NRC Licensing for Yttrium-90 Microsphere Brachytherapy

An Overview of Licensing Guidance and Analysis of Reported Medical Events

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Licensing Guidance

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- Title 10 Code of Federal Regulations (CFR) Part 35 Subpart K – Other Medical Uses of Byproduct Material or Radiation from Byproduct Material (10 CFR 35.1000)

- Medical Uses Licensee Toolkit
  - http://www.nrc.gov/materials/miau/med-use-toolkit.html#guidance

Training & Experience

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- Existing AU for § 35.400 or § 35.300; or
- Meets criteria in § 35.490 or § 35.390; or
- Interventional Radiologist criteria

AND

- Microsphere-specific training provided by
  - An existing AU or
  - The manufacturer

License Commitments

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- Microsphere-specific training provided by manufacturer
  - Complete at least the first three hands-on patient cases supervised in the physical presence of a manufacturer representative
  - Submit documentation of completion from manufacturer to the NRC within 30 days

License Commitments

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- Written Directive (WD)
  - Dose or activity may be used
  - the statement “or dose/activity delivered at stasis”, if appropriate
  - Modify WD within 24 hours due to emergent patient conditions (e.g. artery spasm or sudden change in blood pressure)
  - Same or different AU can sign WD after procedure, if stasis or any changes made to WD; otherwise, another individual can document procedure performed in accordance with WD

License Commitments

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- Manufacturer's procedures
- Inventory
- Patient release
- Labeling
- Medical Event (ME) reporting

Medical Events FY 2000 - 2012

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FY	# of MEs TheraSphere	# of MEs SIRSpheres	Total MEs
2000	1	0	1
2001	2	0	2
2002	0-2?	0-2?	2
2003	1	2	3
2004	0-1?	0-1?	1
2005	0	2	2
2006	0	1	1
2007	6	2	8
2008	3-4?	0-1?	4
2009	5	4	9
2010	2	2	4
2011	9	3	12
2012	12	7	19
TOTAL			68

FY	Incidence Rate TheraSphere	Incidence Rate SIRSpheres	Total % Incidence
2007	2.34%	0.14%	0.47%
2008	unknown	unknown	0.13%
2009	0.30%	0.17%	0.23%
2010	0.10%	0.08%	0.09%
2011	0.29%	0.10%	0.20%
2012	0.36%	0.18%	0.26%
TOTAL			0.26%

Medical Events by State FY 2000-2012

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State	MEs	State	MEs	State	MEs
AR	2	MD	1	RI	1
CA	1	MI	3	SC	1
CO	1	MN	2	TN	2
FL	4	MS	1	TX	5
GA	1	NY	1	UT	1
IL	3	NC	7	VA	3
IN	3	OH	2	WV	1
IA	0	OR	3	WI	3
KY	1	PA	15	**Others**	**0**

pennsylvania
DEPARTMENT OF ENVIRONMENTAL PROTECTION

NRC states: IN, MI & WV

Medical Events NRC Analysis

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- Patient-related factors
  - Backpressure/vasculature resistance, shunting
- Equipment problems & human errors
  - Stopcocks, catheters, clamps; leaks; residual spheres in system
    - Settling, adherence to vial, catheters, or junctions
  - Switching patient doses
  - Treating wrong lobe of liver
  - Improper kit assembly
- Unknown

- ~90% medical events reported were underdoses

Medical Events Advisory Committee Analysis

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- Complexity of devices
- Low flow due to pause, clumping, or leaking of priming line and reduced pressure
- Slow delivery that led to settling
- Needles inserted at an angle
- Defective, pinched, or occluded catheters
- Piece of septum within vial impeded flow
- Clamp not fully opened
- Microspheres stuck to septum because the bottle was shipped upside down

Medical Events Advisory Committee Analysis

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- No obvious root cause
- No indication why one product has been involved in more MEs than the other
- Device changes may require regulatory approval and could introduce additional failures
- Non-statistically significant deviation from background in a procedure that has a low baseline medical event rate

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Questions?