Implementation Experience with Y-90 Microsphere Brachytherapy Licensing Guidance

Ashley Cockerham

Founder & Principal Consultant

Organization of Agreement States Annual Meeting

August 17, 2021

Disclosures

Medical Consultant

Boston Scientific – Peripheral Interventions

Ashley.Cockerham@bsci.com

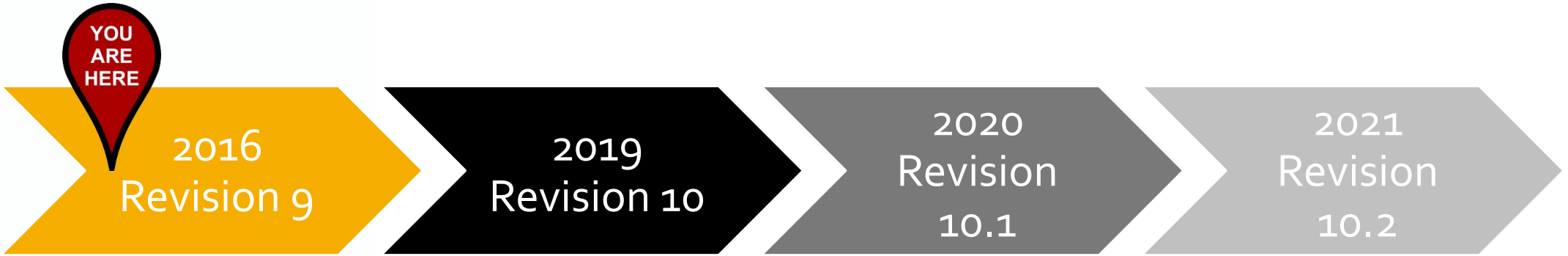
c. (703) 945-5959

Topics for Discussion

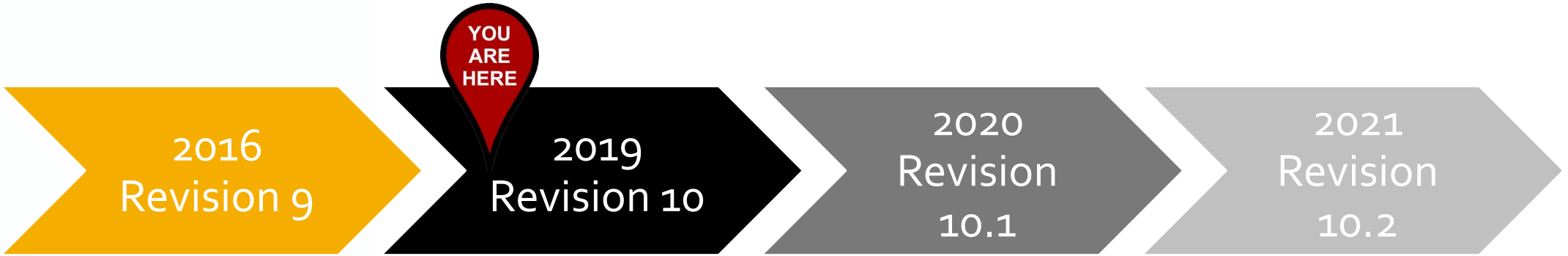
- Overview of NRC Guidance changes from 2016-2021
  - Minor changes
  - Major changes - AU to AU training & proctoring; attestation

- Other state-specific requirements or license commitments
  - Attestations for board certified individuals
  - Physical presence
  - Semi-annual physical inventories
  - Nuclear medicine technician accreditation
  - Possession licensing language
  - Authorized use licensing language

Review of NRC Guidance Changes

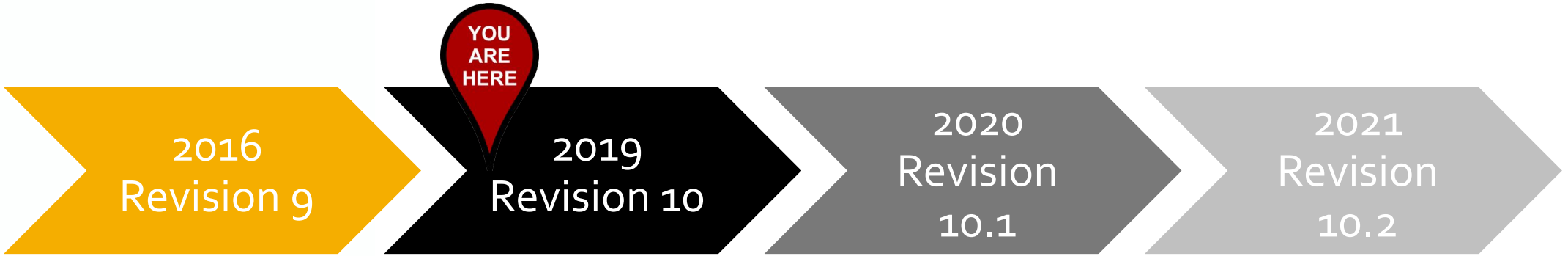


Review of NRC Guidance Changes - Minor



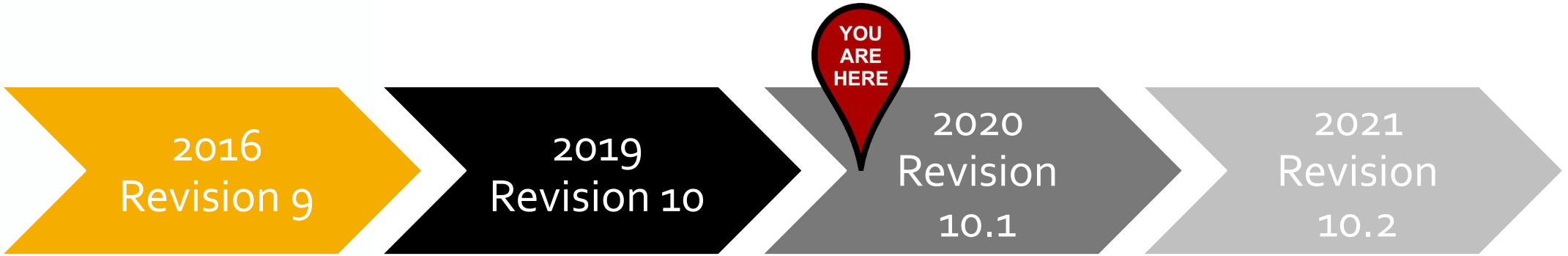
- Deleted per vial limits and 2 Ci total limit suggestion
  - Now listed as 'X' Ci total only
- Added license commitment for therapeutic use as approved in the SSDR, including max activity per vial limit
- Revised requirement for semi-annual physical inventory due to short half life of Y-90 and other requirements for accountability

Review of NRC Guidance Changes - Major



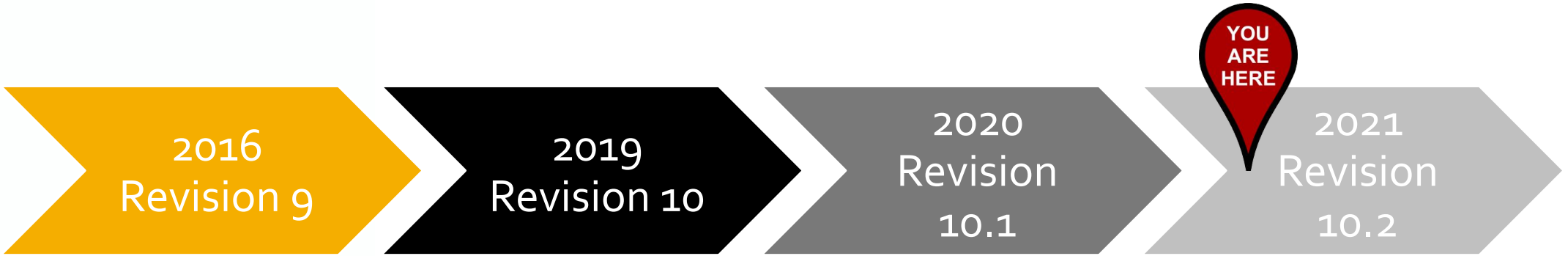
- Authorized Individuals
  - Existing AUs for Y-90 recognized
  - Certain parts of old "A-G" training must be supervised by an existing AU instead of the manufacturer
  - Time limits regarding proctored cases (initiate within 6 months; 12 months to complete; documentation in 60 days)
  - Recentness of training requirements now applicable
  - **AU to AU proctoring required effective May 6, 2020**
  - **Written attestation required**

Review of NRC Guidance Changes



- Authorized Individuals
  - Existing AUs for Y-90 recognized
  - Certain parts of old "A-G" training must be supervised by an existing AU instead of the manufacturer
  - Time limits regarding proctored cases (initiate within 6 months; 12 months to complete; paperwork in 60 days)
  - Recentness of training requirements now applicable
  - **AU to AU proctoring required effective November 8, 2021**
  - Written attestation required

Review of NRC Guidance Changes



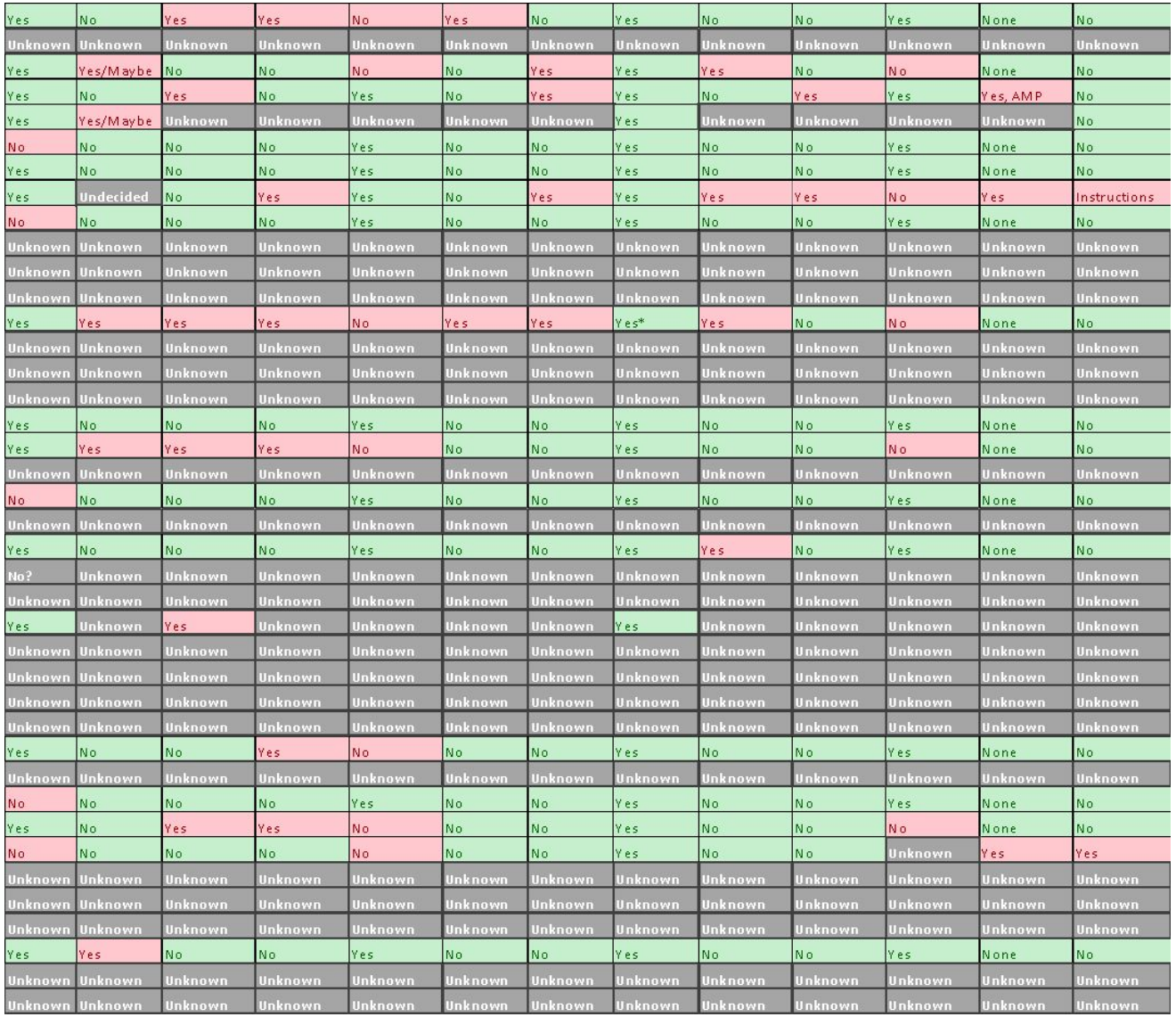
- TheraSphere™ receives FDA Pre-Market Approval March 21, 2021
  - Guidance revised to remove references to Humanitarian Device Exemption and Institutional Review Boards

Agreement State Survey

- Does your state allow manufacturer representatives to proctor?
- If so, will you continue to allow it after Nov 8, 2021?
- Any other requirements (e.g., physical presence)?
- Do you publish your own Y-90 microsphere guidance?

Take the survey!

Agreement State Implementation



Yes	No	Yes	Yes	No	Yes	No	Yes	No	No	Yes	None	No
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Yes	Yes/Maybe	No	No	No	No	Yes	Yes	Yes	No	No	None	No
Yes	No	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes, AMP	No
Yes	Yes/Maybe	Unknown	Unknown	Unknown	Unknown	Unknown	Yes	Unknown	Unknown	Unknown	Unknown	No
No	No	No	No	Yes	No	No	Yes	No	No	Yes	None	No
Yes	No	No	No	Yes	No	No	Yes	No	No	Yes	None	No
Yes	Undecided	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Instructions
No	No	No	No	Yes	No	No	Yes	No	No	Yes	None	No
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Yes	Yes	Yes	Yes	No	Yes	Yes	Yes*	Yes	No	No	None	No
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Yes	No	No	No	Yes	No	No	Yes	No	No	Yes	None	No
Yes	Yes	Yes	Yes	No	No	No	Yes	No	No	No	None	No
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
No	No	No	No	Yes	No	No	Yes	No	No	Yes	None	No
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Yes	No	No	No	Yes	No	No	Yes	Yes	No	Yes	None	No
No?	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Yes	Unknown	Yes	Unknown	Unknown	Unknown	Unknown	Yes	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Yes	No	No	Yes	No	No	No	Yes	No	No	Yes	None	No
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
No	No	No	No	Yes	No	No	Yes	No	No	Yes	None	No
Yes	No	Yes	Yes	No	No	No	Yes	No	No	No	None	No
No	No	No	No	No	No	No	Yes	No	No	Unknown	Yes	Yes
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Yes	Yes	No	No	Yes	No	No	Yes	No	No	Yes	None	No
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown

- 40% response rate
- Red = different from NRC regulations or guidance

Agreement State Implementation

- 73% allow manufacturer representatives to proctor
- 36% may continue to allow manufacturer representatives to proctor or are undecided
- 32% require preceptor attestations for board certified physicians
- 32% require semi-annual physical inventories for Y-90 microspheres
- 11% list specific tumor types or clinical indications on the license

Agreement State Implementation

- 58% allow licensees to request ability to provide notification for an existing AU at a new site
- 53% allow licensees to request ability to make rad safety program changes without an amendment
- 21% require accreditation for nuclear medicine technologist
- 21% require physical presence of AU or AMP or RSO
- 11% require Institutional Review Board in license

Most Difficult to Implement - Training and Attestations

- AU to AU proctoring
  - New NRC Guidance "Part B"
- Attestations for Y-90 microsphere brachytherapy training and experience and ability to fulfill radiation safety-related duties as an AU
  - New NRC Guidance "Part C"
- Parts of "A-G" training must now be supervised by an AU
  - Preparing and administering patient dosage
  - Using administrative controls to prevent medical event
  - Evaluation of patient to determine if medical event occurred

---

- Attestations for diagnostic radiology training and experience
  - Even for board certified individuals

79%

2 states issue their own guidance or checklists for Y-90 licensing

2 states are in full alignment with NRC now and going forward

Agreement State Implementation Summary

Licensing Examples - Possession

- SSDR per vial limit for SIR-Spheres 189 mCi
- SSDR per vial limit for TheraSphere 540 mCi

	TheraSphere®	SIR-Spheres®
Radionuclides (NRC Form 313 Item 5a)	Yttrium-90	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., **BWXT Medical Ltd.** Model TheraSphere®])	Resin microsphere (current manufacturer as listed in the Sealed Source and Device Registry [e.g., Sirtex Model SIR-Spheres®])
Maximum Possession Limit (NRC Form 313 Item 5c)	X* Ci total	X* Ci total
Purpose of Use (NRC Form 313 Item 6)	TheraSphere® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry	SIR-Spheres® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry

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

D. Yttium 90	D. Microsphere	D. 200 millicuries

KK. Yurium 90	KK. Glass microspheres (MDS Nordion Therasphere and/or Sir/Tex SIR-Spheres)	KK. 3 Curies

6. Byproduct, source, and/or special nuclear material	7. Chemical and/or physical form	8. Maximum amount that licensee may possess at any one time under this license
H. Yttrium 90	H. Sealed sources (MDS Nordion Model TheraSpheres and Sirtex Medical, Limited Model SIR-Spheres)	H. Not to exceed 540 millicuries per source and 2,160 millicuries total

- Form sometimes listed as
  - radiopharmaceutical
  - liquid
  - solution

Licensing Examples – Authorized Use

Purpose of Use (NRC Form 313 Item 6)	TheraSphere® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry	SIR-Spheres® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry

F. To be used in MDS Nordion model TheraSpheres® Mark III Administration Set brachytherapy afterloader for treatment of malignant hepatic tumors. ***NOTE: As of this amendment, there are no AUR for this material.***

H. Medical use with the MDS Nordion TheraSphere delivery system and the Sirtex SIR-Sphere delivery system.

R. For use in a Sirtex brachytherapy afterloader for the treatment of non-resectable liver cell tumors.

GG. For use in a Radioembolization with a Microsphere Brachytherapy Device (RMBD) for the treatment of liver malignancies in humans.

L. For use of SIRTEX Medical Model SIR- Spheres® for treatment of unresectable hepatocellular carcinoma.

Licensing Examples – Authorized Use

Purpose of Use (NRC Form 313 Item 6)	TheraSphere® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry	SIR-Spheres® for permanent brachytherapy using delivery system as listed in the Sealed Source and Device Registry

liver
intravenous

Treatment of Hepatic, Kidney and Adrenal Tumors

Y	90	Total	1 Ci	Microshpheres*	MDS Nordion Model Theraspheres	Treatment of Metastatic Kidney Tumors

D. No single vial of solution to exceed 189 millicuries Total: 500 millicuries	**D. Interstitial treatment of cancer as indicated in** [state manual brachytherapy regs]

HH. Y-90	HH. Sealed source (microspheres in solution)	HH. No single source to exceed 540 mCi Total:1.4 Ci	HH. Interstitial treatment of cancer as indicated in [state manual brachytherapy regs]

Authorized Users

- Should license indicate an AU still needs to complete proctored cases?
  - NRC and most Agreement States are issuing one amendment
  - Licensee must provide follow-up documentation
  - Can be verified during inspection
  - At least one state is opting to amend license twice to add/remove conditional authorization

[Physician Name] **TheraSphere Y-90 microspheres use permitted by** **[state regs for manual brachytherapy]** **(This authorization is limited to proctored cases and expires on June 4, 2022)**

Questions

- What are biggest challenges for understanding or implementing latest NRC guidance?
- How to best communicate state-specific requirements and license commitments to licensees?

SCAN ME

Acronyms & References

AU – Authorized User

AMP – Authorized Medical Physicist

IRB – Institutional Review Board

RSO – Radiation Safety Officer

SSDR – Sealed Source and Device Registry

NRC Y-90 Microsphere Licensing Guidance – Revision 9 (Feb 2016) ML15350A099

NRC Y-90 Microsphere Licensing Guidance – Revision 10 (November 2019) ML19338E099

NRC Y-90 Microsphere Licensing Guidance – Revision 10.1 (March 2020) ML20080J208

NRC Y-90 Microsphere Licensing Guidance – Revision 10.2 (April 2021) ML21089A364