBq (5.81 mCi)
  - Measurement of the vial following treatment showed a significant amount of activity remaining in the vial
  - Root cause is under investigation but is suspected to be due to a kink in the catheter
  - Patient will likely require further treatment
  - The licensee will send the device back to the manufacturer for investigation following decay

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230261]
  - Patient prescribed 2.54 GBq (68.5 mCi), received 0.13 GBq (3.6 mCi)
  - Post-treatment surveys discovered microspheres blocked in a tubing connector
  - No spillage or contamination was identified
  - Investigation is ongoing

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230230]
  - Patient prescribed 518 MBq (14 mCi), received 31.45 MBq (0.85 mCi)
  - Obstruction was noticed early during the treatment
  - Administration was halted following the discovery of the obstruction
  - A similar event has occurred at this licensee regarding Y-90 devices from the same batch
  - All microsphere administrations from that batch have been paused
  - Investigation is ongoing

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230221]
  - Patient prescribed 742.22 MBq (20.06 mCi), received 34.41 MBq (0.93 mCi)
  - Obstruction was noticed early during the treatment
  - Administration was halted following the discovery of the obstruction
  - A similar event has occurred at this licensee regarding Y-90 devices from the same batch
  - All microsphere administrations from that batch have been paused
  - Investigation is ongoing

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230211]
  - Patient prescribed 1.03 GBq (27.72 mCi), received 0.64 GBq (17.38 mCi)
  - During treatment a 2.4 French TriNav anti-reflux catheter was attached to the delivery device
  - No microspheres were found in the tubing or delivery system post-treatment
  - Surveys of the catheters found high residual activity remaining
  - Post-treatment scans revealed activity in the left hepaitic lobe with unusual uptake in the spleen/gastric region

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230211](cont.)
  - Root cause is suspected to be a microcatheter rupture during administration, resulting in high residual activity in the catheter and unusual distribution
  - Patient was admitted for observation and remained asymptomatic
  - Corrective actions included discontinuing use of the anti-reflux catheters and retraining

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230193]
  - Patient prescribed 1.282 GBq (34.7 mCi), received 0.981 GBq (26.5 mCi)
  - Post-treatment imaging revealed microspheres remaining in the delivery kit tubing
  - Root cause was determined to be human error
    - The AU could not recall if the microcatheter connection had been placed in the holder on the extension arm
    - The dosimeter did not detect microspheres moving through the tubing
  - No adverse effects are expected
  - Corrective actions included reminders of best practices during a Y-90 treatment and additional surveys of the tubing for verification that microspheres have moved through during the treatment

35.1000 TheraSphere™

- Y-90 TheraSphere™ wrong site [230101]
  - Patient prescribed 0.8 GBq (21.62 mCi) for one liver segment and 1.93 GBq (52.16 mCi) for another, these doses were switched during the administration
  - The physician asked for the first dose but was brought the second dose
  - After verbally reading the dose, the vial was connected and delivered
  - Root cause was determined to be human error
  - Corrective actions included a radiation dosing education program with event background and call back procedures, as well as additional training for personnel

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230029]
  - Patient prescribed 1.377 GBq (37.22 mCi), received 0.451 GBq (12.19 mCi)
  - Treatment was administered according to manufacturer requirements with no errors
  - During the second saline flush a technologist noticed that liquid was pooling inside the acrylic pot inside the lead pig
  - Multiple attempts to stop the pooling were unsuccessful and the administration was halted

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230029](cont.)
  - Surveying of the waste container gave an estimate of the activity actually administered
  - The patient will be evaluated at follow up for future treatment
  - No root cause was able to be identified
  - No specific corrective actions were implemented
  - The administration kit will be returned to the manufacturer for analysis after decay

35.1000 TheraSphere™

- Y-90 TheraSphere™ wrong site [220509]
  - Patient prescribed 666 MBq (18 mCi) to segment 5 of the liver, received 520 MBq (14.05 mCi) to segments 7 and 8
  - A stenosis in the target vessel required changing the treatment vessel to the origin of the vessel
  - An unexpectedly large volume of the microsphere refluxed into the wrong segments of the liver
  - No corrective actions were taken

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230021]
  - Patient prescribed 1.377 GBq (37.22 mCi), received 0.903 GBq (24.41 mCi)
  - The licensee suspected low flow rates had caused occlusion I the catheter
  - After analysis by the manufacturer determined that the injector needles were bent at a 90 degree angle and there was a kink in the tubing at the pinch clamp
    - Could not verify if these were problems pre or post-treatment
  - Blood clots and microspheres were also found in the waste collection vial

35.1000 TheraSphere™

- Y-90 TheraSphere™ underdose [230021](cont.)
  - Root cause was determined to be low flow rate, the cause of which could not be identified
  - No adverse effects are expected and the dose was determined to be medically sufficient
  - Corrective actions included the use of a electronic dosimeter near the patient to identify blockages or buildup of material between the device and the patient

35.1000 TheraSphere™

- Y-90 TheraSphere™ wrong site [220433]
  - Patient prescribed 848.4 MBq (23.2 mCi) to left lobe segments 5 and 8, received 847.3 MBq (22.9 mCi) to left lobe segment 4
  - Written directive error, the dose was originally intended to be given to segment 4 but a typographical error resulted in the wrong written directive being produced
  - No effects are expected to the patient
  - Corrective actions included specifying the treated segment in writing with a formal review of the directive by the treating interventional radiologist
  - Additionally, the treatment quality control will include a verbal verification of the treatment site prior to administering the dose

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® underdose [230209]
  - Patient prescribed 536.5 MBq (14.5 mCi) and 802.9 MBq (21.7 mCi), received 196.1 MBq (5.3 mCi) and 455.47 MBq (12.31 mCi) respectively
  - Patient prescribed 2 vials of microspheres for the treatment
  - Manufacturer could not find any residual microspheres in the device and testing revealed no errors
  - Root cause was determined to be a leak between the delivery system and the administration catheter
  - Corrective actions included procedure modifications, additional training, and obtaining new equipment

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® overdose [230155]
  - Patient prescribed 1.6 GBq (43.2 mCi) and 0.7 GBq (18.9 mCi), received 2.34 GBq (63.2 mCi) and 0.77 GBq (20.8 mCi)
  - One written directive for a split dose administration, 2 doses for 2 separate locations
  - RSO inadvertently entered the total of both doses into the prescribed dose section of the treatment planning spreadsheet
  - Additionally, only GBq were used, disguising the unexpectedly large dose for the first administration
  - No adverse effects are expected
  - Corrective actions included revision of procedures and the calculation spreadsheet, preparing separate written directives for spilt doses, listing the activity in both GBq and mCi on relevant forms and containers, and creating a no distraction zone in the preparation hot lab

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® underdose [220404]
  - Patient prescribed 0.407 GBq (11 mCi), received 1.4 GBq (37.9 mCi)
  - Intended to be a two-step successive administration
  - Technologist drew 2.23 GBq (60.3 mCi) for the first step instead of the intended 0.223 GBq (6.03 mCi)
  - Statis administration of this dose was estimated and no further administration to the patient occurred

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® underdose [220404](cont.)
  - Root cause was determined to be a lack of standardized written NM procedures for microsphere administration verification and inexperience by the administering technologist
  - Corrective actions included formalized staff retraining, rewritten procedures, establishment of a secondary verification during dose preparation, use of a volume determination spreadsheet, and use of a chart of expected measurements for known amounts of activity

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® wrong site [230065]
  - Patient prescribed 1.32 GBq (35.74 mCi) to the right lobe of the liver, received 1.35 GBq (36.48 mCi) to the left lobe of the liver
  - Root cause was determined to be human error
  - No adverse effects are expected, the left lobe of the liver was intended to be treated under a different written directive after this event occurred with a dose within 20% of this administered dose
  - Corrective actions included procedure modifications and additional training
  - The procedure was updated to require verbal verification of the lobe being treated and an additional review by the physician prior to treatment

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® underdose [230026]
  - Patient prescribed 53.65 MBq (1.45 mCi), received 19.61 MBq (0.53 mCi)
  - Update required

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® underdose [220537]
  - Patient prescribed 700.41 MBq (19.93 mCi), received 557.59 MBq (15.07 mCi)
  - Treatment was delivered without error
  - Further investigation discovered that the procedure had reached stasis
  - Root cause was determined to be failure to identify stasis and lack of sufficient training
  - Corrective actions included additional training

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® underdose [220521]
  - Patient prescribed 3.39 GBq (91.6 mCi), received 2.02 GBq (54.6 mCi)
  - Did not appear to involve stasis
  - Root cause was determined to be equipment failure
  - Corrective actions included disposal of the involved equipment

35.1000 SIR-Spheres®

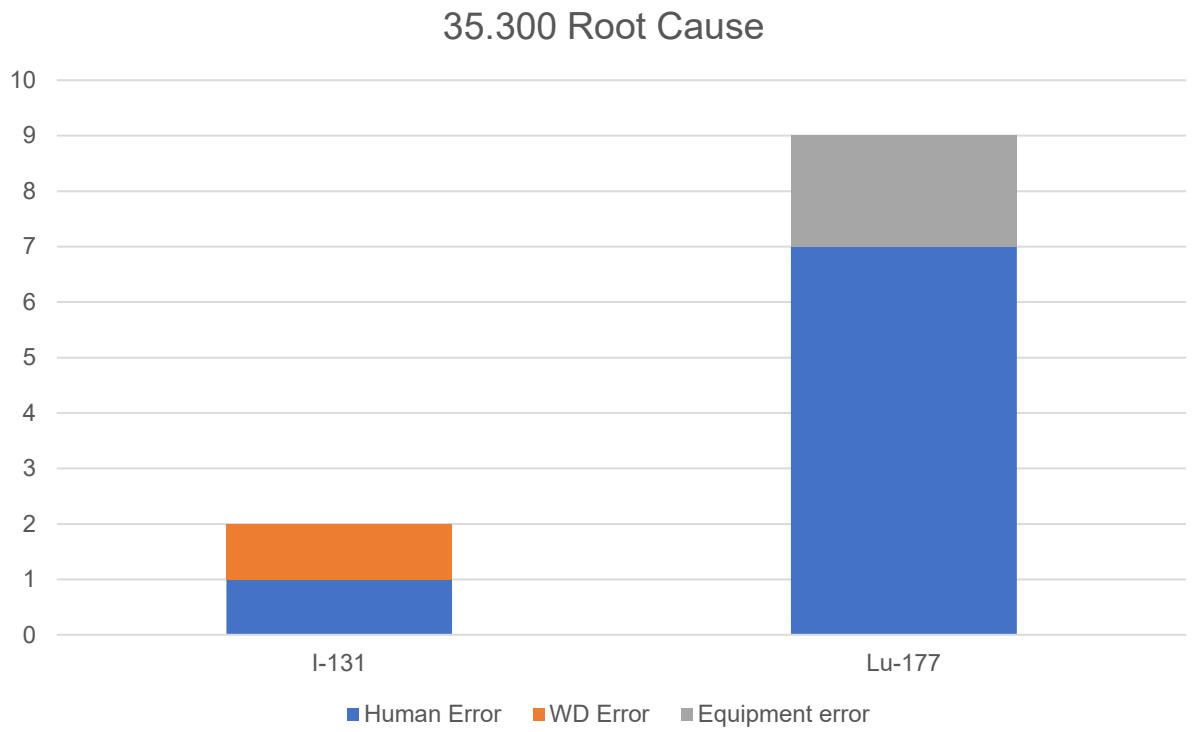
- Y-90 SIR-Spheres® underdose [220505]
  - Patient prescribed 495.8 MBq (13.4 mCi), received 305.62 MBq (8.26 mCi)
  - Procedure occurred without incident, no stasis
  - Post-treatment survey of the tubing found a significant amount of microspheres remaining in the catheter
  - No leakage or contamination was found
  - The procedure was followed correctly and the equipment used was in line with manufacturer recommendations
  - Root cause was suspected by the manufacturer to be a premature air pause
  - Corrective actions included refresher training

35.1000 SIR-Spheres®

- Y-90 SIR-Spheres® underdose [210474]
  - Patient prescribed 399.6 MBq (10.8 mCi), received 160.2 MBq (4.33 mCi)
  - An appropriately sized catheter was used
  - Vascular access to the treatment site was unusually tortuous
  - Manufacturer representatives observing the treatment noted no deviations from recommended protocols
  - Root cause was suspected to be collection of the microspheres to the catheter walls due to tortuous anatomy or excessive bends in the line
  - Corrective actions are pending

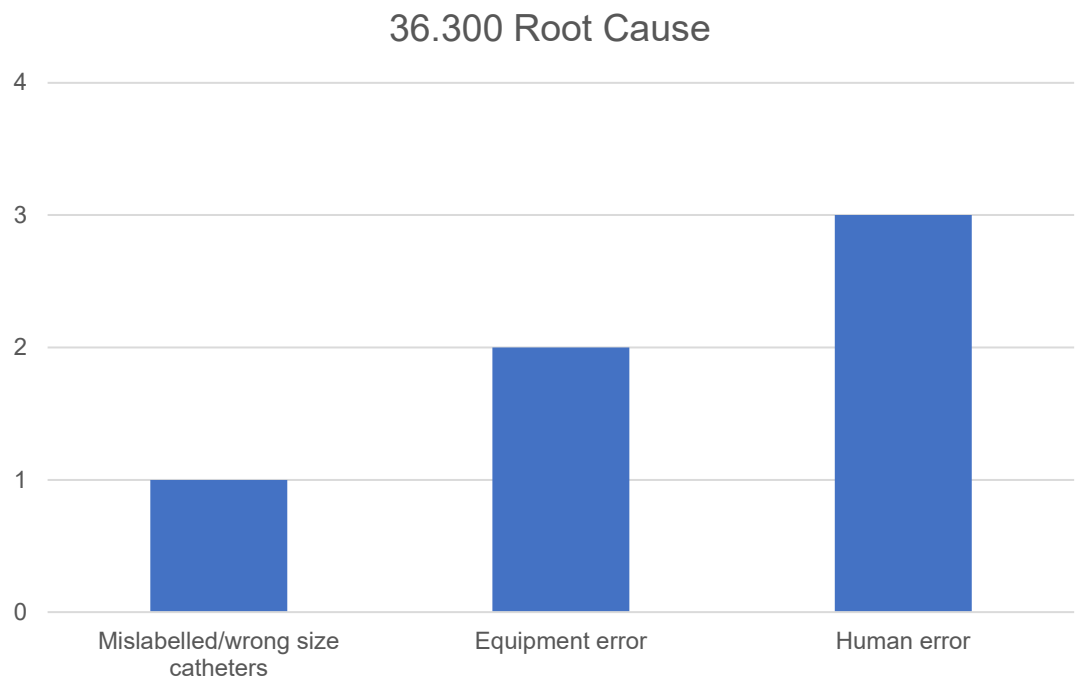
Summary

- 35.300
  - Primarily Lu-177 events, huma error underdoses
  - Mix-up Lutathera and Pluvicto, mix-ups on patients
  - Supply chain issues for delivery equipment



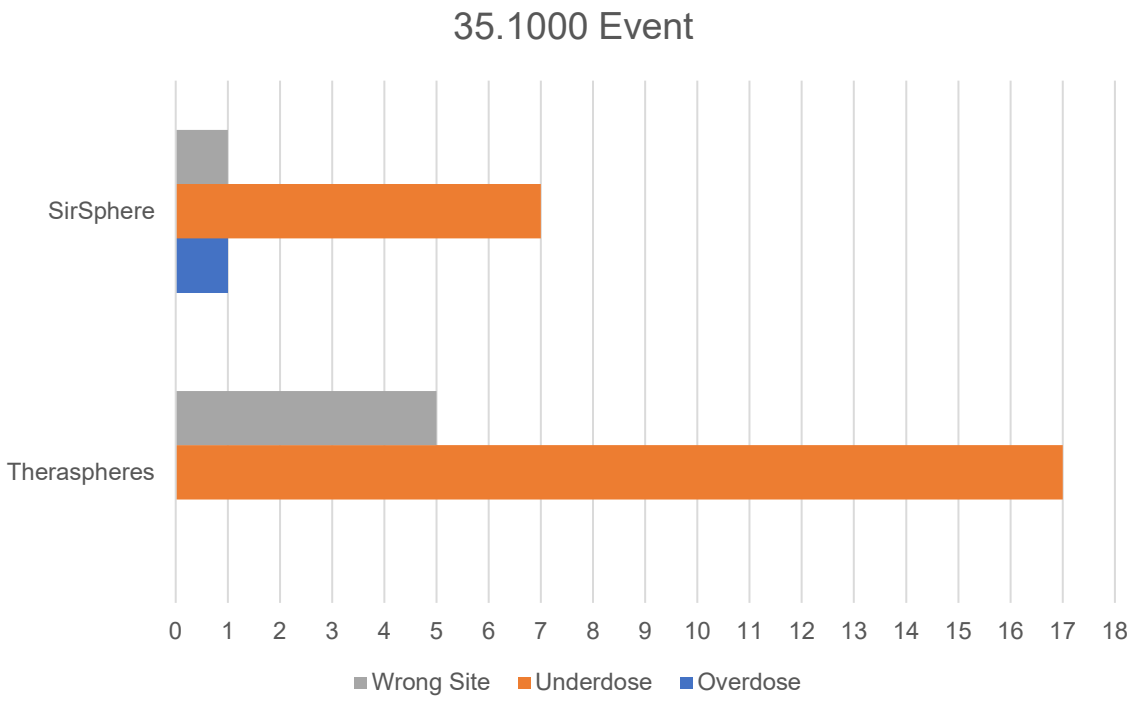
Summary

- 35.600
  - Primarily human error events, few equipment failures
  - Full dose delivery in one fraction
  - Incorrect anatomical placement



Summary

- 35.1000
  - Primarily Y-90 Theraspheres, primarily underdoses
  - Collaboration with manufacturers
  - Possible complications with catheter supplements (anti-reflux cage, extension)



Acronyms

- µCi – microcurie
- AMP – authorized medical physicist
- AU – Authorized User
- Cs-131 – Cesium-131
- cGy – centiGray
- CT – Computed tomography
- FY – Fiscal Year
- GBq – Giga Becquerel
- Gy – Gray
- HDR – High Dose Rate Remote Afterloader

Acronyms

- I-125 – Iodine-125
- I-192 –Iridium-192
- IVB – Intravascular Brachytherapy
- Lu-177 – Lutetium-177
- MBq – Mega Becquerel
- µCi - microcurie
- mCi – millicurie
- NMT – Nuclear medicine technician
- RSO – radiation safety officer
- SI units – International System of Units
- WD- Written Directive
- Y-90 – Yttrium-90

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

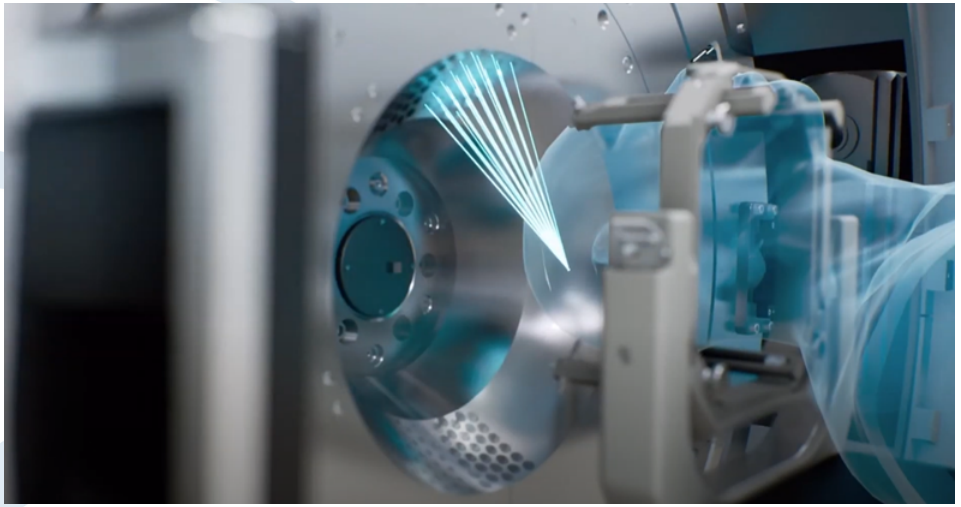
QUESTIONS?

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

ACMUI Comments on the Akesis Galaxy® RTi Draft Licensing Guidance

Harvey B Wolkov, M.D.
Subcommittee Chair

April 8, 2024



Akesis Galaxy® RTi Licensing Guidance Subcommittee

Members:

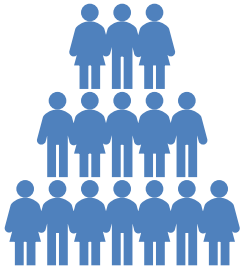
Rebecca Allen, M.S.

Richard Harvey, DrPH.

Zoubir Ouhib, M.S.

Megan Shober, M.S.

Harvey Wolkov, M.D. (Chair)



NRC Staff Resource:

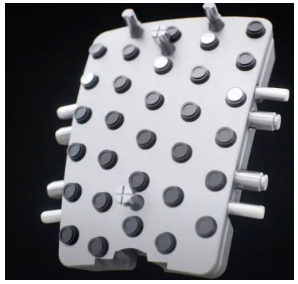
Daniel Shaw

Subcommittee Charge

- Review and comment on the NRC staff's draft Akesis Galaxy® RTi Licensing Guidance

Background

- The Akesis Galaxy RTi is a non-invasive gamma stereotactic radiosurgery (GSR) unit containing 30 Cobalt-60 sources with approximately 6000 curies total initial source activity.



- The unit is paired with an image guidance system (IGS) that uses reference images to move the treatment couch (patient) to the target position for lesion treatment.

Background

- The radiation sources align with the selected secondary collimators of sizes 4, 8, 14 and 18 mm and one blocking position.

- Unlike the Gamma Knife unit, the source and collimating system rotate simultaneously during treatment to form 30 non-overlapping convergent 360 degree arcs.

Background

- All 30 beams are directed towards the target.
- The device has real-time, in-line Cone-beam CT (CBCT) and kV/kV imaging.

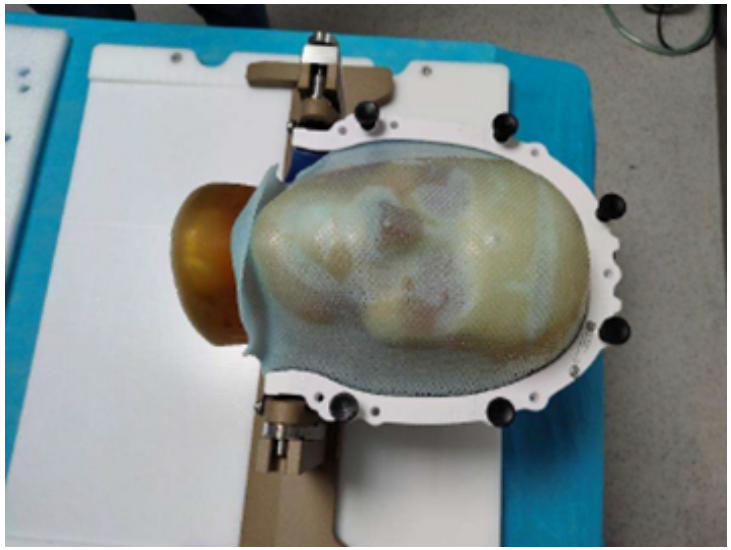
Background

- Prior to treatment, a treatment plan is generated for each patient for adequate dose coverage of the target and sparing of normal structures.

- On the day of treatment, the patient position and target shape are confirmed by co-registration of CT- scans and/or MRI scans.

Background

- Before treatment, the patient is immobilized using a frameless mask or headframe.



Background

- Once the treatment parameters are verified and accepted, the control system automatically executes the planned treatment.

Background

- The first Akesis Galaxy® RTi unit is scheduled to be operational in the U.S. at Case Western Reserve Medical Center in 2024.

- The NRC staff has determined that the Akesis Galaxy® RTi should be regulated under 10 CFR Part 35, Subpart K (10 CFR 35.1000).

Subcommittee Recommendations: Training and Experience

1) Due to similarities between the Akesis Galaxy RTi and the Elekta Gamma Knife (GK), the Subcommittee recommends that the draft guidance be modified to not require attestation for AU's AMP's and RSO's who are qualified for GK.

2)The draft guidance recommends training on the differences between the Akesis Galaxy RTi and GK that must include hands-on device operation, safety procedures, and clinical use.

Subcommittee Recommendations: Training and Experience

3) Training requirements satisfied by completion of training program by vendor or by AU or AMP who is authorized for Akesis Galaxy® RTi use.

Subcommittee Recommendations: Physical Presence Requirement

4) The proposed physical presence requirements are similar to that of HDR brachytherapy and the requirements for both the Leksell Gamma Knife® Perfexion and Icon units.

Subcommittee Recommendations: Physical Presence Requirement

- The draft guidance recommends the AU and AMP be physically present during *initiation* of all treatments.

- The AMP and AU or physician will be physically present during continuation of all patient treatments.

- If treatment is interrupted, the AU will return to the console to evaluate the situation and ensure treatment delivery IAW the treatment plan and written directive prior to re-initiation of treatment.

Acronyms

- AMP – Authorized Medical Physicist
- AU – Authorized User
- CBCT – Cone Beam Computed Tomography
- CFR – Code of Federal Regulations
- HDR – High Dose Rate (Remote Afterloader)
- IAW – In Accordance With
- KV/KV – Kilovolt/Kilovolt
- MRI – Magnetic Resonance Imaging
- NRC – U.S. Nuclear Regulatory Commission
- RSO – Radiation Safety Officer
- SRS – Stereotactic Radiosurgery

U.S. Nuclear Regulatory Commission
Advisory Committee on the Medical Use of Isotopes

Subcommittee Review and Comments on

Akesis Galaxy® RTi Draft Licensing Guidance

Draft Report

Submitted on March 6, 2024

Subcommittee Members:

Rebecca Allen
Richard Harvey PhD
Zoubir Ouhib, MS
Megan Shober, MS
Harvey Wolkov, MD (Chair)

NRC Staff Resource: Daniel Shaw

Background:

The Subcommittee and its Chair were appointed by Advisory Committee on the Medical Uses of Isotopes (ACMUI) Chair, Darlene Metter, on December 8, 2023. The subcommittee charge was to review and comment on the U.S. Nuclear Regulatory Commission (NRC) staff's draft Akesis Galaxy® RTi Licensing Guidance.

Introduction:

The Akesis Galaxy® RTi is a gamma stereotactic radiosurgery (GSR) unit that contains thirty Cobalt-60 sources with approximately 6000 curies (Ci) total initial source activity. The unit is paired with an Image Guidance System (IGS) that uses reference images to move the treatment couch to the correct target position for lesion treatment. During treatment, the radiation sources will be aligned with the user selected secondary collimators. The source and the collimating structures rotate simultaneously during treatment to form thirty non-overlapping convergent 360° gamma ray arcs. All thirty beams are directed towards the target to deliver the desired prescribed dose. The NRC staff has determined that the Akesis Galaxy® RTi is regulated under 10 CFR Part 35, Subpart K, "Other Medical Uses of Byproduct Material or Radiation From Byproduct Material." [10 CFR 35.1000].

Discussion:

The subcommittee reviewed the licensing guidance (LG) and provided the following significant comments.

- Section 1. The committee discussed the determination for why the device was licensed under 35.1000. “As a result…” was removed from the last paragraph of the working draft as it’s misleading to indicate the engineering changes were the driver.

- Section 4.1.1, paragraph 2. The subcommittee decided to remove “preparing treatment plans and calculating treatment doses and times” from the Authorized User (AU) training and experience (T&E) requirements.

- Section 4.1.2, paragraph 2. The subcommittee suggested that the statement “In order to function independently as an Authorized Medical Physicist (AMP), the individual shall have demonstrated familiarity with the treatment using both a stereotactic frame and the patient immobilization system which is a frameless system” be added as an AMP T&E requirement. This statement is consistent with Leksell Gamma Kinfe® Perfexion and Leksell Gamma Kinfe® Icon licensing guidance.

- Section 4.2, paragraph 3. The subcommittee recommended that the statement “The written attestation is not required for individuals who hold certification by a recognized specialty board or are not already authorized for use of another Akesis® model or other gamma stereotactic radiosurgery units licensed under 10 CFR 35.600” be added to the attestation for the Radiation Safety Officer (RSO) to be consistent with Leksell Gamma Kinfe® Perfexion and Leksell Gamma Kinfe® Icon licensing guidance.

- Section 5.2. The Subcommittee asked that the following requirement be added as follows “The spot test and full calibration test, *completed and reviewed per 10 CFR 35.645…”*

The Subcommittee discussed the availability of the Sealed Source and Device (SS&D) certificate. The NRC staff indicated that the SS&D was not yet published by California Department of Public Health (CDPH). CDPH has provided NRC’s Medical Safety and Events Assessment Branch (MSEB) a draft of the SS&D during an October 2023 meeting, but that document cannot be shared with the public. It was further stated that the NRC staff would share the SS&D as soon as it was published.

The Subcommittee also discussed the following coming action items:

- Draft Report for Subcommittee Review and Comments on Draft Akesis Galaxy® RTi

- ACMUI Presentation Report for the Akesis Galaxy® RTi Draft Licensing Guidance

Respectfully submitted on March 6, 2024,
Subcommittee on Akesis Galaxy® RTi Guidance
Advisory Committee on the Medical Uses of Isotopes
Nuclear Regulatory Commission

Akesis Galaxy® RTi Licensing Guidance

November 30, 2023, Revision 0

U.S. Nuclear Regulatory Commission Contact
Daniel Shaw (301) 415-3649; Katie Tapp (301) 415-0236
MedicalQuestions.Resource@nrc.gov

Table of Contents

1. 10 CFR 35.1000 Use

The term Stereotactic radiosurgery is commonly used to indicate the application of radiation beams coming from many directions. The Akesis Galaxy® RTi is a gamma stereotactic radiosurgery (GSR) unit that contains thirty Cobalt-60 sources with approximately 6000 curies (Ci) total initial source activity. The unit is paired with an Image Guidance System (IGS) that uses reference images to move the treatment couch to the correct target position for lesion treatment. During treatment, the radiation sources will be aligned with the user selected secondary collimators. The source and the collimating structures rotate simultaneously during treatment to form thirty non-overlapping convergent 360° gamma ray arcs. Since all thirty beams are directed towards the target, the target will receive a high radiation dose proportional to the total irradiation time. The surrounding normal tissues only receive a transient irradiation. The target spot is sometimes referred to as the "focal-spot" or "focus". The description "focus" describes the concentration of all beams in one intersecting point on the rotational axis but ignores the fact that the radiation beams diverge from the source and cover an extended volume at the intersection point. Before the treatment, the patient (with head frame or mask attached) will be positioned on the treatment couch. Based on the head frame or mask, CT-scans and/or MRI-scans, the target shape and patient position (X, Y, Z coordinates) will be confirmed. After the operator accepts the treatment parameters, the control system automatically executes the planned treatment. No further operator intervention is required during a normal treatment.

Note, Akesis uses the terms focus, focal-spot, target, and target-spot interchangeably for the focal point.

Although the Akesis Galaxy® RTi is a GSR unit, the device includes a number of engineering changes that make the components and operation significantly different from the GSR units currently regulated in 10 CFR Part 35, Subpart H, "Photon Emitting Remote Afterloader Units, Teletherapy Units, and Gamma Stereotactic Radiosurgery Units." These engineering changes include the absence of helmets, relative helmet factors, helmet microswitches, hydraulic backups, trunnions and a trunnion centricity point. In addition, Akesis Galaxy® RTi engineering changes include:

- A beam-collimating system for collimating, focusing and shielding the radiation beams, consisting of a shielding hemisphere, a tungsten-alloy shielding block, 30 rotating radiation sources, a source drawer, and a source carrier.

- A moveable (X, Y, Z) treatment couch that is used with the patient supine during the treatment process that moves the patient to the target position (focal point so that the target in the treatment plan coincides with the focal point of the device.

- As part of the IGS, the Akesis Galaxy® RTi includes the addition of an x-ray tube system mounted onto the unit to take cone beam computed tomography (CBCT) images to obtain patient positioning and verification with use of reference images.

- The Akesis Galaxy® RTi unit can immobilize the patient's head with either a rigid-fixation stereotactic head frame or with a double shell mask positioning system manufactured by MacroMedics. The immobilization of the patient's head is achieved via the headframe interface system that includes a frame-locking interface assembly (U-Frame) and adapter (L-Frame). The U-frame is permanently fixed to the treatment couch and

provides a fixed reference of table position to beam center. When mated to the patient's headframe, the specified positional accuracy of the beam is achieved by precise table movements. Either an independently 510(k) cleared and compatible mask-based or a rigid-fixation head frame must be properly attached to the head frame interface

- The Akesis Galaxy® RTi will use the real-time image-guided radiation therapy (RT-IGRT) system to monitor movements of the patient during setup and treatment while immobilized by the head frame interface.

As a result, the Akesis Galaxy® RTi is regulated under 10 CFR Part 35, Subpart K, "Other Medical Uses of Byproduct Material or Radiation From Byproduct Material." [10 CFR 35.1000]

2. Licensing Guidance

Applicants may refer to NUREG-1556, Volume 9, Revision 3, "Consolidated Guidance About Material Licenses: Program-Specific Guidance About Medical Use Licenses," as it provides overall licensing guidance for all medical uses of byproduct material, including information on how to submit facility's address and description and applicable model procedures for audits, occupational dose monitoring programs, and surveys. Applicants should also refer to https://www.nrc.gov/reading-rm/sensitive-info/materials.html for information regarding submissions of information containing sensitive security-related information, such as information about quantities and locations of radioactive materials at licensed facilities.

This guidance provides applicants with an acceptable means of satisfying the requirements for a license for the use of the Akesis Galaxy® RTi, however, it is not intended to be the only means of satisfying requirements for a license. The applicant must submit the information required by 10 CFR 30.33 and 10 CFR 35.12 as described below. The applicant must submit additional information and commitments requested below or may, unless the information is specifically required by regulation, submit alternative commitments for review by the U.S. Nuclear Regulatory Commission (NRC) staff to determine whether the regulatory requirements are met. The licensee commitments are incorporated into the applicant's license by conditions and will be reviewed during routine inspections. Applicants are reminded that licenses issued pursuant to 10 CFR 35.1000[1] must still meet the general requirements in 10 CFR Part 35, Subparts A, B, C, H, L, M and N, except as specified in this guidance. Additionally, applicants must meet applicable requirements of 10 CFR Parts 19, 20, 30, 37 and 71.

The Akesis Galaxy® RTi makes use of an integrated CBCT imaging system (i.e the IGS) to ensure the patient is properly positioned for and during treatment. The specific license issued by the NRC does not authorize the licensee to possess and use the CBCT imaging system. This authorization must be obtained from the applicable state agency having jurisdiction over computed tomography scanning equipment. The CBCT is not licensed or registered by the NRC. However, because the CBCT is critical to verifying the accuracy of the patient positioning, NRC will require licensees to commit to certain quality assurance (QA) measurements as outlined in the section titled, "Specific Information on Radiation Safety Precautions and Instructions."

[1] Medical uses of byproduct material licensed under 10 CFR 35.1000 are designated as Compatibility Category D. Agreement States are not required to adopt these regulations for purposes of compatibility.

3. General

3.1. Sensitive Security-Related Information

Certain sensitive security-related information such as quantities and locations of radioactive materials at licensed facilities are no longer released to the public. Submission of this type of information in an application should be marked as specified in Regulatory Issue Summary 2005-31, Revision 1, "NRC Regulatory Issue Summary 2005-31, Control of Security Related Sensitive Unclassified Non-Safeguards Information Handled by Individuals, Firms, and Entities Subject to NRC Regulation of the Use of Source, Byproduct, and Special Nuclear Material".

Additional information on procedures handling and marking security-related information and any updates are available at https://www.nrc.gov/reading-rm/sensitive-info.html.

3.2. 10 CFR Part 37

Applicants requesting authorization for the Akesis Galaxy® RTi unit must comply with 10 CFR Part 37 before installing sources for this unit.

Members who have not been granted unescorted access in accordance with 10 CFR Part 37 must be escorted at all times, such as individuals who service the CBCT component or are inspecting (i.e., NRC or Agreement State inspectors) the Akesis Galaxy® RTi must be escorted at all times unless they fall under the relief granted under 10 CFR 37.29. For more information, see NUREG-1556, Volume 9, Revision 3, "Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses;" NUREG-2155, "Implementation Guidance for 10 CFR Part 37, 'Physical Protection of Category 1 and Category 2 Quantities of Radioactive Material;'" and NUREG-2166, "Physical Security Best Practices for the Protection of Risk-Significant Radioactive Material."

3.3. Radionuclides, Form, Possession Limits, and Purpose of Use

Per the requirements of 10 CFR 35.12, the applicant shall identify the radionuclides, chemical/physical form, requested maximum possession limit, and purpose of use. For guidance to meet the requirement, refer to NUREG 1556, Volume 9, Revision 3 "Contents of and Application" additional information. NRC Form 313, "Application for Materials License" may be used to submit this information. For example, the following provides the format for an acceptable request:

Radionuclides NRC Form 313, Section 5.a.)	Cobalt-60
Chemical/Physical Form (NRC Form 313, Section 5.b.)	Sealed sources (Manufacturer and Model Number, e.g., XXXXXXX)
Maximum Possession Limit (NRC Form 313, Section 5.c.)	200 curies per source not to exceed 6000 curies total (or 10000 curies during source exchange)
Authorized Use (NRC Form 313, Section 6)	For 10 CFR 35.1000 medical use in the Akesis Galaxy® RTi gamma stereotactic radiosurgery unit

3.4. Facility Address and Description [10 CFR 30.33(a)(2) and 10 CFR 35.12(b)(1)]

Provide an address of use, submit a facility diagram, and description of the location where the Akesis Galaxy® RTi GSR unit will be used or stored.

4. Training and Experience

4.1. Authorized Individuals [10 CFR 30.33(a)(3); 10 CFR 35.12(b)(1); 35.50; 35.51; and 35.690]

The NRC has determined that individuals meeting the guidance provided below will be considered qualified and authorized for the Akesis Galaxy® RTi GSR unit. Applicants may also submit alternative training and experience commitments to be reviewed on a case-by-case basis by the NRC staff. The alternative information should include an explanation of why the applicant believes the alternative information demonstrates that the individuals are qualified to be authorized individuals.

Because there are minimal Akesis Galaxy RTi units approved for medical use in the United States at the time this licensing guidance was initially published in 2024, there are a limited number of preceptors available to sign attestations. Therefore, the NRC is postponing requiring a written attestation until Month/Day/Year. At that time, attestations will be required for individuals who do not hold certification by a recognized specialty board or are not already authorized for use of other gamma stereotactic radiosurgery units. The NRC will continue to review the availability of preceptors and may revise this guidance if it determines that sufficient preceptors have not become available. In addition, all individuals seeking authorization for use of the Icon™ must submit documentation of successful completion of required training.

4.1.1. Authorized User

Applicants and licensees should identify each authorized user (AU) of the Akesis Galaxy® RTi GSR unit and provide documentation of their training and experience in the use of the unit. The NRC Form 313A (AUS), "Authorized User Training and Experience and Preceptor Attestation (for uses defined under 35.400 and 35.600) [10 CFR 35.490, 35.491, and 35.690]," or other formats may be used to document this training and experience. The physician will be considered qualified for use of the Akesis Galaxy® RTi GSR unit if the individual meets the following:

1) Is listed on a license or permit (NRC, Agreement State, Broad Scope License or NRC Master Materials License) as an AU for 10 CFR 35.600 medical use of a GSR unit; an AU for 10 CFR 35.1000 medical use of the Akesis Galaxy® RTi ; or is board certified by a recognized board listed on the NRC's Web site "Specialty Board Certifications Recognized by NRC Under 10 CFR Part 35" under section 10 CFR 35.690, "Training for use of remote afterloader units, teletherapy units, and gamma stereotactic radiosurgery units," or meets the criteria in 10 CFR 35.690(b)(1) and (2) for GSR unit use;

AND

2) Received documented training in hands-on device operation, safety procedures, and clinical use, which includes headframe or mask fitment, preparing treatment plans and calculating treatment doses and times, for the Akesis Galaxy® RTi GSR unit. If the

individual is already an AU for a GSR unit, in accordance with 10 CFR 35.690(c), this training must also include the differences in the device operation, safety procedures, and clinical use of the Galaxy RTi and the other GSR unit(s) that the individual is authorized to use. This training requirement may be satisfied by satisfactory completion of a training program provided by the Akesis vendor or by receiving training supervised by an AU or authorized medical physicist (AMP), as appropriate, who is authorized for the Akesis Galaxy® RTi use;

AND

3) Obtain a written attestation that the individual has satisfactorily completed the above training and is able to independently fulfill the radiation safety related duties as an AU for the Akesis Galaxy unit. The written attestation must be signed by a preceptor AU who is authorized for the Akesis Galaxy® RTi unit. The written attestation is not required for individuals who hold certification by a recognized specialty board.

4.1.2. Authorized Medical Physicists

Identify each AMP for the Akesis Galaxy® RTi GSR unit and provide documentation of his/her training and experience in the use of the unit. The NRC Form 313A (AMP), "Authorized Medical Physicist Training and Experience and Preceptor Attestation [10 CFR 35.51]," or other formats may be used to document this training and experience. The medical physicist shall be considered qualified for use of the Akesis Galaxy® RTi GSR unit, if the individual meets the following:

1) Is listed on a license or permit (NRC, Agreement State, Broad Scope License or NRC Master Materials License) as an AMP for GSR unit use; or is board certified by a board listed on the NRC's Web site "Specialty Board Certifications Recognized by NRC Under 10 CFR Part 35" under section 10 CFR 35.51, "Training for an Authorized Medical Physicist;" or meets the criteria in 35.51(b)(1) and (2) for gamma stereotactic radiosurgery unit use;

AND

2) Received documented training in hands-on device operation, safety procedures, clinical use, and the operation of a treatment planning system for the Akesis Galaxy® RTi unit. If the individual is already an AMP for a GSR unit, in accordance with 10 CFR 35.51(c), this training must also include the differences in the device operation, safety procedures, clinical use, and the operation of a treatment planning system of the Akesis Galaxy® RTi and other GSR units for which the individual is authorized. This training requirement may be satisfied by satisfactorily completing either a training program provided by the Akesis vendor or by training supervised by an AMP authorized for Akesis Galaxy® RTi use;

AND

3) Obtained a written attestation that the individual has satisfactorily completed the above training and is able to independently fulfill the radiation safety-related duties as an AMP for the Akesis Galaxy® RTi unit. The written attestation must be signed by a preceptor

AMP authorized for the Galaxy RTi unit. The written attestation is not required for individuals who hold certification by a recognized specialty board.

4.2. Radiation Safety Officer

Identify the Radiation Safety Officer (RSO) with responsibility for the Akesis Galaxy® RTi GSR unit and provide documentation of his/her training and experience in radiation safety for the unit. NRC Form 313A (RSO), "Radiation Safety Officer Training and Experience and Preceptor Attestation [10 CFR 35.50]," or other formats may be used to document this training and experience. The NRC recognizes that some applicants with new installations could have an individual who will have RSO responsibilities for the Akesis Galaxy® RTi unit but may not have access to an operational unit at the time of the radiation safety, regulatory issues, and emergency procedures training. For this reason, the applicant may commit that the individual will complete supplemental hands-on radiation safety and emergency procedure training before first patient treatment using the GSR unit. The individual shall be considered qualified to be the RSO for the Akesis Galaxy® RTi GSR unit if the individual meets the following:

1) Is listed as an RSO on an NRC or Agreement State license (or NRC Master Materials License permit) authorizing GSR unit medical use, or is board certified by a board listed on the NRC's Web site "Specialty Board Certifications Recognized by NRC Under 10 CFR Part 35" under section 10 CFR 35.50, "Training for Radiation Safety Officer," or meets the criteria 35.50(b)(1), or 35.50(c)(1) or (2) for GSR unit use;

AND

2) Received documented training in the radiation safety, regulatory issues, and emergency procedures for the Akesis Galaxy® RTi GSR unit. If the individual already has RSO responsibilities for a GSR unit, in accordance with 10 CFR 35.50(e), the training must also include instruction in the differences in the radiation safety, regulatory issues, and emergency procedures of the Akesis Galaxy® RTi unit and other GSR units for which the individual has RSO responsibility. This training requirement may be satisfied by completing training that is provided by the Akesis vendor or supervised by an individual (RSO or AMP or AU) that is authorized for the Galaxy RTi unit. The individual should complete or commit to complete supplemental hands-on radiation safety and emergency procedures training on an operational Akesis unit before first use of the unit for patient treatment;

AND

3) Obtained a written attestation that the individual has satisfactorily completed the above training and is able to independently fulfill the radiation safety-related duties as a RSO for the medical use of the Akesis Galaxy® RTi GSR unit. The written attestation must be signed by a preceptor RSO, AMP, or AU authorized for the Akesis unit. The written attestation is not required for individuals who hold certification by a recognized specialty board.

5. Licensing Commitments

5.1. Written Directive: [10 CFR 35.40]

The Akesis Galaxy® RTi stereotactic radiosurgery unit delivers a therapeutic dose of radiation from byproduct material and under 10 CFR 35.40 requires a written directive. Calculation of the dose to the treatment site is dependent on the shaping of the radiation field at the focal point by selection of different collimators. Therefore, to assure the dose is delivered in accordance with the AU's direction, the written directive should include the collimator specifications, the treatment plan of the single shot or the multi-shot irradiation according to the position and coordinates of the target. The applicant should provide the following commitment:

> "For the Akesis Galaxy® RTi GSR unit use, the written directive will contain the patient or human research subject's name; the total dose; the treatment site; dose per fraction; number of fractions; and the X, Y, Z target coordinate values; gamma angle; beam rotation start and stop angle and collimator size for each treatment shot within an anatomically distinct treatment site."

When a written directive is needed, licensees are required under 10 CFR 35.41(a)(2) to have procedures that provide high confidence that each administration is in accordance with the written directive. Under 10 CFR 35.41(b)(4) these procedures are required to address, among other things, verification that any computer-generated dose calculations are correctly transferred into the control system of GSR units authorized by 10 CFR 35.600. This verification is also applicable to GSR units regulated under 10 CFR 35.1000. For the Akesis Galaxy® RTi GSR unit, the computer-generated dose calculations for each shot (i.e., each set of target coordinates) should also include the collimator settings for that shot. For this reason, the applicant should provide the following commitment:

> "For the Akesis Galaxy® RTi GSR unit, procedures that provide high confidence that each administration is in accordance with the written directive will address verification that any computer-generated dose calculations are correctly transferred into the Akesis Galaxy® RTi control system."

A number of medical events with earlier models of GSR units resulted from movement of the head frame or head frame pins during coughing and other patient movement. As part of its program to provide high confidence that the administration is in accordance with the written directive, the applicant should develop written procedures for the following: (1) pausing treatment and checking the patient set-up if a patient is observed to move during the course of a treatment shot and (2) visually checking the patient set up each time the gamma angle is changed or at the end of the treatment run, whichever comes first.

The applicant should confirm the following for the Akesis Galaxy® RTi:

> "In order to provide high confidence that the administration is in accordance with the written directive our program will include written procedures for: (1) verification of the integrity of the fixation before starting the treatment (2) pausing treatment and checking the patient set-up if a patient is observed to move during the course of a treatment and every time the real-time image-guided radiation therapy (RT-IGRT) system pauses the system due to patient movement outside the set limit and (3) visually checking the patient set up each time the gamma angle is changed or at the end of the treatment run, whichever comes first."

5.2. Specific Information on Radiation Safety Precautions and Instructions: [10 CFR 35.12(d)(3)(i)]

The applicant must submit the information required by 10 CFR 35.12(d). Because the Akesis Galaxy® RTi unit is a GSR unit, the applicant may simplify its submission by confirming the following:

> "For use of the Akesis Galaxy® RTi , we will meet the following requirements for a GSR unit in 10 CFR Part 35, Subpart H:
>
> Section 35.600,
>
> Section 35.605 (and retain records of the information described in Section 35.2605 for 3 years),
>
> Section 35.610 (and retain procedures described in Sections 35.610(a)(4) and (d)(2) for the retention period stated in Section 35.2610, and retain instructions described in 35.610(d) for the retention period stated in Section 35.2310.
>
> Section 35.615 (a) through (d), 35.615(f)(4), and 35.615(g)
>
> Section 35.615(f)(3) (with the modifications listed below),
>
> Section 35.630 (and retain a copy of the information described in Section 35.2630 for the duration of the license),
>
> Section 35.635 (with modifications discussed below and retain a copy of the information described in Section 35.2632 with modifications discussed below for the retention period of 3 years),
>
> Section 35.645 (with modifications discussed below and retain a copy of the information described in Section 35.2645 with modifications discussed below for 3 years),
>
> Section 35.655, (and retain records of the inspection as described in Section 35.2655)
>
> Section 35.657,
>
> Section 35.690.

Unlike earlier GSR units licensed under 10 CFR 35.600, the sources in the Akesis Galaxy® RTi unit are in a movable source drawer. Therefore, radiation surveys required in 10 CFR 35.652(b) will be required following any repairs to the source driving unit or to other electronic or mechanical component that could expose the source, reduce the shielding around the sources, or compromise the radiation safety of the unit or the sources. The driving unit includes a motor and gearbox for the outer, primary collimator (source carrier), a motor and gearbox for the inner, secondary collimator, feedback encoders for both, secondary feedback encoders, a position indicator, tensioners, timing belts, and two electromagnetic clutch brakes. The system determines the relative position of the sec-ondary collimator and the source carrier through the position information feedback from the motor en-coders. The system compares the information

from the motor encoders to determine whether the rotating hemispheres' relative position is consistent with the treatment plan and to trigger an interlock should an inconsistency occur. The tensioners are designed to adjust the tension of the timing belts. The manufacturer states that the timing belts must be replaced annually by Akesis service personnel.

The spot test and full calibration test should include assessing whether the patient docking systems function correctly to place the mechanical center) of the stereotactic frame at the radiation focal point, to know the size of the radiation focal point by confirming the collimator sizes, and to test the precision with which the treatment site could be placed at the radiation focal-spot and the accuracy of the dose calculations. New tests should be performed as part of the revised spot test and full calibration test to assess these basic properties for the Akesis Galaxy® RTi unit.

Some of the measurements in 10 CFR 35.635 and 35.645 cannot be performed and the results of such determinations and tests cannot be recorded as described in 10 CFR 35.2632 or 35.2645 because the components specified in those regulatory provisions do not exist in the Akesis Galaxy® RTi unit. For example, for treatment with the Akesis Galaxy® RTi unit, the patient's head is either immobilized with the aid of a stereotactic head frame or with the aid of a double shell mask that is uniquely shaped to each patient. Regardless of the method of immobilization, the patient's head is attached in an "immovable" position to the treatment couch, and the treatment couch itself is moved (X, Y, and Z directions) over small distances to center the treatment site at the radiation focal-spot.

The individual removable collimator helmets in earlier GSR units have been replaced by four permanently installed independently rotating collimators in the Galaxy RTi unit. The sources, housed in a source drawer, and the collimating structures rotate simultaneously during treatment to form thirty non-overlapping convergent 360° gamma ray arcs. The collimator system contains four different sets of fixed collimator apertures (4 mm, 8 mm, 14 mm, and 18 mm) as well as shielded position (Beam-off). The collimator aperture is set so that the focal point remains constant independent of the collimator used. Therefore, the location and function of the collimators, the patient bed, the docking device, the frame adapter, the mask adapter, and the source exposure indicator light on the device are critical to the safe use and proper functioning of the Akesis unit and should be tested as part of the spot-checks (referred to as QA checks in the operator's manual) and full calibration test. Also, the condition and function of the clearance test tool and QA test tool are critical to determine the location of the radiation focal point, table location, and frame adapter function. For Akesis unit, the verification of the accuracy of the patient positioning with the CBCT is critical and therefore the QA measurements described in the vendor-supplied Instructions for Use shall be performed exactly as stated.

The Akesis Galaxy® RTi will use the real-time image-guided system (IGS) to monitor movements of the patient during setup and treatment while immobilized by the mask. The imaging focus of IGS coincides with the focal-spot of the treatment device. The equipped IGS can register the acquired images with the reference images in the treatment plan and send the position deviation to the Recording and Verification System (RVS). According to the position deviation sent by IGS, the control system moves the treatment couch to the correct target position, and then treatment can be performed. The RVS will pause the patient treatment in the event that the treatment couch position is out of tolerance during the irradiation process by ±0.5 mm in X, Y, and Z directions.

The applicant should confirm the following for the Akesis Galaxy:

"We will follow the survey requirements of 10 CFR 35.652 and make the surveys at installation of a new source and following repairs to the driving unit or other electronic or mechanical component that could expose the source, reduce the shielding around the sources, or compromise the radiation safety of the unit or the sources. The driving unit includes a motor and gearbox for collimating structure, a motor and gearbox for the source carrier, position indicating device, a tensioner, and two clutch brakes. The two driving devices are used to drive the collimating structure and source carrier, respectively. We will retain information described in Section 35.2652 for the period stated in Section 35.2652."

"We will follow the applicable full calibration requirements of 10 CFR 35.635 and the spot-check requirements in 10 CFR 35.645 and retain the information described in 10 CFR 35.2632 for each full calibration and 10 CFR 35.2645 for each check except for those involving helmets, helmet factors, helmet micro-switches, trunnions, and hydraulic backup of the treatment table retraction system. We will keep each record of the full calibration and spot-checks for 3 years."

"Before the first use of the Akesis Galaxy® RTi unit each day, we will confirm that the docking device is securely mounted to the treatment couch (table) and that the frame adapter can be correctly docked in the docking device. This test and the description of the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"Before each patient use, the patient is immobilized with the stereotactic U-frame, we will confirm that the L-frame adapter is functioning correctly and can be attached correctly to the coordinate frame. This test and the description of the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"On a monthly basis, we will confirm that the location of the radiation focal point (isocenter accuracy), with respect to the treatment couch position, is within the specifications provided by the manufacturer. This test and the description of the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"On a monthly basis, we will confirm that the location of the treatment couch at a number of off-center positions is within the collision specifications provided by the manufacturer. This test and the description of the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"Approximately every six months (with exact date subject to vendor service availability), we will confirm that the beam collimating system is within appropriate tolerance limits. This test and the description of the record of the test will be included in the spot-check

procedures. The test will also be performed during the full calibration measurements of the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"During installation and approximately every six months (with exact date subject to vendor service availability, i.e., planned maintenance), we will confirm that the vendor will verify that the location of the radiation focal point, with respect to the treatment couch, is within the specifications using measurements conducted in an off-centered position. This test and the description of the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"We confirm that if the frame adapter or mask adapter fails to perform as designed, we will remove it from service until repaired."

"We confirm that if the source carrier or treatment couch positioning fail to perform as designed, we will lock the control console in the off position and not use the unit except as necessary to repair, replace, or check the malfunctioning system."

"We confirm that removal or major repair of the components associated with the source carrier and collimator assemblies will be considered a major repair of the source assembly and will require full calibration."

"Before the first use of the Akesis unit each day, when using the CBCT system during patient setup, we will confirm that the precision of the CBCT system is within the specifications provided by the manufacturer. This test and the description of the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of the Akesis unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"Before each patient use, and when the patient is immobilized with a mask, we will confirm that the mask fits the patient's head, the mask adapter is functioning correctly and can be attached correctly to the docking device. This test and the description of the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of the Akesis unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"Before each patient use of the Akesis Galaxy® RTi unit, we will confirm that the IGS is working properly. This is done by verifying that a IGS starts real-time image guidance through use of the Akesis provided phantom. The test will also be performed during the full calibration measurements of the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"On a monthly basis, we will confirm that the CBCT image quality is satisfactory. The description of the test and the record of the test will be included in the spot-check procedures. The test will also be performed during the full calibration measurements of

the Akesis Galaxy® RTi unit. We will keep each record of the results of this test performed during the full calibration measurement and spot-check for 3 years."

"We confirm that if the CBCT-system and/or the IGS system fails to function as specified by the manufacturer, we will have the system(s) repaired or replaced before the next patient treatment requiring the proper function of these system."

"Every year, we will have the timing belt replaced by Akesis service personnel."

5.3. Physical Presence Required by 35.615(f)(3)

As stated in 10 CFR 35.615(f)(3), an AU and an AMP are required to be physically present throughout all patient treatments involving GSR units. However, unlike the Leksell Gamma Knife® models, the Akesis Galaxy® RTi unit has additional safety functions and utilizes a completely automated treatment system to deliver dose to the patient. Internal collimation alleviates the need to change collimator helmets and patients are positioned as required by the treatment plan by moving the treatment couch. The CBCT and IGS ensure the patient is properly positioned prior to treatment and any movement during treatment causes the sources to move to the "blocked" position. An auto dry-run test is accomplished prior to patient treatments. The Akesis Galaxy® RTi has twenty-two (22) independent interlocks to ensure patient safety during the treatment. These interlocks ensure the room is safe, the patient is in the proper position and secure, and that the beam and collimators are in position and indicated per TPS. As such, the physical presence of the AU throughout all patient treatments required by 10 CFR 35.615(f)(3) for other types of GSR units is unnecessary for the Akesis Galaxy® RTi unit, provided an AMP and a physician, under the supervision of an AU, are present throughout the duration of all treatments.

Therefore, Akesis Galaxy® RTi unit licensees should confirm they are meeting the requirements in 10 CFR 35.615(f)(3) or the following:

1) An authorized user and an authorized medical physicist will be physically present during the initiation of all patient treatments involving the Akesis Galaxy® RTi unit;

2) An authorized medical physicist and either an authorized user or a physician, under the supervision of an authorized user, who has been trained in the operation and emergency response for the unit, will be physically present during continuation of all patient treatments involving the Akesis Galaxy® RTi unit; and

3) An authorized user will return to the Akesis unit console if there is an interruption of treatment to evaluate the patient, to review any information related to an abnormal situation, and to ensure that the treatment is being delivered in accordance with the treatment plan and written directive prior to re-initiation of the treatment.

5.4. Procedures required by 10 CFR 35.610 and 35.645 [10 CFR 30.33(a)(3) and 10 CFR 35.12(b)(2)]

The applicant is required by 10 CFR 35.12(b)(2) to provide the procedures in 10 CFR 35.610, 35.642, 35.643, and 35.645, as applicable. For the Akesis Galaxy® RTi radiation safety program only the procedures in 10 CFR 35.610 and 35.645 are appropriate.

The Akesis Galaxy RTi unit does not have helmet microswitches or trunnion centricity. Therefore, the applicant will not be required to provide spot-check procedures for those particular components. However, the applicant should provide additional daily spot-check procedures for proper operation of the frame adapter or mask adapter docking device, additional monthly spot-check procedures for the location of the radiation focal point with respect to the treatment couch position, and collision table location, and a six month spot-check procedure (with exact date subject to vendor service availability) for verification of correct sector movement and location.

The applicant must provide a copy of:

- Safety procedures and instruction for the Akesis Galaxy® RTi unit and
- Spot-check procedures for unit.

5.5. Published Protocols Accepted by Nationally Recognized Bodies

Full calibration measurement procedures for GSR units are required by 10 CFR 35.635(d) to be performed in accordance with published protocols accepted by nationally recognized bodies. However, the Akesis Galaxy® RTi unit contains components and features that are not addressed in the full calibration procedures accepted and published by nationally recognized bodies. In this case, the applicant may use procedures developed by the manufacturer.

The applicant should confirm the following:

> "We will perform full calibration measurement procedures in accordance with published protocols accepted by nationally recognized bodies, except when nationally recognized bodies have not published required full calibration procedures for components and features of the Akesis Galaxy® RTi unit. In the absence of published protocols for the Akesis Galaxy® RTi unit accepted by nationally recognized bodies, we will use procedures developed by the manufacturer."

5.6. Full Inspection and Service of the Akesis Galaxy® RTi Unit [10 CFR 35.655]

The NRC requires the full inspection and servicing of GSR units to assure proper functioning of the source exposure mechanism and other safety components. While a number of systems external to the radiation vault can be inspected and serviced prior to source replacement, areas inside the vault can only be inspected and serviced in the absence of the sources. Therefore, the full inspection and service of the Akesis Galaxy® RTi unit can only be performed at source exchange.

The applicant should confirm the following:

> "We will commit to have each Akesis Galaxy® RTi GSR unit fully inspected and serviced during source replacement to assure proper functioning of the source exposure mechanism and other safety components. The interval between each full-inspection servicing shall not exceed 7 years for each unit."
>
> This inspection and servicing will only be performed by persons specifically licensed to do so by the Commission or an Agreement State.

We will retain records of the information described in Section 10 CFR 35.2655 for the duration of use of the unit."

6. Notes to Licensees

6.1. Alterations to the Akesis Galaxy® RTi

This licensing guidance is based on the sealed source and device (SS&D) safety evaluation in registration certificate XX-XXXX-X-XXX-X. Modification of the sources, the device (including the CBCT approved in the SS&D certificate), or the source-device combination, will require an amended SS&D certificate (or safety evaluation by the broad scope medical use licensee) that addresses the conditions of use and safety of the modified Akesis unit.

6.2. Changes in Physical Conditions of Use

If the physical conditions of use exceed those reported in the SS&D certificate, the limited specific medical use licensee should request an amendment for the new conditions, and a broad scope licensee should perform its own engineering and radiation safety evaluation addressing those differences.

6.3. Notification for AUs and AMPs

The NRC recognizes that if an AU or AMP satisfies the training and experience listed in the NRC's licensing guidance for the Akesis Galaxy® RTi unit and is currently listed on a Commission or Agreement State medical use license or permit for the GSR unit, the AU or AMP should be allowed to work under a different license for the medical use of the Akesis Galaxy® RTi unit. A limited specific medical use applicant initially applying for authorization for the medical use of the Akesis Galaxy® RTi unit or an existing licensee applying for an amendment may request authorization to notify the NRC in the future that it has permitted an AU to work at its facility without the need to request an additional license amendment, provided the following conditions are met:

1) The AU or AMP meets the training and experience criteria listed in NRC's licensing guidance for the Akesis Galaxy® RTi unit; and

2) The AU or AMP is currently listed for the Akesis Galaxy® RTi unit use on a Commission or Agreement State license, a permit issued by a Commission master material license, a permit issued by a Commission or Agreement State licensee of a broad scope, or a permit issued by a Commission master material license broad scope permittee; and

3) The licensee provides NRC a copy of the license or permit on which the AU or AMP was originally listed for the Akesis Galaxy® RTi unit; and

4) The licensee provides documentation to NRC for each AU or AMP of the above listed conditions no later than 30 days after the date that the licensee allows the AU or AMP to work as an AU or AMP for the Akesis Galaxy® RTi unit.

If this authorization is approved, these notification conditions will be incorporated as license conditions in the licensee's license.

6.4. Grandfathering

If a licensee adopts this revision of the Akesis Galaxy® RTi training and experience criteria, AUs, AMPs, or RSOs who are currently authorized for the medical use of the Galaxy RTi under previous criteria do not have to meet the revised criteria for the device.

6.5. Revisions to Existing Akesis Galaxy® RTi Radiation Safety Programs to Conform to Future Changes in Licensing Guidance and Additional Safety Recommendations from the Manufacturer

Requesting authorization in accordance with this guidance will permit a licensee to make certain changes under 10 CFR 35.26, "Radiation protection program changes," to the Akesis Galaxy® RTi GSR unit safety program that might otherwise require a license amendment.

This licensing guidance and safety recommendations from the manufacturer may be revised as the regulator and manufacturer gain additional experience regarding medical use of the Akesis Galaxy® RTi GSR unit. Therefore, in contrast to 10 CFR 35.26, a licensee already authorized to use the Akesis Galaxy® RTi GSR unit and committed by license condition to follow the provisions in this guidance and the operators' manual existing at the time of commitment must apply for and receive an amendment to its license prior to making changes to conform to the revised guidance and additional radiation safety recommendations.

An applicant initially applying for authorization for medical use of the Akesis Galaxy® RTi GSR unit (or a licensee applying for an amendment to conform with this revision of the guidance) may request authorization to allow future changes to its radiation safety program, provided the following conditions are met:

1. The revision is in compliance with the regulations of the NRC or Agreement State;

2. The revision is based upon NRC's current guidance for the Akesis Galaxy® RTi GSR unit medical use under 35.1000 use posted on the NRC web site or the current operators' manual and additional safety recommendations from the manufacturer;

3. The revision has been reviewed and approved by the licensee's RSO and management; and

4. The affected individuals are instructed on the revised program before the change is implemented; and

5. The licensee will retain a record of each change for 5 years; and

6. The record will include a copy of the appropriate licensing guidance, the old procedure, the new procedure, the effective date of the change, and the signature of the licensee's management representative who reviewed and approved the change.

If the NRC approves this authorization, these conditions will be incorporated as license conditions in the licensee's license. This may be done by incorporating the commitments in the tie down condition.

7. Note to Regulators

7.1. Inspection Frequency

Licenses authorizing Akesis Galaxy® RTi units should be inspected every two years. Per Enclosure 1 to Inspection Manual Chapter 2800, licenses authorizing emerging technology in 10 CFR 35.1000 are assigned a Priority 2 inspection code.

7.2. Program Code

The NRC regions should use program code 02240.

8. Paperwork Reduction Act Statement

The information collections contained in this guidance are covered by the requirements of 10 CFR Parts 30, 32 and 35, which were approved by the Office of Management and Budget (OMB), approval numbers 3150-0017, 3150-0001, and 3150-0010, as well as, 3150- 0120 for filling out the NRC Form 313.

9. Public Protection Notification

The NRC may not conduct or sponsor, and a person is not required to respond to, a request for information or an information collection requirement, unless the requesting document displays a currently valid OMB control number.

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Protecting People and the Environment

A Review of Prescription Error Reduction Methods

Richard L. Green

Advisory Committee on the Medical Uses of Isotopes

April 8, 2024

Background

- The impetus for this presentation was an event that occurred 7 Dec 2022 NMED item # 220531
  - "…reported that two radiopharmaceutical misadministrations occurred … scheduled two patients who were each to receive 7.4 GBq (200 mCi) of Lu-177."
  - "One patient was to receive Lutathera (Lu-177 dototate) and the other patient was to receive Pluvicto (Lu-177 vipivotide tetraxetan). The Lutathera patient was mistakenly administered the Pluvicto and the Pluvicto patient was mistakenly administered the Lutathera."

What Contributed to the Error?

- “mistakenly administered”
- “complacency”
- “may have treated the tasks of the day, such as opening packages, as mundane and could have not been paying attention to the circumstances”
- “training/awareness”

What Contributed to the Error?

- recentness of handling
- “shipping practices”
- “package labeling and coloring”
- “identical dosages for both patients”

Corrective Actions Taken

- “implementing a new scheduling process so that Lutathera patients and Pluvicto patients are not scheduled on the same day”
- “dual verification process where the authorized user must verify the correctness of the radiopharmaceutical”

Corrective Actions Taken

- “re-education on proper procedures”
- “verify each patient’s identity using at least two methods of verification prior to administration”

A Deeper Look at Medication Errors

Since the publication of the Institute of Medicine report *To Err Is Human*, health systems have adopted technology and information systems to improve the medication use process and reduce errors.

*1

Rights!

The “five rights” of Medication Administration:

- the right patient
- the right drug
- the right dose
- the right route
- the right time

*2

Medication Use Phases

1. Prescription Phase

Provider chooses correct medication and dose based on diagnosis, patient characteristics, other medications, allergies, etc.

2. Transcription Phase

Medication is recorded in medication administration record. This information is transferred to the pharmacy.

3. Dispensing Phase

The pharmacy staff retrieve the correct medication, which is transported to the patient's floor.

4. Administration Phase

The medication is administered to the patient.

5. Monitoring Phase

Some drugs, such as heparin, require further monitoring.

*3

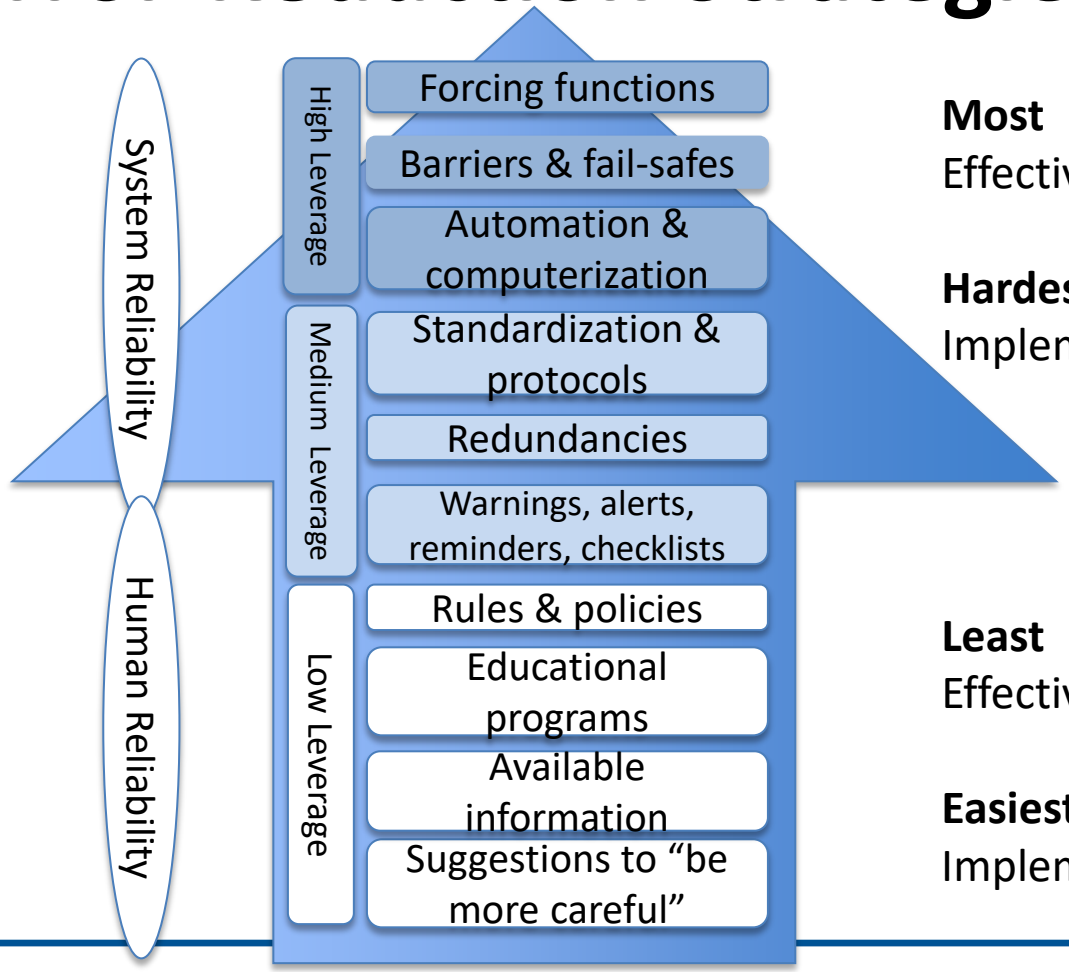
Fixes?

- Color Coding (CC)
- Scheduling of patients
- Limiting procedures performed
- Label design
- Time-outs

Solutions

- CPOE - computerized prescription order entry
- IVWMS- IV Workflow Management Systems
- eMAR - electronic medication administration records
- BCMA - barcode medication administration

ISMP Hierarchy of Error-Reduction Strategies



*4

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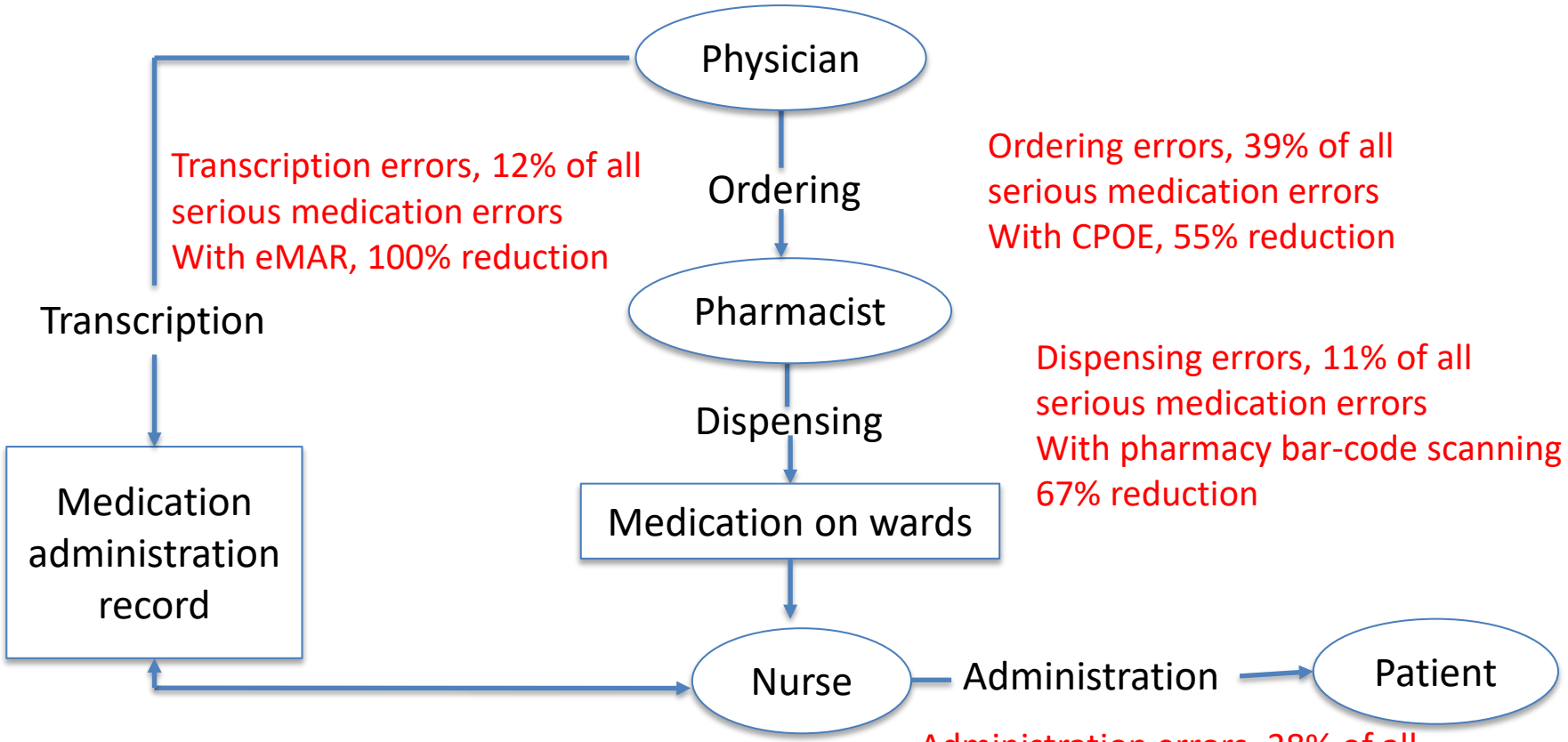
Effect of HIT at Key Stages in the Process of Medication Use



*5

Results of ADE Reducing HIT

- eMAR –
  - 41.4% reduction in non-timing administration errors
- BCMA –
  - 57.4% reduction in wrong medication errors
  - 41.9% reduction in wrong dose errors
  - 80.3% reduction in administration documentation errors

HIT NM Depts Can Use to Reduce ADEs

- CPOE
- IVWMS
- BCMA
- eMAR

Citations

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3. Truitt E, Thompson R, et al, *Effect of the Implementation of Barcode Technology and an Electronic Medication Administration Record on Adverse Drug Events*, Hosp Pharm 2016;51(6):474–483
4. Pharmacy Practice News Special Edition Dec 2023, *January through December 2022 Medication Errors: The Year in Review*
5. Poon E, Keohane C, et al, *Effect of Bar-Code Technology on the Safety of Medication Administration*, N Engl J Med, 2010; 362:1698-707
6. Bonkowski J, Carnes C, et al, *Effect of Barcode-assisted Medication Administration on Emergency Department Medication Errors*, Academic Emergency Medicine 2013; 20:801-806
7. Filiatrault P, Hyland S, *Point Counterpoint – Does Colour-Coded Labeling Reduce the Risk of Medication Error?*, CJHP, Vol 62, No. 2 March, April 2009
8. *A Spectrum of Problems with Using Color*, Institute for Safe Medication Practices, Nov 13, 2023
9. McDaniel P, *Color Me Wrong – Medication Errors and Color Coding*, American Journal of Nursing, Feb 19, 2010
10. Lesar T, *IV Product Labeling: Practices to Improve Patient Safety*, Pharmacy Purchasing & Products, Jan 2008

Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- ADE – adverse drug event
- ADAMS – Agencywide Documents Access and Management System
- ANP – authorized nuclear pharmacist
- AU – authorized user
- BCMA – barcode medication administration
- CC – color coding
- CFR – Code of Federal Regulations

Acronyms (cont'd.)

- CPOE – computerized prescription order entry
- eMAR – electronic medication administration record
- FMEA – failure mode effects analysis
- HIT – health information technology
- ISMP – Institute for Safe Medication Practices
- IVWMS – IV workflow management system
- NM – nuclear medicine
- NRC – U.S. Nuclear Regulatory Commission
- SNMMI – Society of Nuclear Medicine and Molecular Imaging

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Comments on "Yttrium-90 Microsphere Brachytherapy Sources and Devices Eye90 Microspheres® Licensing Guidance"

Michael R. Folkert, MD PhD

Advisory Committee on the Medical Uses of Isotopes

April 8, 2024

Subcommittee Membership

- Michael Folkert, MD PhD (Chair)
- Rebecca Allen, MS
- Andrew Einstein, MD PhD
- Darlene Metter, MD
- Zoubir Ouhib, MS
- Consultant to Subcommittee: John Angle, MD
- NRC Staff Resource: Sarah Spence, CHP

Charge

- On November 3rd, 2023, the ACMUI Chairman, Dr. Darlene Metter, charged the Eye90 Y-90 Microsphere Subcommittee to review and comment on the NRC staff's draft licensing guidance for the ABK Biomedical, Inc. Eye90 microspheres® manual brachytherapy device for hepatocellular carcinoma.

Background

- The liver is a target site for both primary and metastatic cancers.
- Transarterial radioembolization is a technique that takes advantage of tortuous tumor vasculature to concentrate permanent implantable microspheres, delivering localized radiation to treat disease.
- Eye90 Microspheres® are radiopaque glass yttrium-90 microspheres that can be directly imaged fluoroscopically during the procedure and using any x-ray imaging modality post-procedure.

- The NRC determined that Eye90 Microspheres® will be licensed under 10 CFR 35.1000, similar to other yttrium-90 microsphere brachytherapy devices.

Recommendations

- The subcommittee agrees that the Eye90 microspheres® product needs to be licensed under 10 CFR 35.1000, similar to other yttrium-90 microsphere brachytherapy devices.

- The guidance reviewed is substantially similar to that previously issued for other Yttrium-90 microsphere therapy devices (TheraSpheres and SIR-Spheres): “Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance” (ML21089A364), which is appropriate due to the similarity of these devices, their indications and the technical approaches used in administration.

Questions - Training

- As the Eye90 microspheres® product is a new device approved by the FDA under an IDE for clinical trial use, there are a limited number of AUs available to provide training.
  - Should there be unique requirements for training in this situation?

Recommendations

- The Subcommittee recommended that in person training is necessary for initial qualification for the Eye90 microspheres® product for unsupervised use.
  - This training must be hands on and conducted in the physical presence of an AU who is authorized for the Eye90 microspheres® product. At least 3 cases must be performed in the presence of the AU.
  - The AU may be provided by the vendor for training purposes.

Questions - Documentation

- The Subcommittee noted that the use of dose and activity should be consistent in the WD and in subsequent documentation.

Recommendations

- If ”dose” is used, reported dose should indicate absorbed dose to the treatment site(s) and/or to dose limiting structures/organs.
- Nomenclature should be consistent in this, and other licensing guidance provided by the NRC/ACMUI.

Other Questions or Comments?

Abbreviations

- 10 CRF: Title 10 of the *Code of Federal Regulations*
- Y-90: Yttrium-90
- FDA: Food and Drug Administration
- IDE: Investigational device exemption
- AU: Authorized user
- mCi: Millicurie
- GBq: Gigabecquerel
- Gy: Gray
- Sv: Sievert
- SSD: Sealed source and device
- WD: Written directive

U.S. Nuclear Regulatory Commission (NRC)
Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Subcommittee Review and Comments on

Draft Licensing Guidance for Yttrium-90 Microsphere Brachytherapy Eye90 Microspheres Device

Draft Report
Submitted: March 16, 2024

Subcommittee Members:

Michael Folkert, MD PhD (chair)
Rebecca Allen, MS
Andrew Einstein, MD PhD
Darlene Metter, MD
Zoubir Ouhib, MS

Consultant to Subcommittee: John Angle, MD
NRC Staff Resource: Sarah Spence, CHP

Charge

On November 3rd, 2023, the ACMUI Chair, Dr. Darlene Metter, charged the Eye90 Y-90 Microsphere Subcommittee to review and comment on the NRC staff's draft licensing guidance for the ABK Biomedical, Inc. Eye90 microspheres® manual brachytherapy device for hepatocellular carcinoma.

Background

The liver is a common site for malignant involvement, including primary cancers such as hepatocellular carcinoma and cholangiocarcinoma, and secondary cancers metastasizing from other organs such as the colon and rectum, pancreas, small intestine, and breast. Transarterial radioembolization is an interventional technique used to treat hepatic sites of disease with permanent implantable radiopaque glass Y-90 microspheres. The microspheres are delivered to tumor vasculature via an intra-arterial catheter placed under fluoroscopic guidance, usually by an interventional radiologist.

A new yttrium-90 microsphere brachytherapy device called Eye90 microspheres® has recently been approved by the Food and Drug Administration (FDA) under an Investigational Device Exemption (IDE) for use in a clinical trial. It uses a proprietary delivery system comprised of a sterile, single-use delivery device and a re-useable, nonsterile system container. This product is unique to the existing FDA-approved yttrium-90 microsphere products at the time of publication, due to the radiopaque quality of the microspheres. The authorized user (AU) may choose to use fluoroscopy to directly image the radiopaque microspheres in the tumor vasculature during administration and via any x-ray imaging modality thereafter.

The NRC staff have determined that this product needs to be licensed under 10 CFR 35.1000, similar to other yttrium-90 microsphere brachytherapy devices. The NRC staff developed the draft licensing guidance to support future licensing, adapted from the existing guidance for other microsphere brachytherapy, "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance" (ML21089A364) revised in April 2021.

General Comments:

1. The subcommittee agrees that the Eye90 microspheres® product needs to be licensed under 10 CFR 35.1000, similar to other yttrium-90 microsphere brachytherapy devices.
2. The guidance reviewed is substantially similar to that previously issued for other Yttrium-90 microsphere therapy devices (TheraSpheres and SIR-Spheres): "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance" (ML21089A364), which is appropriate due to the similarity of these devices, their indications and the technical approaches used in administration.
3. Use of the term "dose" alone may be ambiguous. In this and other therapeutic application guidance from the NRC, should be consistent in terms of the dose definition used, specified target and organs at risk, and units. Likewise, use of "dose equivalent" vs "equivalent dose" in reporting of medical events/exposures.

Specific Comments:

1. Background section, 2nd paragraph: add "Following angiographic pre-therapy evaluation for extrahepatic shunting,"
2. Training and experience, section 5.1.A.3.ii.b: add "and" to note that in addition to the experience and classroom/laboratory training requirement, the relevant supervised work experience is also required.
3. Training and experience, section 5.1.B: change "should" to "must" as the consensus of the group is that there must be hands on training in the Eye90 microspheres® product by an AU, vendor training alone would be insufficient.
4. Training and experience, section 5.1.B: note that the hands-on cases are "conducted in the physical presence of an AU".
5. Training and experience, section 5.1.B: change "above, including case work" to "at the beginning of this section" to reduce redundancy.
6. Training and experience, section 5.1.C: include "fellowship" as an addition/alternative to residency training throughout.
7. Team approach, section 5.4: add "ordering" to the participating individuals to whom training must be provided.
8. Written directives, section 6.2 written directive condition: removed "or manufacturer" as the Eye90 microspheres® product could change ownership.
9. Written directives, section 6.2: for clarity, in the written directive, "prescribed activity (mCi or GBq) means the total activity administered whereas "prescribed dose" means the total planned dose (rad or Gy). The choice of prescribed activity or prescribed dose should be used consistently for all subsequent documentation and evaluations."
10. Written directives, section 6.2: Reported dose should indicate absorbed dose to the treatment site (liver, liver lobe, liver segment, or liver lesion) or to the dose limiting structure (liver absorbed dose or lung absorbed dose).

11. Medical event reporting, Section 6.3: “0.5 Sv (50 rem) dose equivalent to an organ or tissue per 10 CFR 35.3045”; use of “dose equivalent” vs “equivalent dose” uniformity throughout NRC guidance recommended. Added “equivalent” to dose to skin/organ/tissue.
12. Surveys, section 6.8: changed to “As the Eye90 microspheres® are too small to be seen, licensees should survey, with an appropriate calibrated radiation detection survey instrument (per 10 CFR 35.61),”.
13. Section 7.4: changed heading to “Explanted Tissues, Autopsy and Cremation“ and added language about management of explanted tissues as patients may undergo removal of the treated liver as part of a liver transplant: “However, when managing explanted tissues treated with Eye90 microspheres, or in the case of autopsy or cremation, a radiation hazard exists for individuals who handle tissues that may contain radioactive material, especially if the event of explantation or death occurs within 1 month after treatment with Eye90 microspheres®.” One month was specified as this would allow sufficient decay of an yttrium-90 source.

Respectfully submitted on March 16, 2024,

Subcommittee on “Draft Licensing Guidance for Yttrium-90 Microsphere Brachytherapy Eye90 Microspheres Device”
Advisory Committee on the Medical Use of Isotopes
U.S. Nuclear Regulatory Commission

DRAFT FOR ACMUI REVIEW

Yttrium-90 Microsphere Brachytherapy Sources and Devices

Eye90 Microspheres® Licensing Guidance

[XXXX XX, 2023]

NRC Contact
Sarah Spence
MedicalQuestions.Resource@nrc.gov

Table of Contents

1. Background

This licensing guidance for yttrium-90 (Y-90) microsphere brachytherapy is exclusively for the use of Eye90 microspheres®. At the time of publication of this guidance, Eye90 microspheres® is a new microsphere device approved by the Food and Drug Administration (FDA) under an Investigational Device Exemption (IDE) for clinical trial.

Eye90 microspheres® are permanent implantable radiopaque glass Y-90 microspheres used for treatment of conditions of the liver. The microspheres are provided as a unit dose in 2.5 mL saline, contained in an acrylic shield. The microspheres are delivered to tumor vasculature via a catheter placed under fluoroscopy guidance using a proprietary delivery system comprised of a sterile, single-use delivery device and a re-useable, nonsterile system container. This product is unique to the existing FDA-approved Y-90 microsphere products at the time of publication, due to the radiopaque quality of the microspheres. The AU may choose to use fluoroscopy to directly image the radiopaque microspheres in the tumor vasculature during administration and via any x-ray imaging modality thereafter.

At the time of publication of this guidance, Eye90 microspheres® does not have an SSDR safety certificate.

This document has been adapted from the existing guidance for other microsphere brachytherapy, “Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance” (ML20080J208) revised in March 2020, to reflect necessary changes unique to Eye90 microspheres®, in particular the ability to visualize the microspheres during administration via fluoroscopy. Because this product is new and still being investigated in early clinical trials at the time of publication, a separate guidance was needed to facilitate any necessary future revisions as the NRC and medical communities gain experience with Eye90 microspheres®.

2. 10 CFR 35.1000 Use

Although Eye90 microspheres® are manual brachytherapy sources used for permanent implantation therapy, Eye90 microspheres® have many unique properties that merit radiation safety considerations other than those required by 10 CFR Part 35, “Medical Use of Byproduct

Material," Subpart F, "Manual Brachytherapy." These unique properties include the microspheres' small size, the large number of microspheres used in a treatment, and the route of administration. As a result, Eye90 microspheres® brachytherapy is regulated under 10 CFR 35.1000, "Other medical uses of byproduct material or radiation from byproduct material[1]."

3. Licensing Guidance

This guidance provides applicants with an acceptable means of satisfying the requirements for a license for the use of Eye90 microspheres® and is not intended to be the only means of satisfying the requirements for a license. The applicant must submit the information required to meet 10 CFR 30.33 and 35.12, as described below. The applicant should submit additional information and commitments requested below or may, unless the information is specifically required by regulation, submit alternative information and commitments for review by the NRC to make a licensing determination. The commitments incorporated into the license by license condition will be reviewed during routine inspections. If an applicant commits to the guidance provided below, the applicant is committing to follow commitments described with the use of the word "should."

4. General

4.1 Requirements not Specific to 10 CFR 35.1000 Use

Applicants must commit to meet the general requirements in 10 CFR Part 35, Subpart A, "General Information;" Subpart B, "General Administrative Requirements;" Subpart C, "General Technical Requirements;" Subpart L, "Records;" Subpart M, "Reports;" and Subpart N, "Enforcement," except as specified in this guidance. Additionally, applicants must meet applicable requirements of 10 CFR Part 19, "Notices, Instructions and Reports to Workers: Inspection and Investigations;" Part 20, "Standards for Protection Against Radiation;"[2] Part 30, "Rules of General Applicability to

[1] 10 CFR 35.1000 is designated as Compatibility Category D. Agreement States are not required to adopt these regulations for purposes of compatibility but are not prohibited from adopting Compatibility Category D regulations if they so choose. If Agreement States choose to adopt this licensing guidance, references to 10 CFR should be changed to the equivalent Agreement State regulations.

[2] Refer to IN-21-02 for further information regarding compliance with Part 20.

Domestic Licensing of Byproduct Material;" and Part 71, "Packaging and Transformation of Radioactive Material."

4.2 Radionuclides, Form, Possession Limits, and Purpose of Use

Pursuant to 10 CFR 35.12, the applicant shall identify the radionuclide, chemical/physical form, requested maximum possession limit, and purpose of use. This information may be submitted under a signed, dated letter or NRC Form 313, "Application for Materials License." The following table provides the format for an acceptable request.

	Eye90 Microspheres®	
Radionuclides (NRC Form 313 Item 5a)	Yttrium-90	
Chemical/Physical Form (NRC Form 313 Item 5b)	Glass microsphere (current manufacturer as listed in the Sealed Source and Device Registry [e.g., ABK Biomedical, Inc. Model Eye90 microspheres®])	**For broad scope licensees using the SSD exemption in 10 CFR 35.15(g):** Glass microsphere (current manufacturer as approved for IDE by the FDA [e.g., ABK Biomedical, Inc. Model Eye90 microspheres®])
Maximum Possession Limit (NRC Form 313 Item 5c)	X* Ci total	

Purpose of Use (NRC Form 313 Item 6)	Eye90 microspheres® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry	**For broad scope licensees using the SSD exemption in 10 CFR 35.15(g):** Eye90 microspheres® for permanent brachytherapy using delivery system as described in the FDA-approved IDE research protocol

***** Based on the maximum amount the applicant anticipates having at one time (i.e., 3 Ci)

4.3 Facility Address and Description

Provide an address of use and description of the location where the Eye90 microspheres® will be used and stored.

4.4 Leak Tests

Leak tests are not required for Eye90 microspheres®. The small size and large number of Y-90 microspheres make leak testing, as required by 10 CFR 35.67(b), impractical. Further, leak testing is not required as the activity of each Y-90 microsphere is below the threshold in 10 CFR 35.67(f)(3).

5. Training and Experience

5.1 Authorized Users

NRC has determined that individuals meeting the Authorized User (AU) training and experience (T&E) criteria A, B, and C provided below can be authorized for the use of Eye90 microspheres® brachytherapy. Applicants may also submit alternative T&E criteria to be reviewed on a case-by-case basis by NRC staff. The alternative T&E commitments should include an explanation of

why the applicant believes the alternative T&E commitments demonstrate that the individuals are qualified to be an AU.

A.

1. Is identified as an AU for medical use in 10 CFR 35.1000 for Y-90 microspheres, 10 CFR 35.400, "Use of sources for manual brachytherapy," or for medical uses in 10 CFR 35.300, "Use of unsealed byproduct material for which a written directive is required," that includes the use described in 10 CFR 35.390(b)(1)(ii)(G)(3) on one of the following licenses or permits that authorizes the medical use of byproduct material: A Commission or Agreement State license, a permit issued by a Commission master materials licensee, a permit issued by a Commission or Agreement State licensee of broad scope, or a permit issued by a Commission master materials license broad scope permittee; or
2. Meets the training and experience requirements of 10 CFR 35.390 or 10 CFR 35.490; or
3. Meets the training and experience guidelines as follows:

   i.

   a. Experience in diagnostic radiology demonstrated by:
      (a) Board certification in interventional radiology/diagnostic radiology by the American Board of Radiology (ABR)[2]; or
      (b) Board certification in diagnostic radiology by the ABR[2]; or
      (c) Board certification in diagnostic radiology by the American Osteopathic Board of Radiology (AOBR)[3]; or
      (d) Three years supervised clinical experience in diagnostic radiology; and
   b. Experience in interventional radiology demonstrated by:
      (a) Board certification in interventional radiology/diagnostic radiology by the ABR[2]; or
      (b) Board subspecialty certification in interventional radiology by the AOBR[2]; or
      (c) One year of supervised clinical experience in interventional radiology; and

[3] As noted on the NRC's Medical Uses Licensee Toolkit Web site, the NRC-approved ABR and AOBR certificates contain the words "AU eligible" above the ABR or AOBR seal. For the purposes of this guidance, the NRC deems the certificates issued without "AU Eligible" to be adequate to meet the T&E guidelines in criteria A.3.i.a and A.3.i.b.

ii. Has 80 hours of classroom and laboratory training[4] for byproduct material requiring a written directive, applicable to Y-90 microspheres, which may be concurrent with training received in accordance with criterion A.3.i in:
    a. Radiation physics and instrumentation; and
    b. Radiation protection; and
    c. Mathematics pertaining to the use and measurement of radioactivity; and
    d. Radiation biology;
iii. Has work experience under the supervision of an AU for Eye90 microspheres® brachytherapy or training provided by an Eye90 microspheres® manufacturer representative involving:
    a. Ordering, receiving, and unpacking radioactive materials safely and performing the related radiation surveys; and
    b. Performing quality control procedures on instruments used to determine the activity of Eye90 microspheres® and performing checks for proper operation of survey meters; and
    c. Calculating and measuring the activity and safely preparing the Eye90 microspheres® to be delivered to the patient or human research subject; and
    d. Using procedures to control and to contain spilled byproduct material, including Eye90 microspheres®, safely and using proper decontamination procedures. The procedures should address any special circumstances that may be encountered, such as the electrostatic charge of Eye90 microspheres® and the proper survey instrument and survey technique for beta emitters[5]; and
iv. Has work experience or training under the supervision of an AU or manufacturer representative[6] for Eye90 microspheres® brachytherapy, including:
    a. Preparing and administering patient dosage. The individual does not have to be the physician who places the micro-catheter or administers patient dosage, but it is necessary that the individual have training in the administration process,

[4] For Board Certified physicians, if the Board Certification is recognized by the NRC on the NRC's Medical Uses Licensee Toolkit Web site for 10 CFR 35.290, 35.390, 35.392, 35.394, and 35.396, the applicant or licensee need not submit detailed documentation of those AUs' classroom and laboratory training to satisfy section A.3.ii. The applicant or licensee need only confirm that the individual has completed training on the use of Y-90 microspheres.

[5] Appendix N, "Model Emergency Procedures," NUREG-1556, Volume 9 provides additional guidance.

[6] Because there were no licensees approved for Eye90 Microspheres® at the time this licensing guidance was initially published in 2023, there are a limited number of AUs available to provide training. Therefore, training provided by a manufacturer representative will be accepted in lieu of training provided by an AU until [DATE].

including selection of activity of Eye90 microspheres® to be administered to each treatment site and catheter positioning to ensure administration of the Eye90 microspheres® is in accordance with the written directive; and

b. Using administrative controls to prevent a medical event involving the use of byproduct material[7]; and

c. Evaluation of patient or research subject's treatments to determine whether the administered dosage was in accordance with the written directive or if a medical event has occurred.

B.

Has successfully completed training in the operation of the delivery system, safety procedures, and clinical use for Eye90 microspheres®. This requirement may be satisfied by completing a training program provided by the vendor for new users or by receiving training supervised by an AU[8] who is authorized for Eye90 microspheres®. Clinical use training to support unsupervised use should include at least three hands-on patient cases for Eye90 microspheres®, conducted in the physical presence of an AU[6, 9] who is authorized for Eye90 microspheres®.

Additionally, if the proposed AU is already trained on the use of another model of microspheres, they must be trained in the specific differences between Eye90 microspheres® and the other model(s) of microspheres for which they are approved, including activity prescription, written directive preparation, microsphere administration, and spill procedures.

However, if a proposed AU cannot complete patient cases prior to authorization; the licensee may request conditional approval with the proposed AU's completion of at least

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[7] Appendix S, "Model Procedures for Developing, Maintaining, and Implementing Written Directives," NUREG-1556, Volume 9 provides additional guidance.

[8] A physician who is not an AU but who meets the T&E criteria for Eye90 microspheres may be approved to supervise another physician's training or first hands-on patient cases on a case-by-case basis.

[9] Because there were no licensees approved for Eye90 microspheres® at the time this licensing guidance was initially published in [YEAR], there are a limited number of preceptors available to provide training and sign attestations. Therefore, the NRC is postponing requiring a written attestation until [DATE HERE]. At that time, attestations will be required for individuals who are not already authorized for use of Eye90 microspheres®. The NRC will continue to review the availability of preceptors and may revise this guidance if it determines that sufficient preceptors have not become available. In addition, all individuals seeking authorization for use of Eye90 microspheres® must submit documentation of successful completion of required training as provided by the manufacturer.

three mock simulated cases. Mock simulated cases should demonstrate issues that are encountered during Eye90 microspheres® administration procedures and should be completed by the individual in the physical presence of a manufacturer representative or an AU[6] who is authorized Eye90 microspheres®. Following conditional approval, the individual should complete the clinical casework described above, including case work, within a year following the license issuance or amendment that names the individual as an AU for Eye90 microspheres® use. The licensee may submit documentation to the NRC requesting an extension of this timeframe. The supporting documentation should include a commitment to perform continuing T&E (e.g., one additional mock case prior to performing patient cases) in Eye90 microspheres® until the first three patient cases are completed, and

C.

Has obtained written attestation that the individual has satisfactorily completed the requirements in criteria A and B of this section and is able to independently fulfill the radiation safety-related duties as an AU for Eye90 microspheres®. The attestation must be obtained from either:

1. An AU[6, 7] who is authorized forEye90 microspheres®; or
2. A residency program director who affirms in writing that the attestation represents the consensus of the residency program faculty where at least one faculty member is a physician who is an AU[6] for Eye90 microspheres® brachytherapy and concurs with the attestation provided by the residency program director. The residency training program must be approved by the Residency Review Committee of the Accreditation Council for Graduate Medical Education or the Royal College of Physicians and Surgeons of Canada or the Council on Postdoctoral Training of the American Osteopathic Association and must include T&E specified in criteria A and B of this section.

In accordance with 10 CFR 35.59, the T&E specified above must have been obtained within the seven years preceding the date of application or the individual must have had related continuing education and experience since the required T&E was completed. Recent training provided under Section B may be sufficient to show recentness of training. This recentness of training requirement applies to all individuals, including those who are board certified or listed as an AU on an NRC or Agreement State license.

5.2 Radiation Safety Officer

The Radiation Safety Officer (RSO) must have training as specified in 10 CFR 35.50, including training in radiation safety, regulatory issues, and emergency procedures for Y-90 microsphere use. An RSO already listed on a license that includes one type of Y-90 microsphere device does not require additional approval for another type of Y-90 microsphere device but should be familiar with all radiation safety aspects, including cleaning up spills, associated with all devices used at the facility.

5.3 Training and Experience Documentation

The applicant must submit documentation of the above T&E for all physicians requesting authorization to use Eye90 microspheres®. This documentation shall include the clinical use cases and written attestation and supervising physician T&E, if necessary. For individuals completing the patient cases following the license amendment, this documentation shall include documentation from the manufacturer representative or supervising physician of the three mock simulated cases and a commitment that each individual will complete at least the first three hands-on patient cases supervised in the physical presence of an AU[7, 8] who is authorized for the Eye90 microspheres®. The documentation should commit to requiring the individual to perform a mock simulated case if six months or more have passed since last performing a hands-on or mock simulated case. Additionally, for applicants that have individuals completing the patient cases following the license amendment, the applicant's commitment will include submitting documentation from the manufacturer to the appropriate NRC Regional Office within 60 days of when these three patient cases have been satisfactorily completed.

5.4 Team Approach

Microsphere brachytherapy treatment is usually conducted using a multi-disciplinary team approach. The AU should consult with individuals, as necessary, with expertise in:

- cancer management (e.g., radiation or medical oncology);
- catheter placement;
- radiation dosimetry; and
- safe handling of unsealed byproduct material.

One individual may satisfy more than one of the listed areas of expertise. The applicant shall commit to provide training in the licensee's procedures to all individuals involved in Eye90 microspheres® use, commensurate with the individual's duties to be performed. This training must be provided to all individuals preparing, measuring, performing dosimetry calculations, or administering Eye90 microspheres®.

5.5 Notification

The NRC recognizes that, if an AU satisfies the T&E listed in NRC's licensing guidance for Eye90 microspheres® and is currently listed on a Commission or Agreement State medical use license or permit for Eye90 microspheres®, the AU should be allowed to work under a different license for the medical use of Eye90 microspheres®. A limited specific medical use applicant initially applying for authorization for the medical use of Eye90 microspheres® or an existing licensee applying for an amendment may request authorization to notify the NRC in the future that it has permitted an AU to work at its facility without requesting an additional license amendment, provided the following conditions are met:

1. the AU satisfies the T&E listed in this licensing guidance for Eye90microspheres®; and
2. the AU is currently listed for Eye90 microspheres® use on a Commission or Agreement State license, a permit issued by a Commission master materials licensee, a permit issued by a Commission or Agreement State licensee of a broad scope, or a permit issued by a Commission master materials license broad scope permittee; and
3. the licensee provides the NRC a copy of the license or permit on which the AU is listed for Eye90 microspheres® use; and
4. the licensee provides the NRC documentation of the completion of three patient cases if previously not submitted to the NRC; and
5. the licensee provides documentation of the above listed conditions to NRC for each AU no later than 30 days after the date that the licensee allows the AU to work as an AU for the Eye90 microspheres®.

If this authorization is approved, these notification conditions will be incorporated as license conditions on the license.

5.6 Grandfathering

If a licensee adopts this licensing guidance revision, physicians who are currently authorized for the medical use of Eye90 microspheres® under T&E criteria listed in previous revisions do not have to meet the revised criteria in this revision for Eye90 microspheres®.

6. License Commitments

The applicant shall commit to follow all the requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use, except where replaced by the following licensing commitments:

6.1 Procedures for Administration

The licensee must have procedures for administration requiring a written directive as specified in 10 CFR 35.41, specifically to ensure high confidence that the patient's or human research subject's identity is verified before each administration and each administration is in accordance with the written directive. As Eye90 microspheres® are too small to be calibrated in accordance with 10 CFR 35.432, the licensee shall determine and record the activity of each dosage before medical use in accordance with 10 CFR 35.63 and 10 CFR 35.60 even though Eye90 microspheres® are not considered to be unsealed byproduct material. The licensee shall commit to following the manufacturer's procedures or submit alternative methods for calculating and documenting the dose or activity to the treatment site; preparing the dose for administration; determining shunting to non-treatment sites; and determining if a medical event has occurred (e.g., performing pre- and post-vial dose measurements with appropriate instrumentation, evaluating post-treatment imaging). For the purpose of this guidance, shunting is defined as blood flow through pathway or bypass due to patient vasculature causing the Eye90 microspheres® to flow to an unwanted location. Unexpected dose or activity to an organ or tissue other than the treatment site that is caused by catheter placement during delivery of the Eye90 microspheres® is not considered shunting and should be evaluated as a possible medical event.

Administration of Eye90 microspheres® must be performed in accordance with the written directive. The licensee shall record the dose or activity delivered to the treatment site. The record shall be prepared within 24 hours after the completion or termination of the

administration and must include the name of the individual who determined the dose or administered activity and the date the record is completed.

6.2 Written Directives

The licensee must complete a written directive, which must be dated and signed by an AU before the administration in accordance with 10 CFR 35.40(a) and 10 CFR 35.40(c) unless a delay in order to provide a written directive would jeopardize the patient's health, as allowed under 10 CFR 35.40(c)(1). The licensee shall retain a copy of the written directive in accordance with 10 CFR 35.2040.

Due to the unique properties of Eye90 microspheres® brachytherapy, the following written directive condition should be used instead of 10 CFR 35.40(b).

> The written directive shall include the patient or human research subject's name; the treatment site; the radionuclide (including the physical form [Y-90 microspheres]); the model of spheres (e.g. Eye90 microspheres®) or manufacturer; the prescribed dose or activity; and, if appropriate for the type of microsphere used, the statement "or dose or activity delivered at stasis."

For the purpose of written directive and medical event reporting requirements in the Eye90 microspheres® guidance, "prescribed dose" means the total dose (rad or Gy). Alternatively, prescribed activity (mCi or GBq) may be used in lieu of prescribed dose. If prescribed activity is used in lieu of prescribed dose, the activity shall be used for all documentation and evaluations. As described in 10 CFR 35.2, "treatment site" means the anatomical description of the tissue intended to receive a radiation dose, as described in a written directive. For instance, the treatment site may be described as the lobe or segment that is intended to receive the Eye90 microspheres® and the tissue that is expected to receive Eye90 microspheres® due to shunting. For the purpose of this guidance, stasis is defined as a stoppage or slowdown in the flow of blood. The inability to complete administration due to clogging or kinking of the catheter is not considered stasis.

6.2.1 Termination of Treatment Due to Stasis

If the administration was terminated because of stasis, then the total dose or activity to the treatment site is the value of the total dose or activity administered when stasis occurred and the administration was terminated. The record shall be prepared within 24 hours after the completion or termination of the administration and must include the name of the individual who determined the administered dose or activity, the signature of an AU for Eye90 microspheres®, and the date signed.

6.2.2 Emergent Patient Conditions

If the procedure must be modified due to emergent patient conditions that prevent administration in accordance with the written directive (e.g., artery spasm or sudden change in blood pressure), the AU shall document such changes in the written directive within 24 hours after the completion or termination of the administration. The modification to the written directive shall include the reason for not administering the intended dose or activity, the signature of an AU for Eye90 microspheres®, and the date signed.

6.*2.3 Termination of Treatment Due to Observed Deposition*

If the AU decides to terminate administration due to observation of undesired radiopaque microsphere deposition, the AU may make an oral revision to a written directive to modify the prescribed dose or activity. The oral revision must be documented as soon as possible in the patient's record. A revised written directive must be signed by an AU within 24 hours of the oral revision and shall include a reason for the termination, the dose or activity delivered, the signature of an AU for Eye90 microspheres®, and the date signed. If the dose delivered to the unintended target exceeds the thresholds for medical event reporting as outlined in Section 6.3, then the licensee shall comply with the medical event reporting and notification requirements as described in 10 CFR 35.3045(b)-(g).

6.3 Medical Event Reporting

In place of 10 CFR 35.3045(a), the licensee shall commit to report any event, except for an event that is caused by shunting as described in the criteria below, or as a result of patient intervention, as defined in 10 CFR 35.2 as an actions by the patient or human research subject,

whether intentional or unintentional, such as dislodging or removing treatment devices or prematurely terminating the administration. The criteria for event reporting is:

- the administration of byproduct material results in a dose that exceeds 0.05 Sv (5 rem) effective dose equivalent or 0.5 Sv (50 rem) to an organ or tissue; and
    - an administration of the wrong radionuclide or type of microsphere; or
    - an administration to the wrong individual or human research subject; or
    - an administration by the wrong route of administration; or
    - an administration by the wrong mode of treatment; or
- the total dose or activity delivered differs from the prescribed dose or activity, as documented in the written directive, by 20 percent or more, except when stasis or emergent patient conditions are documented and resulted in a total dose or activity administered that was less than that prescribed; or
- A dose to the skin or an organ or tissue other than the treatment site that exceeds by 0.5 Sv (50 rem) to an organ or tissue and 50 percent or more of the dose expected from the administration defined in the written directive (excluding shunting as defined in Section 6.1 when shunting was evaluated prior to the treatment in accordance with the manufacturer's procedures.)

Additionally, the licensee shall comply with the medical event reporting and notification requirements as described in 10 CFR 35.3045(b)-(g).

6.4 Sealed Source and Device Use

The licensee should commit to only use Eye90 microspheres® for therapeutic medical uses as approved in the SSD registration certificate for Eye90 microspheres®, including maximum activity per vial limit.[10]

[10] At the time of publication of this guidance, Eye90 Microspheres® does not have a Sealed Source and Device (SSD) registration certificate. Note that 10 CFR 35.15(g) exempts licensees possessing a Type A specific license of broad scope from the SSD manufacturer requirement in 10 CFR 35.49(a). Broad scope licensees instead must perform their own internal safety evaluation as mentioned in Section 7.1.

6.5 Inventory

Due to the short half-life of Y-90 (64 hours) and the fact that microspheres are not managed as individual discrete sources, the requirements in 10 CFR 35.67 for semi-annual physical inventory of brachytherapy sources and recordkeeping in 10 CFR 35.2406 are not applicable to microspheres. Rather, the requirements for brachytherapy source accountability (10 CFR 35.406), receipt (10 CFR 20.1906), labeling (10 CFR 20.1904 and 10 CFR 35.69), storage (10 CFR 20.1801 and 10 CFR 35.92), and disposal (see the "Waste Disposal Issues" section of this guidance document) are sufficient to ensure accountability of Y-90 in the form of microspheres possessed by a licensee.

6.6 Labeling

The licensee should commit to the following when the Eye90 microspheres® are placed in vials, syringes, or radiation shields that are not labeled by the manufacturer:

- Label vials and vial radiation shields with the radioactive device (i.e. Eye90 microspheres®); and
- Label syringes and syringe radiation shields with the radioactive device.

6.7 Patient Release

The licensee should commit to develop procedures that describe measures taken to ensure that radiation emissions, which may include bremsstrahlung, from each patient or human research subject permits his or her release in accordance with 10 CFR 35.75. Guidance for release of patients or human research subjects following administration of radioactive materials may be found in Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials."

6.8 Surveys

As the Eye90 microspheres® are too small to be seen, licensees should survey, with an appropriate radiation detection survey instrument, all areas that the Eye90 microspheres® are prepared for use or administered. The survey should be conducted immediately following each preparation and administration in unrestricted areas and by the end of the day for restricted areas. A licensee should retain a record of each survey for three years and the record should include the date of the survey, the results of the survey, the instrument used to perform the survey, and

the name of the individual who performed the survey. Licensees do not need to perform surveys in an area(s) where patients or human research subjects are confined when they cannot be released under
10 CFR 35.75.

6.9 Radiation Protection Program Changes

This guidance may be revised as additional experience is gained regarding the medical use of Eye90 microspheres®. A licensee currently authorized to use these products that is committed by license condition to following provisions in a previous revision of this guidance may request a license amendment to commit to following this revision of the guidance instead. The licensee must apply for and receive this license amendment in order to make program changes to conform to this revision of the guidance.

An applicant initially applying for authorization for the medical use of Eye90 microspheres®, or a licensee applying for an amendment to conform with this revision of the guidance 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 to radiation safety programs without a license amendment provided that the change process requires the following conditions to be met for revisions to the radiation safety program:

1. the revision is in compliance with the regulations; and
2. the revision is based upon NRC's current guidance for Eye90 microspheres® Y-90 microspheres 35.1000 use posted on the NRC's Medical Uses Licensee Toolkit Web site; and
3. the revision has been reviewed and approved by the licensee's RSO and licensee's management; and
4. the affected individuals are instructed on the revised program before the change is implemented; and
5. the licensee will retain a record of each change for five years; and
6. the record will include a copy of the appropriate website guidance, the old procedure, the new procedure, the effective date of the change, and the signature of the licensee management that reviewed and approved the change.

If approved, these conditions for use of the updated guidance will be incorporated as license conditions in the license.

7. Notes to Licensees

7.1 Change in Physical Conditions of Use

At the time of publication of this guidance, Eye90 microspheres® is does not have an SSD registration certificate. Upon issuance of an SSD registration certificate for Eye90 microspheres®, the following guidance applies:

If the physical conditions of use exceed those reported in the SSD registration certificate, the limited specific medical use licensee shall request an amendment for the new conditions, and a broad scope licensee shall perform its own engineering and radiation safety evaluation addressing those differences.

7.2 Use of Other Y-90 Microspheres

At the time of publication of this guidance, Eye90 microspheres® is pending an SSD safety evaluation. Upon issuance of an SSD registration certificate for Eye90 microspheres®, the following guidance applies:

The SSD safety evaluation for a specific manufacturer's Y-90 microsphere does not cover the use of any other Y-90 microspheres in its device for administration. The medical use of such a source will require a new SSD registration certificate (or safety evaluation by the broad scope medical use licensee) that addresses the conditions of use, safety of the new Y-90 microspheres, and compatibility of the new microspheres with the microsphere delivery system(s).

The SSD safety evaluation for a given manufacturer's Y-90 microsphere delivery system does not cover the use of that manufacturer's Y-90 microspheres with another manufacturer's delivery system or the use of another manufacturer's Y-90 microspheres with the given manufacturer's delivery system. Before authorization, the medical use of such a delivery system will require a new SSD registration certificate (or safety evaluation by the broad scope medical use licensee) that addresses the conditions of use, safety of the microsphere delivery system, and compatibility of the new delivery system with the Y-90 microspheres.

7.3 Waste Disposal Issues

Y-90 microspheres are known to potentially contain radioactive impurities, some of which are long-lived (i.e., half-lives of greater than 120 days) (Refer to Information Notice (IN) 2007-10, "Yttrium-90 Therasphere® and Sirspheres® Impurities"). Due to different manufacturing processes, the activity and radionuclides of the impurities vary for different Y-90 microsphere products. Impurities that have been recently found in reactor-activated microspheres include small amounts of long-lived radionuclides such as europium-152, europium-154, and cobalt-60.[11] Impurities that have been recently found from microspheres with generator-produced Y-90 include trace amounts of strontium-90.[12] While this IN was generated in response to other products, licensees should be prepared to follow similar precautions and procedures when handling waste generated by Eye90 Microspheres®.

Licensees should be aware that the activity and type of impurities can change and be different from that described above. The NRC does not limit manufacturers to specific manufacturing processes, and it is therefore possible for the activity and types of radionuclide impurities to change for all Y-90 microsphere products. Additionally, unused or partially used vials are likely to contain higher activities of impurities.

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. Specifically, 10 CFR 35.92 requires that licensees monitor byproduct material with a physical half-life of less than or equal to 120 days at the surface before disposal and determine that its radioactivity cannot be distinguished from the background radiation level with an appropriate radiation detection survey meter before disposal. Therefore, regardless of the length of time they have been allowed to decay, licensees are not permitted to dispose of Y-90

[11] J. Metyko, J. Williford, W. Erwin, J. Poston, S. Jiminez. "Long-lived Impurities of ^{90}Y-labeled microspheres, TheraSphere and SIR-Spheres, and the impact on patient dose and waste management." Health Phys. **103**(3), S204-S208 (2012).

[12] J. Metyko, W. Erwin, J. Poston, and S. Jimenez. "^{90}Sr Content in ^{90}Y-labeled SIR-Spheres and Zevalin." Health Phys. **107**(5), S177-S180 (2014)

microspheres if radioactivity can be distinguished from the background radiation level with an appropriate radiation detection survey meter.

If waste is determined to contain impurities with a physical half-life of greater than 120 days that can be distinguished from the background radiation level with an appropriate radiation detection survey meter, the licensee may need to use one or more of the following means to dispose of waste associated with the Eye90 microspheres®:

- return the Eye90 microspheres® to the manufacturer, if the manufacturer is authorized to receive Y-90 microspheres; or
- transfer the Eye90 microspheres® to an authorized recipient pursuant to requirements in 10 CFR Part 20 and Part 30.

See Regulatory Issue Summary 2004-17, Revision 1, "Revised Decay-in-Storage Provisions for the Storage of Radioactive Waste Containing Byproduct Material," for more information regarding requirements for holding waste for decay-in-storage.

7.4 Autopsy and Cremation

Eye90 microspheres® are permanent implants that are not removed from the body by biological methods. Because Y-90 has a 64-hour half-life, Y-90 will likely have significantly decayed before a patient's death. Patients treated with Eye90 microspheres® will not usually represent an external radiation hazard to persons handling the body. However, in the case of autopsy or cremation, the radiation hazard increases due to the need for individuals to handle tissues that may contain radioactive material, especially if the death occurs soon after treatment with Eye90 microspheres®. The National Council on Radiation Protection and Measurements (NCRP) Report No. 155, "Management of Radionuclide Therapy Patients," December 2006, may contain helpful information for radiation safety considerations associated with autopsy or cremation of patients with permanent implants. Additionally, NUREG-1556, Volume 9, Appendix N, "Model Emergency Procedures," contains additional guidance regarding autopsy and cremation of patients who have received therapeutic amounts of radionuclides.

7.5 Radiation Safety Committee

If a licensee is required to have an RSC in accordance with 10 CFR 35.24(f), then the committee must include an AU for the use of Y-90 microspheres.

8. Notes to Regulators

8.1 Inspection Frequency

Licenses authorizing Eye90 microspheres® brachytherapy should be inspected every two years. Per Enclosure 1 to Inspection Manual Chapter 2800, licenses authorizing emerging technology under 10 CFR 35.1000 are assigned a Priority 2 inspection code.

8.2 Program Code

The NRC regions should use program code 02240.

9. Paperwork Reduction Act Statement

This Licensing Guidance provides voluntary guidance for implementing the mandatory information collections in 10 CFR Parts 30 and 35 that are subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et. seq.). These information collection were approved by the Office of Management and Budget (OMB), approval numbers 3150-0017 and 3150-0010. Send comments regarding this information collection to the Information Services Branch (T6-A10M), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, or by e-mail to Infocollects.Resource@nrc.gov, and to the OMB reviewer at: OMB Office of Information and Regulatory Affairs (3150-0017, 3150-0010), Attn: Desk Officer for the Nuclear Regulatory Commission, 725 17th Street, NW Washington, DC 20503;
e-mail: oira_submission@omb.eop.gov.

10. Public Protection Notification

The NRC may not conduct or sponsor, and a person is not required to respond to, a collection of information unless the document requesting or requiring the collection displays a currently valid OMB control number.

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Protecting People and the Environment

ACMUI's Review and Analysis of Reported Medical Events from Fiscal Years 2021-2023

Richard P. Harvey, DrPH

Advisory Committee on the Medical Uses of Isotopes

April 8, 2024

U.S.NRC
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Subcommittee Members

- Richard Harvey, DrPH (Chair)
- Michael Folkert, M.D.
- Richard Green, B.S.
- Darlene Metter, M.D.
- Zoubir Ouhib, M.S.
- Harvey Wolkov, M.D.

- Consultant: John Angle, M.D.
- NRC Staff Resource: Daniel DiMarco, M.S.

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Subcommittee Charge

- Review Medical Events (MEs) to advise the Advisory Committee on the Medical Use of Isotopes (ACMUI) and United States Nuclear Regulatory Commission (NRC) about emerging trends that may need regulatory attention.

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Background

- The NRC and ACMUI review MEs that occur throughout the country on a regular basis.
- MEs occur when radioactive material use in healthcare results in unexpected radiation dose to patients. (Please refer to 10 CFR 35 Subpart M – Reports and more specifically 10 CFR 35.3045 – Report and Notification of a Medical Event for more information.)
- The Medical Events Subcommittee of the ACMUI reviews the data to analyze the nature of medical events, identify emerging trends and provide recommendations to the ACMUI and NRC.

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Medical Event Review

- FY21 – October 1, 2020 to September 30, 2021
- FY22 – October 1, 2021 to September 30, 2022
- FY23 – October 1, 2022 to September 30, 2023

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Summary

- Two overarching themes remain
  - Human Error
    - Communication/feedback
    - Failure to work in teams
  - Inexperience
    - Rapidly evolving use of radiopharmaceuticals
    - Dissemination of use to smaller institutions with lower frequency of procedures performed

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Specific Issues

- Increasing MEs: new and increasing use of current therapeutic radiopharmaceuticals
- ^{90}Y microsphere procedures remain the most common MEs.
    - ACMUI Action: Added 2 specialty-specific subcommittee members
    - ACMUI recommendation: AU adhere to manufacturer recommendations (i.e. avoid aggregation: use recommended catheter size and needle gauge)

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35.200 Use of Unsealed Byproduct Material for Imaging and Localization

Medical Events Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Cause								
Wrong Drug	0	0	0	0	1	0	1	2
Wrong Dosage	2	0	0	0	1	0	0	3
Wrong Patient	1	0	0	0	2	0	0	3
Extravasation*	1	0	0	0	0	0	0	1
Human Error	0	0	1 (8 patients)	0	0	0	0	1 (8 patients)
Total	4	0	1	0	4	0	1	10

5/5 (100%) possibly preventable by time out in 2021 & 2023 (Wrong Drug, Wrong Dosage & Wrong Patient)

*NRC does not have reporting requirement for extravasations

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35.300 Use of Unsealed Byproduct Material, Written Directive Required

Medical Event Summary

	2017	2018	2019	2020	2021	2022	2023	Total
WD not done or incorrectly	2	1	2	0	0	1	1	7
Error in delivery (# capsules)	1	0	1	0	0	1	0	3
Wrong Dose	0	0	0	0	4	3	8	15
Equipment	0	1	4	0	2	1	0	8
Human Error	0	0	1	2	3	4	0	10
Wrong Patient	1	0	1	0	0	0	0	2
Wrong Drug	0	0	0	0	1	0	2	3
Total	4	2	9	2	10	10	11	48

Time out: 2021-5/10 (50%), 2022-3/10 (30%), 2023-10/11 (91%)
(Wrong Drug, Wrong Dosage & Wrong Patient)

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35.400 Manual Brachytherapy

Medical Event Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Applicator issue (e.g. jam, eye plaque dislodged)	0	0	0	2	0	1	1	4
Wrong site implanted (e.g. penile bulb, bladder)	1	1	1	2	2	0	0	7
Activity/prescription error (e.g. air kerma vs mCi, enter wrong activity in planning software)	1	0	1	0	1	0	0	3
Wrong Dose	5	11	3	0	0	0	2	21
New Device	0	1	0	0	0	0	0	1

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35.400 Manual Brachytherapy

Medical Event Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Wrong Source	0	0	0	1	0	0	0	1
Patient Health (?patient intervention)	0	0	0	1	0	0	0	1
Wrong Patient	0	0	0	0	1	0	0	1
Total	7	13	5	6	4	1	3	39
"Time Out" may have prevented	1	0	5	1	2	0	0	9

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35.400 Manual Brachytherapy

Potentially ~23% (9/39) of ME from 2017 to 2023 may be prevented with the use of a “Time Out” (wrong site, wrong source and wrong patient):

- “Time Out” or checklist for 2021 may have prevented: ¾ (75%)
- No benefit in 2022 or 2023

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35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

	2017	2018	2019	2020	2021	2022	2023	Total
Wrong position	2	3	4	7	0	1	3	20
Wrong reference length	2	1	4	2	2	2	0	13
Wrong plan	0	2	0	0	0	0	0	4
Wrong dose/source strength	0	1	0	0	0	0	2	1
Machine/applicator malfunction	2	3	1	1	1	2	2	12
Software/hardware failure	2 (9 patients)	0	1	1	0	0	0	4
Treatment planning	0	0	0	2	1	2	0	5
Human Error	0	0	0	0	1	4	1	6
Total	8	10	10	13	5	11	8	65

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35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

Medical Event Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Location								
Breast	0	1	0	1	0	0	0	2
Gynecological	7	7	8	10	4	2	5	43
Skin/neck	0	1	0	2	1	5	1	10
Bronchus	0	0	0	0	0	0	0	0
Prostate	0	0	0	0	0	0	1	1
Brain	1	1	2	0	0	0	0	4
Unknown	0	0	0	0	0	4	1	5
Total	8	10	10	13	5	11	8	65

GYN tumors most common site of ME

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35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

MEs that may have been prevented by "timeout" (wrong plan or dose)

- 2017 0/8 events
- 2018 3/10 events
- 2019 0/10 events
- 2020 0/13 events
- 2021 0/5 events
- 2022 0/11 events
- 2023 2/8 events

Total 5/65 (8%)

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35.600 Use of a sealed source in a remote afterloader unit, teletherapy unit, or gamma stereotactic unit

MEs caused by "infrequent user/inattention"

This is difficult to determine based on information in NMED. For this assessment, assumed wrong position is a surrogate for "infrequent" user/inattention – improved training may be beneficial

- 2017 2/8 events
- 2018 3/10 events
- 2019 4/10 events
- 2020 7/13 events
- 2021 0/5 events
- 2022 1/11 events
- 2023 3/8 events

Total 20/65 (31%)

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35.1000 Radioactive Seed Localization

Medical Events Summary

	2018	2019	2020	2021	2022	2023
Total Medical Events	0	1	0	1	0	1
Cause:						
Delayed seed removal (patient intervention)	0	1	0	0	0	1
Lost seed	0	0	0	0	0	0
Wrong implant site	0	0	0	0	0	0
Seed migration	0	0	0	1	0	0

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35.1000 Intravenous Cardiac Brachytherapy

Medical Events Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Did not follow proper procedure	0	0	1	0	0	0	0	1
Tortuous vessel anatomy	0	1	1*	0	0	0	0	2
Catheter issue	0	1	0	1	0	0	0	2
Wrong Site	0	0	0	0	0	0	1	1
Total	0	2	2	1	0	0	1	6

*AU felt this is “patient intervention”
No time out issues

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35.1000 Gamma Knife® Perfexion™, Icon™ and Esprit™

Medical Events Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Total Medical Events	0	1	2	2	0	2	1	8
Cause:								
Back-up battery power source failure	0	1	0	0	0	0	0	1
Patient set-up error	0	0	0	1	0	0	0	1
Patient movement	0	0	2	0	0	0	0	2
Wrong site (treatment plan)	0	0	0	0	0	0	0	0
Wrong site (human error-shifting of co-registration images)	0	0	0	1	0	1	0	2
Patient motion management system failure	0	0	0	0	0	1	0	1
Device Malfunction	0	0	0	0	0	0	1	1

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35.1000 ^{90}Y Theraspheres

Medical Events Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Total Medical Events	15	14	15	15	23	23	22	127
Cause:								
> 20% residual activity remaining in delivery device/leakage	7	11	9	12	10	2	11	62
Delivery device set-up error	2	2	1	1	1	0	2	9
Wrong dose (treatment plan calculation error)	4	0	1	0	0	3	1	9
Wrong site (catheter placement error & size)	2	0	0	2	1	7	3	15
Wrong dose vial selected*	0	1	4	0	1	1	1	8
Wrong dose (calibration error)*	0	0	0	0	3	1	0	4
Aggregation of microspheres	0	0	0	0	7	9	4	20

For 2021 - 2023: Time out 4/23 (17%), 2/23 (9%), 1/22 (5%) – Wrong Dose*
Infrequent/inattention 10/23 (43%), 2/23 (9%), 11/22 (50%) – > 20% Residual

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35.1000 ^{90}Y SirSpheres

Medical Events Summary

	2017	2018	2019	2020	2021	2022	2023	Total
Total Medical Events	8	7	11	8	18	9	9	70
Cause:								
> 20% residual activity remaining in delivery device/leakage	7	2	8	8	2	1	6	34
Wrong dose (treatment plan calculation error)	0	2	0	0	2	1	0	5
Wrong site (catheter placement error & defective catheter)	1	2	2	0	4	0	1	10
Wrong site (WD error)	0	1	1	0	1	1	2	6
Aggregation of microspheres	0	0	0	0	9	6	0	15

2021 - 2023: Time out: 1/18(6%), 1/9(11%), 2/9(22%) - Wrong Site (WD)
Infrequent/inattention: 2/18(11%), 1/9(11%), 6/9(67%) - >20% Residual

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Actions to Prevent 35.1000 ^{90}Y Microsphere Medical Events

- Ensure familiarity with the mechanics of ^{90}Y microsphere delivery device and setup procedures
- Confirm all data and calculations in treatment plan
- Perform “Time Out” to assure all elements of treatment are in accordance with Written Directive

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Possible Elements of a "Time Out"

- Identity of patient via two identifiers (e.g. name and DOB)
- Procedure to be performed
- Radiopharmaceutical
- Activity
- Dosage –second check of dosage calculation and that the WD and dosage to be delivered are identical
- Others as applicable
  - units of activity (LDR prostate)
  - anatomic location
  - patient name on treatment plan
  - treatment plan independent second check has been performed
  - reference length (HDR)
  - Implant site location (RSL)

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Acronyms

- 10 CFR – Title 10 of the *Code of Federal Regulations*
- AUs – authorized users
- FY – fiscal year
- GYN – gynecological
- HDR – high dose-rate
- LDR – low dose rate
- mCi – milliCurie
- ME – medical event
- RSL – radioactive seed localization
- WD – written directive
- Y – Yttrium

U.S. Nuclear Regulatory Commission
Advisory Committee on the Medical Uses of Isotopes

Subcommittee on Medical Events

Draft Report
Submitted on March 14, 2024

Subcommittee Members:
Michael Folkert, MD, PhD (Brachytherapy Radiation Oncologist)
Richard Green, BS (Nuclear Pharmacist)
Richard Harvey, DrPH (Radiation Safety Officer; Chair)
Zoubir Ouhib, MS (Therapy Medical Physicist)
Harvey Wolkov, MD (Radiation Oncologist)

Consultant: John Angle, MD (Interventional Radiologist)

NRC Staff Resource: Daniel DiMarco, MS

Subcommittee Charge: Review Medical Events (MEs) to advise the Advisory Committee on the Medical Use of Isotopes (ACMUI) and United States Nuclear Regulatory Commission (NRC) about emerging trends that may need regulatory attention.

Background: The subcommittee reviewed medical events from the Fiscal Year 2021 and 2022 as part of its ongoing biannual review. In addition, the subcommittee reviewed medical events from the Fiscal Year 2023.

Findings: Medical Events in Fiscal Years 2021, 2022 and 2023 were relatively low but there appears to be an increase in Medical Events in 10 CFR 35.300 and 10 CFR 35.1000. The volume of procedures involving ^{177}Lu radiopharmaceuticals has increased during this period and this has resulted in an increased number of Medical Events in the category of 10 CFR 35.300.

Medical Events in 10 CFR 35.1000 have increased for treatments involving ^{90}Y microspheres (for both Theraspheres and SirSpheres). Reducing the number of Medical Events involving ^{90}Y microspheres may be accomplished through improved education with emphasis on appropriate administration of the microspheres and proper set-up of the delivery device. In addition, a "Time-Out may be a tool that can be implemented to reduce the number of Medical Events for procedures using ^{90}Y microspheres.

The committee recognizes past effort and continues to discuss Medical Events that may benefit from a "Time-Out" or those that may be the result of infrequent/inexperience use. Improved education and use of a "Time-Out" may be beneficial in preventing Medical Events.

The Subcommittee will continue to examine Medical Events involving radiopharmaceuticals approved for use under 10 CFR 35.300 as well as treatments performed with ^{90}Y microsphere procedures (10 CFR 35.1000). Furthermore, the subcommittee will monitor trends that may continue and appear to be significant during the biannual review period (Fiscal Year 2021 and 2022) as well as Fiscal Year 2023.

Concluding Remarks: The ACMUI subcommittee on Medical Events appreciates the opportunity to continue reviewing these events. Emphasis will be placed on radiopharmaceuticals in 10 CFR 35.300 and 10 CFR 35.1000, specifically ^{90}Y microsphere procedures, to discern if there are emerging trends in Medical Events involving these treatments. The subcommittee welcomes any comments and/or recommendations.

Respectfully submitted, March 14, 2024
Subcommittee on Medical Events
Advisory Committee on the Medical Uses of Isotopes (ACMUI)
U.S. Nuclear Regulatory Commission (NRC)

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Medical Radiation Safety Team Updates

Celimar Valentín-Rodríguez, PhD
Medical Team Leader, US NRC
April 8, 2024

Outline

01 RULEMAKING

02 GUIDANCE

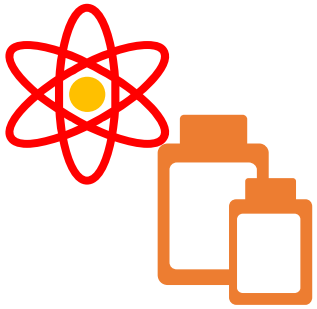
03 OTHER EFFORTS

MEDICAL RULEMAKINGS

Medical Rulemakings

EXTRAVASATIONS

Ongoing rulemaking to amend 10 CFR Part 35 to require reporting of certain nuclear medicine extravasations.



EMT/RB-82 GENERATORS

Ongoing rulemaking to establish requirements for Rb-82 generators and well-established EMTs currently regulated under 10 CFR 35.1000 and establish flexibility for future EMTs.

Reporting Nuclear Medicine Injection Extravasations as Medical Events

- On December 12, 2022, the Commission issued SRM-SECY-22-0043.
  - Approved amending 10 CFR Part 35 requirements to include reporting of certain nuclear medicine injection extravasations.
  - Included additional actions:

01

Can we **reduce reliance on patient reporting?**

02

Should we **require** licensees to have **procedures to detect and report extravasations?**

03

Can we **accelerate the rulemaking schedule** without shortening public comment periods?

04

Develop regulatory guidance for all medical events, not only extravasation events.

Rulemaking Schedule

2022

Dec: Commission issues SRM-SECY-22-0043

2023

Apr 19: NRC issues RFI & preliminary proposed rule language

2024

Aug: Proposed rule and draft implementation guidance to be issued to Commission

2026

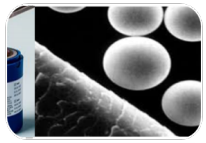
Mar: Final rule and implementation guidance to be issued to Commission

EMT/Rb-82 Generator Rulemaking Background

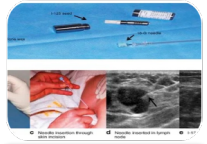
Sr-82/Rb-82 Generator

NorthStar RadioGenix Generator System

RadioMedix™ GeGant Ge-68/Ga-68 Generator System



Y-90 Microspheres



Radioactive Seed Localization

Novoste Beta-Cath Intravascular Brachytherapy System

Gamma Stereotactic RadioSurgery Perfexion and Icon

Gamma Stereotactic RadioSurgery GammaPod

ViewRay™ System Co-60 Radiation Therapy Device

Issues under consideration:

- Challenges associated with licensing Rb-82 generators under 10 CFR Part 35
- Challenges associated with licensing existing and future EMTs under the current medical use regulations in 10 CFR Part 35

Proposed changes to 10 CFR Part 35 regulations:

- Address calibration and dose measurement for Rb-82 generators
- Establish risk-informed, performance-based requirements for some existing and future EMTs within applicable subparts in Part 35, and outside of Subpart K

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EMT/Rb-82 Generator Rulemaking Timeline

July 2023

Issued regulatory basis for public comment

August 2023

Held public meeting to facilitate comments on the reg basis

Winter 2026

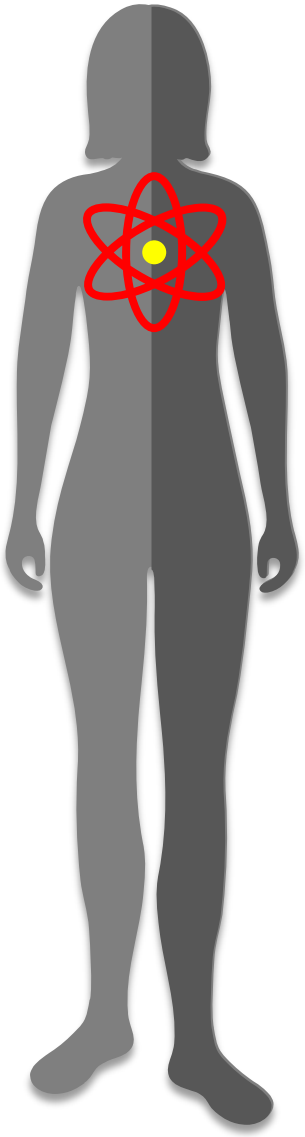
Issue proposed rule and draft implementation guidance to Commission

Winter 2027

Issue final rule and implementation guidance to Commission

Guidance Development and Updates

EMERGING MEDICAL TECHNOLOGIES



CivaDerm™

Temporary radiation therapy product to treat skin cancer and other lesions

Akesis Galaxy® RTi

Gamma stereotactic radiosurgery unit

Eye90 Microspheres®

Y-90 glass microspheres with radioopacity

Thorium Generators

Generators for therapeutic radionuclides from Th-228

Technegas™

Gas-like dispersion of Tc-99m labeled carbon for functional lung imaging

Liberty Vision Y-90 Disc Source

High dose rate Y-90 disc source to treat ocular tumors and benign growths

STATUS

RECENTLY ISSUED

ADDRESSING STAKEHOLDER COMMENTS

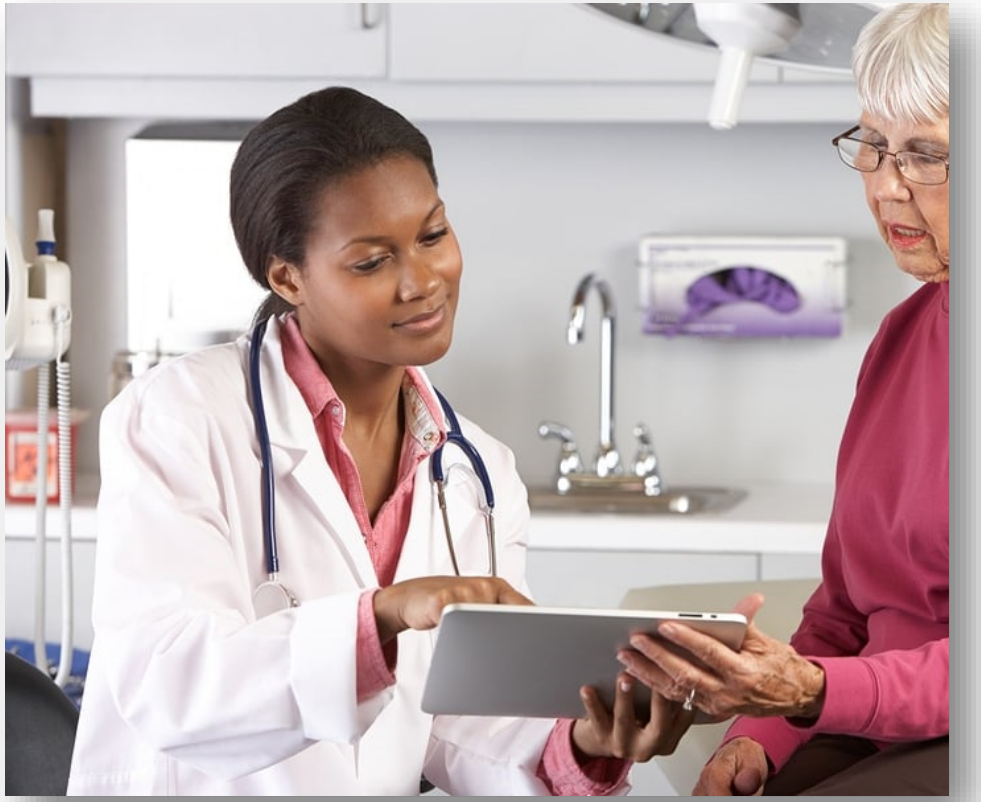
EVALUATING

Training and Experience Implementation Guidance

- The Commission directed the staff to develop implementation guidance to clarify roles and responsibilities of individuals subject to T&E requirements. (SRM-SECY-22-0005)
- Interim staff guidance to be issued by August 2024.

RG 8.39, Release of Patients Administered Radioactive Materials, Rev. 2

- In response to ACMUI comments on the draft proposed revision to RG 8.39, the staff:
  - Revised methodology to allow licensees to change some of the modifying factors, while keeping conservative assumptions for others
  - Included a patient questionnaire to gather information that licensees can use to modify the occupancy factors



RG 8.39, Release of Patients Administered Radioactive Materials, Rev. 2 (cont'd)

Published for public comment on April 21, 2023

- We received over 60 comment letters from diverse stakeholders

We are currently:

- Updating RG 8.39 based on public comments
- Developing a regulatory analysis with a cost-benefit analysis
- Will provide a revised RG 8.39 to ACMUI for another review

Medical Events

Regulatory Guide

- For evaluating and reporting medical events, including extravasations (SRM-22-0043)
- Draft to be issued concurrent with proposed rule for extravasations in August 2024

Information Notice

- In response to the increase in radiopharmaceutical-related medical events
- To be issued later this year

OTHER EFFORTS

ABR Termination

ABR notified NRC and submitted a letter of intent to terminate NRC's recognition of their certification processes (ML22091A272).

ABR will discontinue including AU, AMP, and RSO –Eligible designations on certificates issued after December 31, 2023.

March/April 2022

November 30, 2023

December 31, 2023

NRC issued IN 23-05 to provide information about the discontinuation and the existing T&E pathways for individuals seeking to become authorized individuals on medical use licenses

NRC-Recognized Specialty Boards Website: https://www.nrc.gov/materials/miau/med-use-toolkit/spec-board-cert.html

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Household Waste from Nuclear Medicine Patients

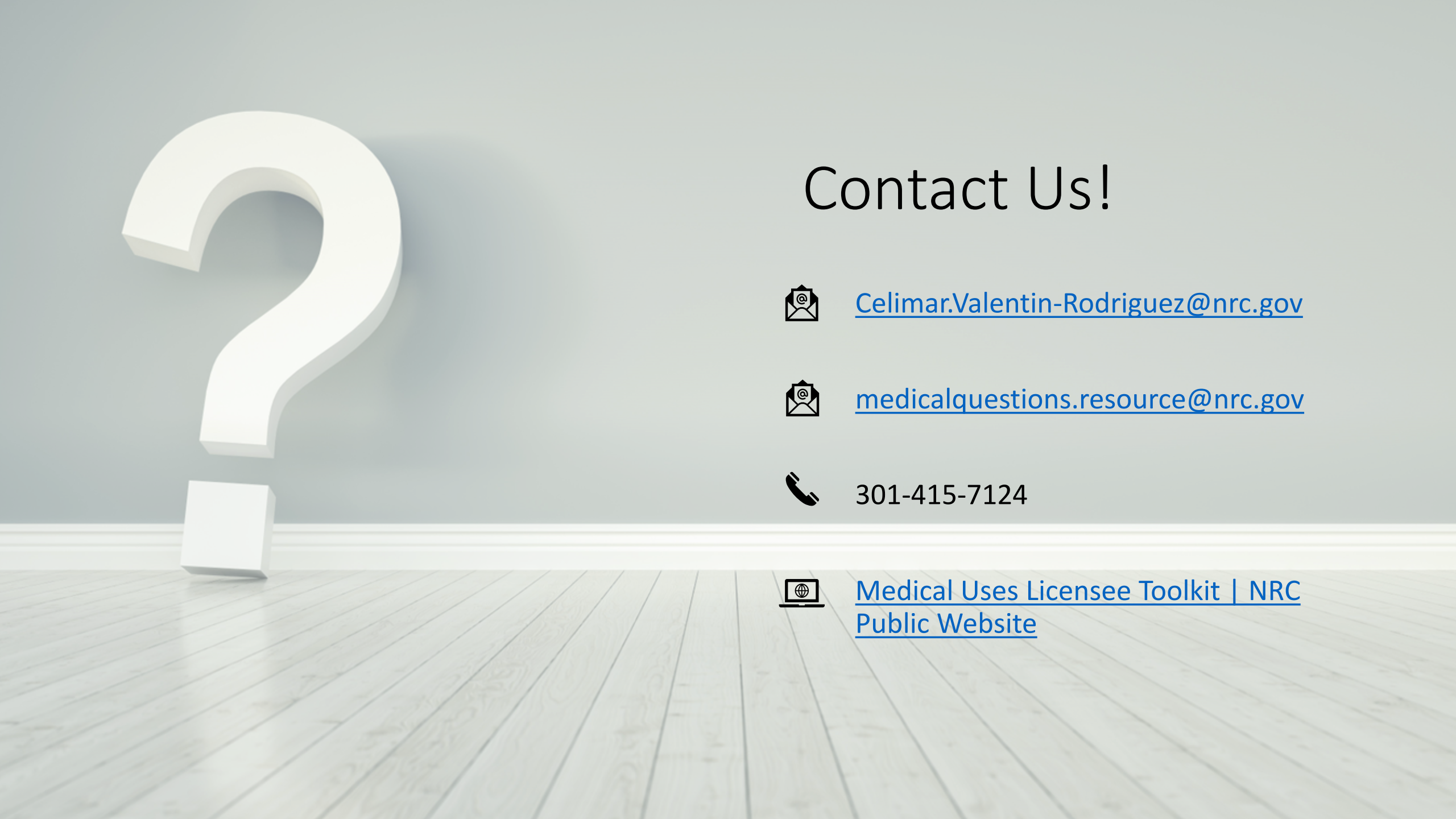
ACMUI recommended that NRC assess the issue of detection of short-lived medical isotopes in municipal waste from nuclear medicine patients

Sent voluntary survey to Agreement States requesting information on best practices and need for additional guidance.

Assessing our regulatory framework regarding waste and developing recommendations to be provided to ACMUI

Acronyms

- ABR – American Board of Radiology
- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- AMP – Authorized medical physicist
- AU – Authorized User
- CFR – Code of Federal Regulations
- Co – Cobalt
- EMT – Emerging medical technology
- IN – Information Notice
- OAS – Organization of Agreement States
- Rb-82 – rubidium-82
- RG – Regulatory guide
- RFI – Request for information
- RSO – Radiation Safety Officer
- Rb – Rubidium
- SRM – Staff requirements memorandum
- Sr - Strontium
- T&E – Training and experience
- Tc – Technetium
- Th – Thorium
- Y – Yttrium



Contact Us!

Celimar.Valentin-Rodriguez@nrc.gov

medicalquestions.resource@nrc.gov

301-415-7124

Medical Uses Licensee Toolkit | NRC Public Website

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Report of the Subcommittee on LV Liberty Vision Y-90 Disc and iWand® Ophthalmic System

Presentation by: Zoubir Ouhib, MS, FABS, FAAPM, FACR, FASTRO (Subcommittee Chair)
Advisory Committee on the Medical Uses of Isotopes
April 8, 2024

Agenda

- Subcommittee Membership
- Subcommittee Charge
- Background
- Device description
- Recommendations and General Comments
- Acronyms

Subcommittee Membership

Rebecca Allen
Michael O'Hara, PhD
Zoubir Ouhib, MS (Chair)
Megan Shober, MS
Harvey Wolkov, MD
Maryann Ayoade (NRC Staff Resource)

Subcommittee Charge

The ACMUI Chair, Dr. Darlene Metter, appointed this subcommittee to review the Liberty Vision technology and comment on the NRC staff's draft licensing guidance for the LV Liberty Vision Corporation Yttrium-90 Disc and iWand® Ophthalmic System.

Background

- Ophthalmic brachytherapy has been used as treatment for both benign and malignant tumors.
- Sources used in the past:
  - High energy LDR cobalt-60
  - Low energy x-rays LDR iodine-125 and LDR palladium-103
  - Beta radiation emitting LDR ruthenium-106 and HDR strontium-90/yttrium-90
- Source being evaluated by this subcommittee is Liberty Vision LV HDR beta emitting radiation Y-90 Disc.

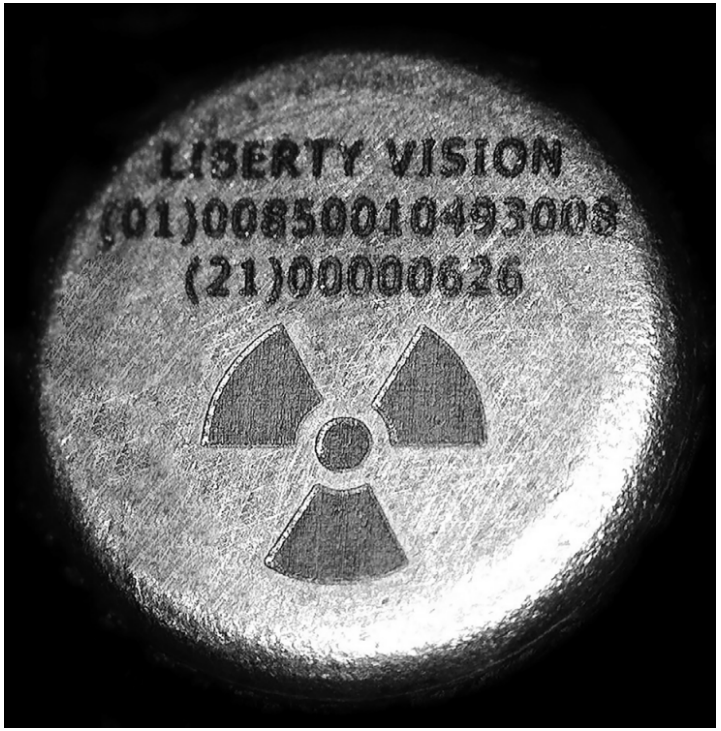
Background (Cont'd)

- Y-90 has been widely used for cancer treatment.
- Provided an effective treatment for episcleral fibrovascular growths.
- Treatment is to be provided by a team: AU who is a radiation oncologist, an ophthalmologist, and AMP.
- Device with LV Y-90 source cleared by FDA with 510(k) with source activity up to 20 mCi at time of treatment and 80 mCi at time of shipment.
- Source can be used for superficial lesions and at desired depth.

Background (Cont'd)

- Source has a short half-life: 64 hr.
- LV Y-90 source is designed for a single use and to be stored for decay or returned to the manufacturer.
- Desired dose prescription at specific depth (superficial or at depth): 26 Gy.

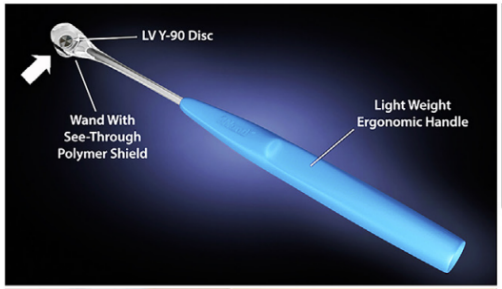
Y-90 source

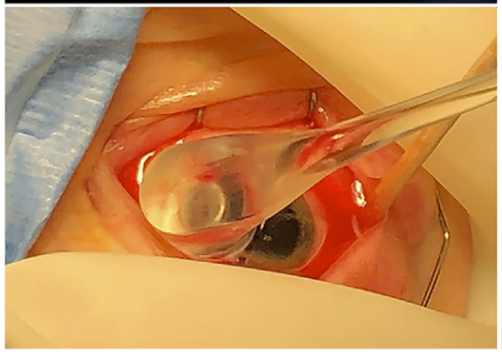


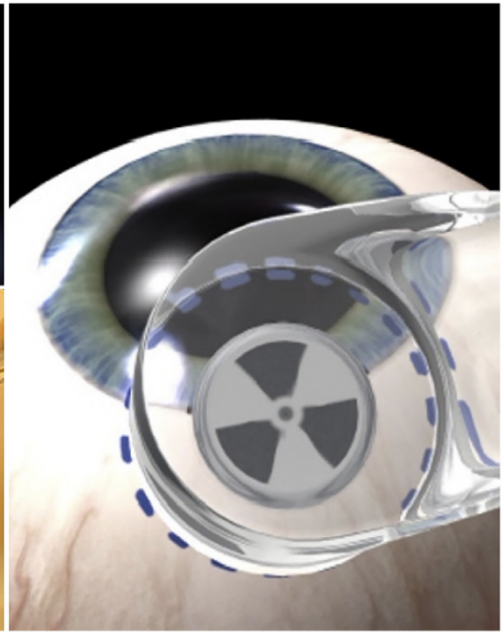
Source: P.T. Finger et al. / Brachytherapy 22 (2023) 416–427

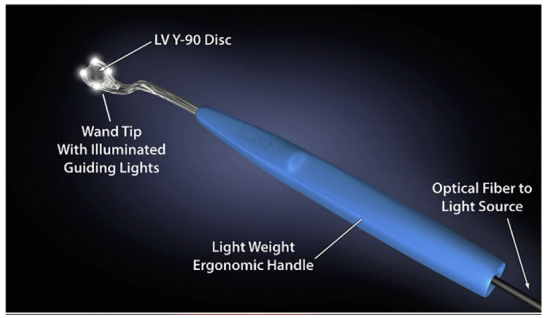
- 6 mm diameter
- 1 mm height

Source Illustration





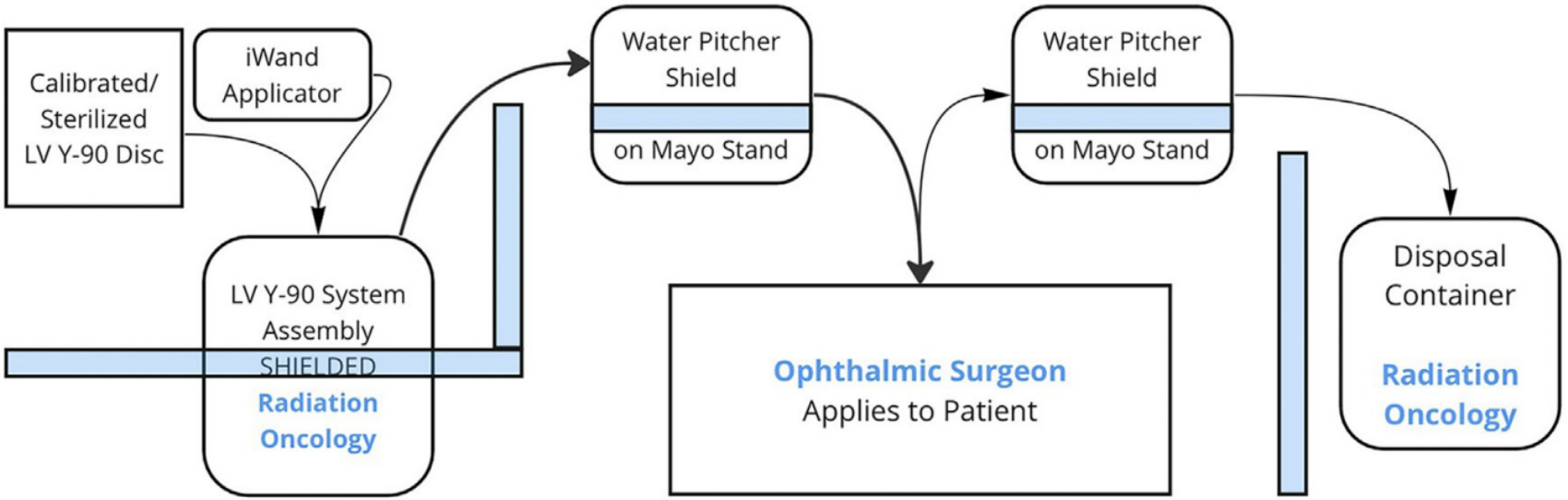




- Top left: iWand A (Anterior) applicator and its module (Lightweight of 8 grams).
- Middle left: Anterior applicator with its embedded Y-90 disc placed to treat an underlying uveal melanoma.
- Bottom left: iWand P (Posterior) applicator designed for treatment of tumors and growths in the posterior aspect of the eye globe.
- Right: Graphic illustration shows the site-defining tissue markings used to guide placement of the iWand A on target.

Source: P.T. Finger et al. / Brachytherapy 22 (2023) 416–427

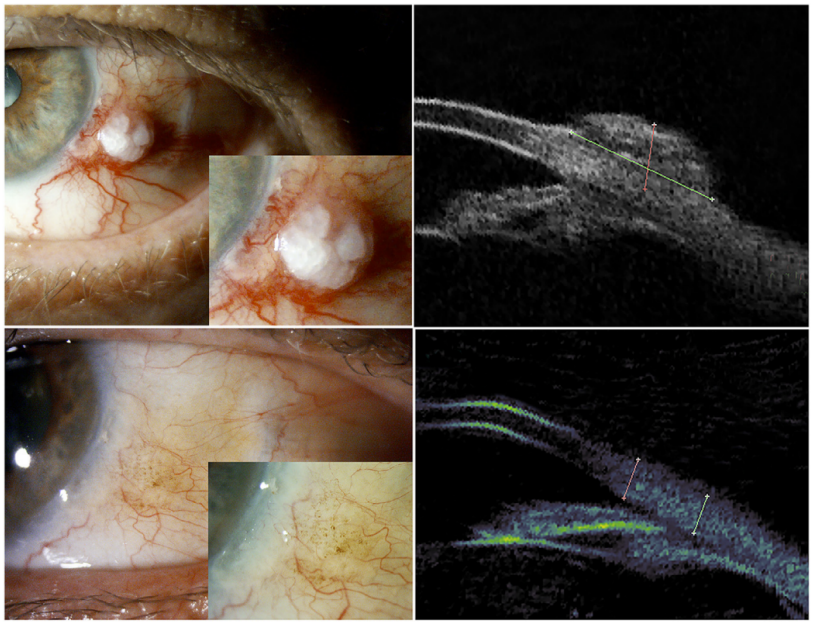
Treatment process for LV Y-90



Source: P.T. Finger et al. / Brachytherapy 22 (2023) 416–427

Tx Illustration with a case

- Case of microinvasive ocular surface malignant squamous carcinoma.
- Slit lamp photograph and high-frequency ultrasound imaging before (top left and top right, respectively) and 1-month follow-up after HDR Y-90 plaque therapy (bottom left and bottom right, respectively).



Source: P.T. Finger et al. / Brachytherapy 22 (2023) 416–427

Patient and Tumor Characteristics (without margins)

Patient and tumor characteristics

Patient	Tumor				AJCC
Age	Location	Thickness	Width	Length	Stage
66	Iris melanoma	0.6	3.0	3.1	cT1a
84	Iridociliary melanoma	0.8	2.9	2.7	cT2a
72	Choroidal melanoma	1.6	4.1	2.9	cT1a
82	Iris melanoma	1.1	2.6	2.7	cT1a
71	Iris melanoma	1.0	3.8	2.7	cT1a
80	M-OSSN	1.7	4.0	3.5	cT3

AJCC = American Joint Committee on Cancer staging system, M-OSSN = malignant ocular surface squamous neoplasia, tumor thickness/width/length = millimeters, Age = years.

Source: P.T. Finger et al. / Brachytherapy 22 (2023) 416–427

Treatment Parameters

Patient specific ^{90}Y plaque treatment parameters

Patient number	^{90}Y source activity	Prescription		
		Depth	Dose	Duration
1	16.0	2.5	25	348
2	8.76	2.5	30	773
3	15.48	1.6	30	219
4	16.63	2.3	30	345
5	13.8	2.5	22	356
6	15.31	2.6	30	476
Mean	14.33	2.3	27.8	420

Activity = mCi = millicurie, Depth = mm, Dose = Gy (1Gy= 100 cGy), Duration = seconds.

Source: P.T. Finger et al. / Brachytherapy 22 (2023) 416–427

Central Axis Dose Falloff

For Y-90 20 mCi source

Depth (mm)	Dose rate (Gy/min)
0.0	30.0
0.6	21.6
1.0	16.2
2.6	4.8

Source: P.T. Finger et al. / Brachytherapy 22 (2023) 416–427

Brachytherapy Team and their Role

- Ophthalmologist: Diagnosis, imaging, target definition, applicator placement.
- AU: Written directives, applicator placement, dose delivery, Tx planning, radiation safety.
- AMP: Determine source activity and place the order, source calibration, Tx time calculation, Tx planning, source sterilization, radiation safety, source disposal.

Specific Recommendations by the Subcommittee

- Section 5.2. The Subcommittee recommends stating clearly the two different training pathways, depending on whether the treatment is prescribed for the surface or prescribed at depth (below the surface).
- Section 5.2.2. should clearly describe that there are different training requirements for AUs treating superficial lesions versus AUs treating at depth (below the surface).
- Section 5.2.2.D. The Subcommittee strongly disagrees with requiring a written attestation statement for "involved non-AUs (i.e., an ophthalmologist)." Non-AUs are supervised individuals and do not require preceptor attestations.
- Section 5.2.3. The Subcommittee recommends that this procedure be performed in the presence of an AMP. The use of Ophthalmic Physicist should be deleted.

Specific Recommendations (Cont'd)

- Section 6.1. The Subcommittee recommends requiring the presence of both the AU and the AMP. This is similar to other procedures, such as Intravascular brachytherapy, prostate, and other procedures where the AU and the AMP are present.
- Section 6.4. Per the manufacturer's recommendation and other AAPM reports, calibration of the LV source must be performed by the user prior to use and compared to the manufacturer's stated activity. This is an important item for patient safety and accurate treatment. Any discrepancies must be resolved according to the AAPM guidelines related to source calibration and manufacturer's recommendations (±5%). [***Example***: Source of activity 8.76 mCi ordered to deliver dose of 25 Gy in 644 sec. Assume source received was 16 mCi and not 8.76 mCi. If not checked for calibration and used for the same treatment time, will deliver approx. 45.7 Gy or 82% more dose.]

Specific Recommendations (Cont'd)

- Section 6.5. Service and maintenance is not needed as this is a single use device. Recommend deleting this section.
- Section 6.6. The subcommittee recommends replacing "returned to the safe shielded position" with "returned to the shielded container."

General Comments on Dosimetry and Safety

The Subcommittee recognizes that the LV Disc and iWand system present few challenges:

a. Accounting for anisotropy of the source when performing the treatment plan.

b. Properly positioning and orienting the iWand.

c. Carefully dispensing the sterile adhesive and allowing it to cure when mounting the source on the iWand.

d. Members of the treatment team should take precautions to assure that their use of the source is in accordance with the manufacturer's instructions.

Acronyms

- AAPM: American Association of Medical Physicists in Medicine
- ACMUI: Advisory Committee on the Medical Use of Isotopes
- AMP: Authorized Medical Physicist
- AU: Authorized User
- Beta radiation: symbol β. High speed electron or positron emitted during the process of beta decay from a radioactive nucleus (Y-90)
- FDA: Food and Drug Administration
- Gy: Gray unit of dose
- HDR: High Dose Rate
- LDR: Low Dose Rate
- LV: Liberty Vision
- NRC: Nuclear Regulatory Commission
- Tx: Treatment
- Y-90: Yttrium 90 (isotope)

U.S. Nuclear Regulatory Commission
Advisory Committee on the Medical Uses of Isotopes
Subcommittee on LV Liberty Vision Y-90 Disc and iWand® Ophthalmic System

Subcommittee Review and Comments on:
LV LIBERTY VISION CORPORATION YTTRIUM-90 DISC AND IWAND® OPHTHALMIC SYSTEM DRAFT LICENSING GUIDANCE

Draft Report
March 11, 2024

Subcommittee Membership:
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Subcommittee Charge:

To review the Liberty Vision technology and comment on the NRC staff's draft licensing guidance for the LV Liberty Vision Corporation Yttrium-90 Disc and iWand® Ophthalmic System. This subcommittee was established by the Advisory Committee on the Medical Use of Isotopes (ACMUI) Chair, Dr. Darlene Metter, during the ACMUI's Fall 2021 Meeting on October 4, 2021. Note that implementation of the subcommittee charge was deferred while the NRC staff focused on high priority rulemaking and NRC-recognized specialty board efforts.

Introduction

The LV Liberty Vision ^{90}Yttrium Disc Source (LV Y-90 Disc Source) is a new eye applicator brachytherapy source for episcleral tumors and benign growths. The episcleral tissue is a thin layer of connective tissue in the eye that lies between the sclera (the white of the eye) and the conjunctiva (transparent membrane). This is a temporary brachytherapy procedure. The source manufactured by LV Liberty Vision Corporation has a sealed source and device certificate with the state of New Hampshire. Each source with activity up to 20 mCi (range of 10-20 mCi) is designed for a single use. The treatment time with such activity is in the order of 3-7 minutes. The NRC has determined that this product needs to be listed under 10 CFR 35.1000 and has developed the draft licensing guidance for this device.

This Subcommittee endorses the proposed draft licensing guidance, subject to the specific changes provided below.

Discussion

A) Specific comments

1) In section 1, the subcommittee recommends the deletion of the statement comparing the beta energy between the LV Y-90 and the Sr-90 sources.

2) In section 3, first paragraph: Recommend changing “upgraded” to “other.” The licensee, if authorized by the license, may possess other approved source models as they become available. These are not necessarily upgraded sources but simply with different diameters etc.
3) In section 5.2, the Subcommittee recommends stating clearly the two different training pathways, depending on whether the treatment is prescribed for the surface or prescribed at depth (below the surface).
4) Section 5.2.2 should clearly describe that there are different training requirements for AUs treating superficial lesions versus AUs treating at depth (below the surface).
5) In section 5.2.2.D, the Subcommittee strongly disagrees with requiring a written attestation statement for “involved non-AUs (i.e., an ophthalmologist).” Non-AUs are supervised individuals and do not require preceptor attestations.
6) In section 5.2.3, the Subcommittee recommends that this procedure be performed in the presence of an AMP. The use of Ophthalmic physicist should be deleted.
7) In section 6.1, the Subcommittee recommends requiring the presence of both the AU and the AMP. This is similar to other procedures, such as Intravascular brachytherapy etc. where the AU and the AMP are present.
8) In section 6.4, as per the manufacturer’s recommendation and other AAPM reports, the calibration of the LIV source must be performed by the user prior to its use and compared to the manufacturer’s stated activity. Any discrepancies must be resolved according to the AAPM guidelines related to source calibration and manufacturer’s recommendations (±5%).
9) In section 6.5, service and maintenance is not needed as this is a single use device. Recommend deleting this section.
10) In section 6.6, the committee recommends replacing “returned to the safe shielded position” with “returned to the shielded container”.

B) General comments

The Subcommittee recognizes that the LV Disc and iWand system present challenges in accounting for anisotropy of the source, properly positioning and orienting the iWand, dispensing sterile adhesive, and allowing the adhesive to cure. Members of the treatment team should take precautions to assure that their use of the source is in accordance with the manufacturer’s instructions.”

Respectfully submitted, March 11, 2024
Subcommittee on LV Liberty Vision Y-90 Disc and iWand® Ophthalmic System.
Advisory Committee on the Medical Use of Isotopes
U.S. Nuclear Regulatory Commission

DRAFT FOR ACMUI REVIEW

LV Liberty Vision Corporation Yttrium-90 Disc and iWand® Ophthalmic System

Licensing Guidance

{{date:long}}

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1. 10 CFR 35.1000 APPLICABILITY AND USE

The LV Liberty Vision ^{90}Yttrium Disc (hereafter the LV Y-90 Disc) is a manual brachytherapy source intended to be used within the Liberty Vision iWand® Ophthalmic System. The LV Y-90 Disc source has unique properties that merit radiation safety considerations and general licensing considerations beyond those required by Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, Subpart F, "Manual Brachytherapy." The LV Y-90 Disc is an yttrium-90 (Y-90) source with higher energy beta radiation compared to the beta radiation energy that is present in the traditional strontium-90 (Sr-90) sources, which are presently used in standard eye applicators for ophthalmic radiotherapy under 10 CFR 35.400, "Use of sources for manual brachytherapy." Furthermore, use of the LV Y-90 Disc falls outside of the requirements for physicians authorized under 10 CFR 35.491, "Training for ophthalmic use of strontium-90," for Sr-90 superficial eye applicator sources. The regulations in 10 CFR 35.433, "Strontium-90 sources for ophthalmic treatments," 10 CFR 35.491, and 10 CFR 35.2433, "Records of decay of Strontium-90 sources for ophthalmic treatments," are specific for the use of Sr-90 sources for ophthalmic radiotherapy by physicians other than radiation oncologists. As a result of these differences from the eye applicator sources currently regulated in 10 CFR Part 35, Subpart F, the use of the LV Y-90 Disc is regulated under the provisions of 10 CFR 35, Subpart K, "Other Medical Uses of Byproduct Material or Radiation from Byproduct Material."[1]

2. DEVICE DESCRIPTION AND USE

The LV Y-90 Disc and iWand® Ophthalmic System are a source and eye applicator system that use high dose rate beta radiation from Y-90 for episcleral brachytherapy of tumors and benign growths. The LV Y-90 Disc is temporarily positioned on the treatment area using the LV Liberty Vision Corporation iWand® applicator series – iWand® Anterior (A) for anterior placement or iWand® Posterior (P) for posterior placement. The applicator systems have operational commonality with the source affixed to the applicators and the applicator handles allowing for manipulation of the source. The source is comprised of a single solid metal cylindrical disc of Y-90 encapsulated in titanium. Y-90 has a half-life of 2.67 days or 64.1 hrs., and decays by beta emission with average energy of 934 keV (max energy 2,280 keV). Both the source and the iWand® applicators are single or one-time use and the source can be disposed of by decay-in-storage or by return to manufacturer or authorized recipient.

The LV Y-90 Disc was approved by the U.S. Food and Drug Administration with the trade/device name – "LV Liberty Vision Model 1 ^{90}Yttrium" (in a Section 510(k) Number K163571 premarket notification of intent to market, dated March 15, 2017), for episcleral brachytherapy of tumors and benign growths and for use within a manual brachytherapy system. The Sealed Source and Device (SS&D) registration certificate for the source includes a source model – "Model 1 ^{90}Yttrium Brachytherapy Source" with a source diameter size of 6.0 millimeters (mm). More information about the source can be found in its SS&D registration certificate, NH-1501-S-101-S. This licensing guidance is applicable to the Model 1, 6 mm source that was approved in the SS&D registration certificate at the time of issuance of the guidance.

[1] 10 CFR 35.1000 is designated as Compatibility Category D. Agreement States are not required to adopt these regulations for purposes of compatibility but are not prohibited from adopting Compatibility Category D regulations if they so choose. If Agreement States choose to adopt this licensing guidance, references to 10 CFR should be changed to the equivalent Agreement State regulations.

3. LICENSING GUIDANCE

The license conditions in this guidance provide applicants with one acceptable means of satisfying the requirements for a license to authorize the use of the LV Y-90 Disc in the manufacturer's iWand® applicator device/system. This information is not intended to be the only means of satisfying the requirements. While the guidance refers generically to the LV Y-90 Disc, under 10 CFR 30.33(a)(3), the applicant or licensee must document the model that will be possessed and used, but the NRC will not include the model number on the license. There are provisions and commitments in sections 5, 7 and 8 of this guidance that if authorized on the license, will permit the licensee to possess and use upgraded source models, as appropriate.

The applicant must submit the information required by 10 CFR 30.33, "General Requirements for Issuance of Specific Licenses," and 35.12, "Application for License, Amendment, and Renewal," as described below. The applicant should submit additional information and commitments requested below or may, unless the information is specifically required by regulation, submit alternative information and commitments for review by the U.S. Nuclear Regulatory Commission (NRC) staff to make a licensing determination. The commitments incorporated by license condition into the applicant's license will be reviewed during routine inspections. If an applicant commits to the guidance provided below, the applicant must follow commitments described with the use of the word "should." This guidance may be revised as additional experience is gained regarding the medical use of the LV Y-90 Disc.

Applicants should also refer to NUREG-1556, Volume 9, Revision 3, "Consolidated Guidance About Material Licenses: Program-Specific Guidance about Medical Use Licenses," as it provides overall licensing guidance for all medical uses of byproduct material, including applicable model procedures for audits, occupational dose monitoring program and surveys. Guidance specific for the use of the LV Y-90 Disc under 10 CFR 35.1000, "Other medical uses of byproduct material or radiation from byproduct material" are contained herein.

4. REQUIREMENTS NOT SPECIFIC TO 10 CFR 35.1000 USE

In addition to meeting the applicable regulation in Subpart F – Manual Brachytherapy, applicants must commit to meet the general requirements in 10 CFR Part 35, Subpart A — General Information; Subpart B —General Administrative Requirements; Subpart C —General Technical Requirements; Subpart L —Records; and Subpart M —Reports; except as specified in this guidance. Additionally, applicants must meet applicable requirements of 10 CFR Part 19, "Notices, Instructions and Reports to Workers: Inspection and Investigations;" Part 20, "Standards for Protection Against Radiation;" Part 30, "Rules of General Applicability to Domestic Licensing of byproduct material," and Part 71, "Packaging and Transportation of Radioactive Material." The enclosed consolidated technical analysis table provides guidance on applicable requirements.

5. SPECIFIC LICENSING GUIDANCE FOR THE LV LIBERTY VISION YTTRIUM-90 DISC

5.1. Radionuclides, Form, Possession Limits, and Purpose of Use

Pursuant to 10 CFR 35.12(c), the applicant must identify the radionuclide, chemical/physical form, requested maximum possession limit, and purpose of use. The NRC Form 313, "Application for Materials License," may be used to submit this information. The information in the table below provides the suggested format and information for completing Item 5 (Radioactive Material) and Item 6 (Purpose of Use) on the NRC Form 313, "Application for Materials License."

Radionuclides: (NRC Form 313 Item 5a)	Yttrium-90 permitted by 10 CFR 35.1000
Chemical/Physical Form: (NRC Form 313 Item 5b)	Sealed sources (Manufacturer and Model Number, e.g., LV Liberty Vision Corporation, LV Model 1 Y-90 Disc)
Maximum Possession Limit: (NRC Form 313 Item 5c)	___ mCi[2]
Purpose of Use: (NRC Form 313 Item 6)	For medical use in the Liberty Vision iWand® Anterior Applicator or iWand® Applicator Posterior permitted by 10 CFR 35.1000.

5.2. Training and Experience

Licensees must have at least one Authorized User (AU), one Authorized Medical Physicist (AMP), and one Radiation Safety Officer (RSO) for medical use of the LV Y-90 Disc for the source to be added to the license. The NRC has determined that individuals meeting the training and experience (T&E) criteria below will be considered qualified and can be authorized for use of the LV Y-90 Disc within the Liberty Vision iWand® Applicator Systems, for episcleral brachytherapy of tumors and benign growths or for superficial episcleral brachytherapy (i.e., ophthalmic radiotherapy that is not beyond the surface or at a depth beyond the surface). Applicants must submit documentation showing these criteria are met. Alternatively, applicants may also submit alternative T&E commitments to be reviewed on a case-by-case basis by NRC staff. The commitments should include an explanation of why the applicant believes the alternative T&E commitments demonstrate that the individual is qualified to be an authorized individual.

5.2.1. Grandfathering

If the NRC revises the T&E criteria (i.e., in subsequent revisions to this guidance), individuals previously considered to be qualified and authorized for use of a specific

[2] Maximum limit for the LV Model 1 Y-90 Disc as listed in SS&D registration certificate (20 millicuries at time of treatment and 80 millicuries at time of shipment to treatment facility).

model of the LV Y-90 Disc and Liberty Vision iWand® Applicator Systems do not have to meet the revised criteria for that model.

5.2.2. Authorized User (AU)

Applicants and licensees should identify each AU and provide documentation of T&E in the use of the LV Y-90 Disc within the Liberty Vision iWand® Applicator Systems. The NRC Form 313A (AUS), "Authorized User Training, Experience, and Preceptor Attestation (for uses defined under 10 CFR 35.400 and 35.600) [10 CFR 35.57, 35.490, 35.491, and 35.690]," or other formats which capture equivalent information may be used to document this T&E.

The NRC has determined that there are two categories of AUs for the medical use of the LV Y-90 Disc within the Liberty Vision iWand® Applicator Systems.

A. An AU for medical use of the LV Y-90 Disc for episcleral brachytherapy, including superficial ophthalmic radiotherapy. This AU is a physician:

   ~~1.~~ Currently identified as an AU for— (i) medical use permitted by 10 CFR 35.400 or 35.600, or (ii) medical use of the LV Y-90 Disc permitted by 10 CFR 35.1000; AND meets the additional device and clinical use T&E criteria in Item C;

   OR

   2. That meets the T&E requirements in 10 CFR 35.490, "Training for use of manual brachytherapy sources," or 10 CFR 35.690, "Training for use of remote afterloader units, teletherapy units, and gamma stereotactic radiosurgery units," or 10 CFR 35.57, "Training for experienced Radiation Safety Officer, teletherapy or medical physicist, authorized medical physicist, authorized user, nuclear pharmacist, and authorized nuclear pharmacist;" and meets the additional T&E criteria in Items C and D.

B. An AU for medical use of the LV Y-90 Disc for superficial episcleral brachytherapy (i.e., superficial ophthalmic radiotherapy that is not beyond the surface or at a depth beyond the surface). This AU is a physician:

   1. Currently identified as an AU for— (i) medical use permitted by 10 CFR 35.400 or 35.600, or (ii) medical use of the LV Y-90 Disc permitted by 10 CFR 35.1000, or (iii) medical use of the LV Y-90 Disc for superficial ophthalmic radiotherapy permitted by 10 CFR 35.1000; AND meets the additional training criteria in Item C;

   OR

2. That meets the T&E requirements in 10 CFR 35.490, “Training for use of manual brachytherapy sources,” or 10 CFR 35.57, “Training for experienced Radiation Safety Officer, teletherapy or medical physicist, authorized medical physicist, authorized user, nuclear pharmacist, and authorized nuclear pharmacist;” and meets the additional training criteria in Item C and as applicable in Item D;

OR

3. Listed on an NRC or Agreement State license (or NRC Master Materials License) as an AU for – Strontium-90 for ophthalmic radiotherapy permitted by 10 CFR 35.400; and meets the additional training criteria in Items C and D;

OR

4. That meets the T&E requirements in 10 CFR 35.491, "Training for ophthalmic use of strontium-90,” by successfully completing the minimum number of hours of classroom and laboratory training and the supervised clinical training to include all the topics described in paragraphs (b)(1) and (b)(2), but specifically for use of the LV Y-90 Disc; and meets the additional training criteria in Items C and D.

C. Both categories of AUs and involved non-AUs (i.e., an ophthalmologist) should receive and successfully complete additional training in the hands-on device operation, safety procedures, and clinical use for the same model of the LV Y-90 Disc and the LV iWand® Applicator Systems (i.e., iWand® A and iWand® P) for which authorization is sought. This training may be satisfied by completing training provided by the LV Y-90 Disc vendor; or by completing training that is supervised by an AU or authorized medical physicist (AMP), as appropriate, who is authorized for use of the same model of the LV Y-90 Disc and the LV iWand® Applicator Systems for which the individual is seeking authorization.

D. Both categories of AUs and involved non-AUs (i.e., an ophthalmologist), except the individuals listed in Items A.1. and B.1., should obtain a written attestation affirming that the individual has satisfactorily completed the above training and is able to independently fulfill the radiation safety-related duties as an AU for applicable use of the LV Y-90 Disc and the LV iWand® Applicator Systems. The written attestation must be signed by a preceptor AU who is authorized for use of the same model of the LV Y-90 Disc and the LV iWand® Applicator Systems that is being requested or a residency program director, similar to that in 10 CFR 35.490, but with the faculty member physician that is an AU for the same model of the LV Y-90 Disc and the LV iWand® Applicator Systems for which the individual is seeking authorization. The written attestation is not required for individuals who hold certification by a recognized specialty board or are already authorized for use of another manual brachytherapy source under 10 CFR 35.400.

5.2.3. Authorized Medical Physicist (AMP)

Applicants and licensees should identify each AMP and provide documentation of T&E in the use of the LV Y-90 Disc and the LV iWand® Applicator Systems. The NRC Form 313A (AMP), "Authorized Medical Physicist Training, Experience, and Preceptor Attestation [10 CFR 35.51, 35.57(a)(3), and 35.433]," or other formats which capture equivalent information may be used to document this T&E.

An AMP for medical use of the LV Y-90 Disc is an individual:

1. Currently identified as an AMP for— (i) medical use of the LV Y-90 Disc and iWand® Applicator Systems permitted by 10 CFR 35.1000; or (ii) meets the T&E requirements in 10 CFR 35.51, "Training for an authorized medical physicist;" or the definition of *authorized medical physicist* in 10 CFR 35.2, "Definitions;" or the requirements in 10 CFR 35.57;

   AND

2. That has received and successfully completed additional training in the hands-on device operation, safety procedures, and clinical use of the LV Y-90 Disc and the LV iWand® Applicator Systems (i.e., iWand® A and iWand® P). This training may be satisfied by completing training provided by the LV Y-90 Disc vendor, or by completing training that is supervised by an AMP authorized for use of the same model of the LV Y-90 Disc and iWand® Applicator Systems for which the individual is seeking authorization.

   AND

3. That has obtained a written attestation affirming that the individual has satisfactorily completed the above training and is able to independently fulfill the radiation safety-related duties as an AMP for use of the LV Y-90 Disc and iWand® Applicator Systems. The written attestation must be signed by a preceptor AMP that is authorized for the use of the same model of the LV Y-90 Disc and the LV iWand® Applicator Systems that is being requested. The written attestation is not required for individuals who hold certification by a recognized specialty board or are already authorized for use of the LV Y-90 Disc.

The applicant must submit documentation for all of the above T&E for each AMP of the LV Y-90 Disc and the applicable LV iWand® Applicator System. The NRC Form 313A (AMP), "Authorized Medical Physicist or Ophthalmic Physicist, Training, Experience and Preceptor Attestation [10 CFR 35.51, 35.57(a)(3), 35.433]," or other formats which capture equivalent information may be used to document T&E.

5.2.3. Ophthalmic Physicist

An ophthalmic physicist for medical use of the LV Y-90 Disc is an individual:

1. Listed on an NRC or Agreement State license (or NRC Master Materials License) as an AMP for medical use of the LV Y-90 Disc and iWand® Applicator Systems; or meets the T&E criteria 10 CFR 35.51, “Training for an authorized medical physicist;” or the definition of *authorized medical physicist* in 10 CFR 35.2, “Definitions;” or the requirements in 10 CFR 35.57;

   AND

2. That has received and successfully completed additional training in the operation, safety procedures, and clinical use of the LV Y-90 Disc and the applicable LV iWand® Applicator Systems. This training should include hands-on device operation commensurate with the individual’s duties. This training may be satisfied by completing training provided by the LV Y-90 Disc vendor; or by completing training that is supervised by an AMP authorized for the LV Y-90 Disc and iWand® Applicator Systems.

   AND

3. That has obtained a written attestation that the individual has satisfactorily completed these requirements and is able to independently fulfill the radiation safety-related duties as an AMP for use of the LV Y-90 Disc and iWand® Applicator Systems. The written attestation must be signed by a preceptor AMP that is authorized for the use of the LV Y-90 Disc and the LV iWand® Applicator Systems that is being requested. The written attestation is not required for individuals who hold certification by a recognized specialty board or are already authorized for use of the LV Y-90 Disc.

The applicant must submit documentation for all of the above T&E for each AMP of the LV Y-90 Disc and the applicable LV iWand® Applicator System. The NRC Form 313A (AMP), “Authorized Medical Physicist or Ophthalmic Physicist, Training, Experience and Preceptor Attestation [10 CFR 35.51, 35.57(a)(3), 35.433],” or other formats which capture equivalent information may be used to document T&E.

5.2.4. Radiation Safety Officer (RSO) and Associate Radiation Safety Officer

An RSO with responsibility for the LV Y-90 Disc within the LV iWand® Applicator Systems is an individual:

a. Listed as an RSO on an NRC or Agreement State license (or NRC Master Materials License) for the LV Y-90 Disc and iWand® Applicator Systems; or that meets the T&E criteria in 10 CFR 35.50, "Training for Radiation Safety Officer;” or the definition of Radiation Safety Officer in 10 CFR 35.2, “Definitions;” or the requirements in 10 CFR 35.57;

AND

That has received and successfully completed additional training in the radiation safety, regulatory issues, and emergency procedures of the LV Y-90 Disc and IiWand® Applicator Systems. This training requirement may be satisfied by completing training provided by the LV Y-90 Disc vendor or by completing training that is supervised by an individual (AU, AMP or RSO, as appropriate) who is authorized for the LV Y-90 Disc.

The applicant must submit documentation for all the above T&E for the RSO of the LV Y-90 Disc. NRC Form 313A (RSO), "Radiation Safety Officer Training and Experience and Preceptor Attestation [10 CFR 35.50]," or other formats which capture equivalent information may be used to document T&E.

6. LICENSE CONDITIONS

The applicant or licensee shall commit to follow all applicable requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use. The table contained in the appendix to this licensing guidance document provides more details on applicable 10 CFR Part 35 requirements. If this authorization is approved, these conditions will be incorporated as license conditions in the licensee's license. This may be done by incorporating the commitments in the tie down condition. The applicant or licensee shall commit to the following licensing commitments.

6.1. Physical Presence

1. Use of the LV Y-90 Disc for superficial episcleral brachytherapy (i.e., ophthalmic radiotherapy that is not beyond the surface or at a depth beyond the surface) will be conducted in the physical presence of an:

    a. AMP authorized for use of the LV Y-90 Disc and iWand® Ophthalmic System; or

    b. AU authorized for episcleral brachytherapy, including superficial episcleral brachytherapy; or

    c. RSO authorized for the LV Y-90 Disc and iWand® Ophthalmic System (except an RSO who is an AU authorized only for superficial episcleral brachytherapy).

2. For all procedures beyond superficial episcleral brachytherapy, the AU will consult with the ophthalmologist and an AMP authorized for use of the LV Y-90 Disc and iWand® Ophthalmic System before initiating treatment. The procedures will be conducted in the physical presence of either the AU authorized for procedures beyond superficial episcleral brachytherapy, or AMP authorized for the LV Y-90 Disc and iWand® Ophthalmic System.

6.2. Radiation Protection Program Changes

The above licensing guidance may be revised as additional experience is gained regarding medical use of the LV Y-90 Disc by the regulator or manufacturer. Therefore, in contrast with 10 CFR 35.26, a licensee already authorized to use the LV Y-90 Disc and that has committed, by license conditions, to follow the provisions in this guidance existing at the time of commitment, must apply for and receive an amendment to its license prior to making changes to conform to the revised guidance and additional radiation safety recommendations.

An applicant initially applying for authorization for medical use of LV Y-90 Disc (or a licensee applying later for an amendment to conform to revisions in this guidance) may request authorization to allow future changes to its radiation safety program, provided the following conditions are met:

1. The revision is in compliance with the regulations of the NRC or Agreement State;

2. The revision is based on the current licensing guidance for the LV Y-90 Disc under 10 CFR 35.1000 use posted on the NRC Web site;

3. The revision has been reviewed and approved by the licensee's RSO and management;

4. The affected individuals are instructed on the revised program before the change is implemented;

5. The licensee will retain a record of each change for five years; and

6. The record will include a copy of the appropriate NRC Web site guidance, the old procedure, the new procedure, the effective date of the change, and the signature of the licensee's management representative who reviewed and approved the change.

6.3. Written Directives

The licensee should complete a written directive in accordance with 10 CFR 35.40, "Written directives." In addition, the applicant or licensee should commit to including the source activity as part of the written directive. As the intended use of the LV Y-90 Disc is similar to Sr-90 sources used for ophthalmic radiotherapy under 10 CFR 35.400, the activity of the Y-90 source should also be calculated to determine the treatment times, similar to the requirement for Sr-90 sources in accordance with 10 CFR 35.433. For use of the LV Y-90 Disc, the written directive shall, before treatment, be signed and dated by an AU, and contain the patient or human research subject's name, treatment site, radionuclide, source activity, and total dose.

6.4. Calibration

Licensees shall commit to following 10 CFR 35.432, "Calibration measurements of brachytherapy sources," and 10 CFR 35.2432, "Records of calibration measurements of brachytherapy sources," for calibration and recordkeeping. In accordance with 10 CFR 35.432, licensees may use measurements provided by the source manufacturer.

The activity of each Y-90 source that is used to determine the treatment times for brachytherapy treatments will be calculated by either an AMP authorized for the LV Y-90 Disc and iWand® Ophthalmic System or another individual whose calculation will be reviewed by the AMP authorized for the LV Y-90 Disc and iWand® Ophthalmic System. If an individual other than an AMP authorized for the LV Y-90 Disc and iWand® Ophthalmic System calculates the activity of the Y-90 source, the AMP will review the calculated activity within 15 days prior to the first post-calculation treatment utilizing the source. The records will include the name of the individual who performed the activity calculation, the signature of the AMP who reviewed the calculation, and the date of the AMP's review. The decay will be based on the activity determined under 10 CFR 35.432.

6.5. Service and Maintenance

Service and maintenance will be performed only by the manufacturer or persons specifically licensed by NRC or an Agreement State to perform such services. Service and maintenance will be conducted at intervals specified in the SS&D registration certificate.

Prior to each treatment, the LV Y-90 Disc source will be sterilized and installed into the ophthalmic applicator system by the licensee following the manufacturer instructions.

6.6. Surveys

In addition to the surveys after source implant and removal, and surveys of the patient or human research subject, required by 10 CFR 35.404, as well as the area surveys required by 10 CFR Part 20 and 10 CFR 35.70, "Surveys of ambient radiation exposure rate," the licensee shall commit to survey in accordance with the manufacturer's recommended procedures, pre-treatment and post-treatment visual inspections will be conducted, and a survey of the patient or human research subject and ophthalmic applicator system should be conducted with a portable radiation detection survey instrument to confirm that the source has been removed from the patient or human research subject and returned to the safe shielded position. In addition, pretreatment and post-treatment surveys of the storage container, ophthalmic applicator system, and procedure room will be conducted to ensure that the source has been stored in its storage location.

6.7. Emergency Procedures

Written emergency procedures will be developed, implemented, and maintained. As a minimum, these procedures will address appropriate preparation and handling procedures when emergency source manipulation is needed, when emergency operations must be performed, and steps needed when the source or source assembly is damaged. The procedures will include a description of appropriate emergency response equipment, any appropriate surgical interventions, and responsible individuals.

7. NOTES TO LICENSEES

7.1. Alterations to the LV Y-90 Disc and iWand® Ophthalmic System

This licensing guidance is based on the SS&D safety evaluation in Registration Certificate NH-1501-S-101-S. Modification of the source (including source model or size), will require a new or amended SS&D safety evaluation that addresses the conditions of use and safety of the modified LV Y-90 Disc. Additionally, modification of the Liberty Vision iWand® or use of other manual brachytherapy systems or the source-device combination may require a new or amended SS&D safety evaluation that addresses the conditions of use and safety of the modified LV Y-90 Disc and iWand® Ophthalmic System.

7.2. Changes in Physical Conditions of Use

If the physical conditions of use exceed those reported in the SS&D registration certificate, a limited specific medical use licensee shall request an amendment for the new conditions, and a broad scope licensee shall perform its own engineering and radiation safety evaluations addressing those differences.

7.3. Notification for AUs and AMPs

The NRC recognizes that if an AU or AMP satisfies the T&E listed in the NRC's licensing guidance for the LV Y-90 Disc source and is currently listed on a Commission or Agreement State medical use license or permit for episcleral brachytherapy use of the LV Y-90 Disc, the AU or AMP should be allowed to work under a different license for the same medical use. A limited specific medical use applicant initially applying for authorization for the medical use of the LV Y-90 Disc or an existing licensee applying for an amendment for the medical use of the LV Y-90 Disc may request authorization to notify the NRC in the future that it has permitted an AU or AMP to work at its facility without the need to request an additional license amendment, provided the following conditions are met:

- The AU or AMP meets the training and experience criteria listed in NRC's current licensing guidance for the LV Y-90 Disc and iWand® Ophthalmic System; and

- The AU or AMP is currently listed for the LV Y-90 Disc use on a Commission or Agreement State license, a permit issued by a Commission Master Material License, a permit issued by a Commission or Agreement State licensee of a broad scope, or a permit issued by a Commission Master Material License broad scope permittee; and

- The licensee provides NRC a copy of the license or permit on which the AU or AMP was originally listed for the LV Y-90 Disc; and

- The licensee provides documentation to NRC for each AU or AMP of the above listed conditions no later than 30 days after the date that the licensee allows the AU or AMP to work as an AU or AMP for the LV Y-90 Disc.

If this authorization is approved, these notification conditions will be incorporated as license conditions in the licensee's license.

7.4. Brachytherapy Source Accountability

Licensees shall maintain accountability at all times for all brachytherapy sources in storage or use in accordance with 10 CFR 35.406, “Brachytherapy sources accountability.” When not in use, the LV Y-90 Disc and ophthalmic applicator system should be stored in its storage container and the storage container will be locked in an authorized secure location. In addition, licensees shall maintain records of brachytherapy sources accountability in accordance with 10 CFR 35.2406, “Records of brachytherapy source accountability.”

8. NOTES TO REGULATORS

8.1. Alterations to the LV Y-90 Disc and iWand® Ophthalmic System

License reviewers should confirm that the model and size of the source match those listed in the current SS&D registration certificate.

8.2 Inspection Frequency

Licenses authorizing the LV Y-90 Disc should be inspected every two years. Per Enclosure 1 to Inspection Manual Chapter 2800, “Materials Inspection Program,” licenses authorizing emerging technology under 10 CFR 35.1000 are assigned a Priority 2 inspection code.

8.3 Program Code

The NRC Regions should use program code 02240.

9. PAPERWORK REDUCTION ACT STATEMENT

This licensing guidance provides voluntary guidance for implementing the mandatory information collections in 10 CFR Parts 30 and 35 that are subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et. seq.). These information collections were approved by the Office of Management and Budget (OMB), approval numbers 3150-0017 and 3150-0010. Send comments regarding this information collection to the Information Services Branch (T6-A10M), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, or by e-mail to Infocollects.Resource@nrc.gov, and to the OMB reviewer at: OMB Office of Information and Regulatory Affairs (3150-0017 and 3150-0010), Attn: Desk Officer for the Nuclear Regulatory Commission, 725 17th Street, NW Washington, DC 20503; e- mail: oira_submission@omb.eop.gov.

10. PUBLIC PROTECTION NOTIFICATION

The NRC may not conduct or sponsor, and a person is not required to respond to, a collection of information unless the document requesting or requiring the collection displays a currently valid OMB control number.

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

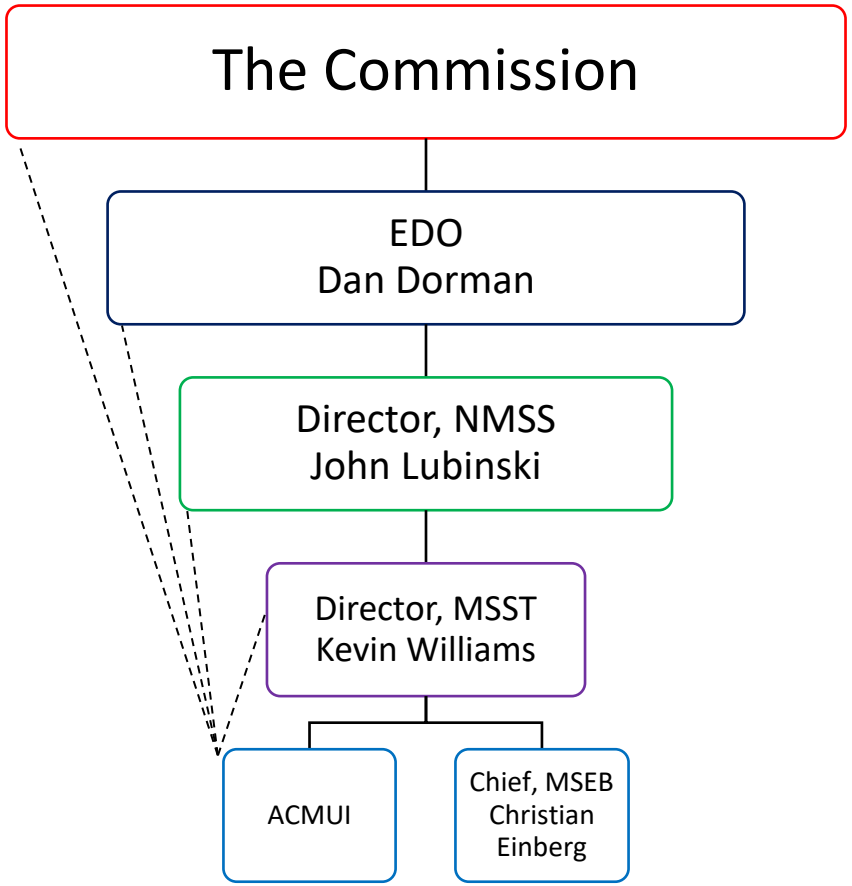
ACMUI Reporting Structure

Lillian Armstead
ACMUI Coordinator
April 8, 2024

Outline

- Current Reporting Structure
- Annual Review
- Meetings
- Discussion

Current Reporting Structure



Annual Review

- In September 2012, the ACMUI recommended to have an annual review of reporting structure.

Meetings

- Two meetings each year
- April/May
- October/November

- Approximately 2-3 teleconferences (as needed)

ACMUI Discussion

Points of Contact

- Kevin Williams – MSST Director
- Kevin.Williams@nrc.gov

- Christian Einberg – Designated Federal Officer (DFO), Chief, MSEB
- Christian.Einberg@nrc.gov

- Lillian Armstead – ACMUI Coordinator
- Lillian.Armstead@nrc.gov

Acronyms

- ACMUI – Advisory Committee on the Medical Uses of Isotopes
- DFO – Designated Federal Officer
- EDO – Executive Director for Operations
- MSST – Division of Materials Safety, Security, States, and Tribal Programs
- MSEB – Medical Safety and Events Assessment Branch
- NMSS – Office of Nuclear Material Safety and Safeguards

OPEN FORUM

(No Handout)

September 2024

Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2 **Labor Day**	3	4	5	6	7
8	9 **Tentative ACMUI Date**	10 **Tentative ACMUI Date**	11	12	13	14
15	16	17	18	19	20	21
22	23 **World Medical Innovation Forum**	24 **World Medical Innovation Forum** **ABMS**	25 **World Medical Innovation Forum** **ABMS**	26 **ABMS**	27	28
29 **ASTRO**	30 **ASTRO**					

October 2024

Sun	Mon	Tue	Wed	Thu	Fri	Sat
		1 **ASTRO**	2 **ASTRO** **Rosh Hashanah**	3 **Rosh Hashanah**	4 **Rosh Hashanah**	5
6	7 **Tentative ACMUI Date**	8 **Tentative ACMUI Date**	9	10	11 **Yom Kippur**	12 **Yom Kippur**
13	14 **Columbus Day**	15	16 **Sukkot**	17 **Sukkot**	18 **Sukkot**	19 **Sukkot** **Annual Advocacy Summit 2024**
20 **Sukkot** **Annual Advocacy Summit 2024**	21 **Sukkot** **Annual Advocacy Summit 2024**	22 **Sukkot**	23 **Sukkot** **Shemini Atzeret & Simchat Torah**	24 **Shemini Atzeret & Simchat Torah**	25 **Shemini Atzeret & Simchat Torah**	26
27	28	29	30	31		

November 2024

Sun	Mon	Tue	Wed	Thu	Fri	Sat
					1	2
3	4 **Tentative ACMUI Date**	5 **Tentative ACMUI Date**	6	7	8	9
10	11 **APG Annual Fall Conference** **Veterans Day**	12 **APG Annual Fall Conference**	13 **APG Annual Fall Conference**	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30