FDA's Role in the Regulatory Clearance of Safe and Effective Radiation Planning and Delivery Devices

William C. Jung, Ph.D.
Branch Chief
Nuclear Medicine and Radiation Therapy
Division Of Radiological Health
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

AAPM July 2018

Disclosure

- None

Outline

- Overview of radiological device regulation
  - Classifications
- Intended use and Indications for use
- Premarket approval and clearances of medical devices
  - Premarket Approval (PMA)
  - Premarket Notification (510(K))
- Pros/Cons for 510(K)

Classes of medical Devices

- **Class I** devices are the low-risk devices and require general controls.
  - 892.5780 Light beam patient position indicator
  - 892.1950 Radiographic anthropomorphic phantom
- **Class II** devices require general controls and special controls.
  - 892.5050 Medical charged particle radiation therapy system
  - 892.5700 Remote controlled radionuclide applicator system
  - 892.1750 Computed tomography x-ray system
  - 892.1650 Image-intensified fluoroscopic x-ray system
- **Class III** require general controls and pre-market approval, PMA and are high risk, generally life-supporting, life sustaining devices
  - Radioactive microspheres
  - Digital Breast Tomosynthesis

Radiation Therapy Devices

Regulation	Device	Class
892.5050	Medical charged-particle, radiation therapy system	II
892.5300	Medical neutron radiation therapy system	II
892.5650	Manual radionuclide applicator system	I exempt
892.5700	Remote controlled radionuclide applicator system	II
892.5710	Radiation therapy beam shaping block	II
892.5730	Radionuclide brachytherapy source	II
892.5740	Radionuclide teletherapy source	I exempt
892.5750	Radionuclide radiation therapy system	II
892.5770	Powered radiation therapy patient support assembly	II
892.5780	Light beam patient position indicator	I
892.5840	Radiation therapy simulator system	II
892.5900	X-ray radiation therapy system	II
892.5930	Therapeutic x-ray tube housing assembly	II

892.5050 Medical Charged-Particle Radiation Therapy System

Product Code	Device	Class
IYE	Accelerator, linear, medical	II
MWW	Accessory, film dosimetry system	II
IYG	Betatron, medical	II
IWK	Cyclotron, medical	II
NZT	Dosimeter, ionizing radiation, implanted	II
JAE	Microtron, medical	II
IWM	Synchrotron, medical	II
LHN	System, radiation therapy, charged-particle	II
MUJ	System, planning radiation therapy treatment	II

510(k) premarket notification

- The 510(k) is the mechanism by which a manufacturer seeks introduction into interstate commerce for commercial distribution of a device
- Device is substantially equivalent to a legally marketed predicate device
- Established special controls applicable to the predicate device need to be addressed by the new device

510(K) Substantial Equivalence

- Means
  - New (subject) device compared to the predicate device has the same intended use
  - Has the same technological characteristics or
  - Has different technological characteristics that do not raise different questions of safety and effectiveness and data demonstrate the device is as safe and as effective as the predicate device

Intended Use

- **Intended use** means the general purpose of the device or its function and encompasses the indications for use.
- **Indications for use** describes the disease or conditions the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended [21 CFR 814.20(b)(3)(i)]
- The indications for use and intended use may be the same for devices with general indications for use that do not specify a disease, condition, or population.
- Intended use of many radiation oncology devices can be very general.

Tool Type Claim

- Devices with general indications for use that do not specify a disease, condition or population (or anatomical site) the intended use is the same as the indications for use.
- Examples
  - scalpels for cutting tissue, same tool for cutting hand or leg
  - Imaging devices for imaging the body, same tool for imaging hand or leg
  - "___ systems are indicated for treatment planning and image guided stereotactic radiosurgery and precision radiotherapy for lesions, tumors and conditions anywhere in the body when radiation treatment is indicated"
  - "____ is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors and conditions anywhere in the body when radiation treatment is indicated"

Data Requirements for Linear Accelerators

- Example Indication for Use
  - Linear Accelerator system A is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors and conditions anywhere in the body where radiation treatment is indicated.
- Data Supplied
  - Biocompatibility – new patient contacting components, previously cleared material
  - Software – supplied material for major level of software concern.
  - Electrical safety testing – Radiotherapy treatment system, conformance to IEC 60601-1-1:2000 Medical Electrical Equipment – Collateral standard: Safety requirements for medical electrical systems (General), Treatment couch, conformance to IEC 60601-2-32:1994 Medical Electrical Equipment –Particular requirements for safety of associated equipment of X-ray equipment – Ed. 10
  - EMC testing for conformance to IEC 60601-1-2:2014 + A1: 2004-Medical electrical equipment – collateral standards: Electromagnetic Compatibility
  - Accelerator beam output characteristics compared to the predicate

Standards Used for Linear Accelerators

- IEC 60601-1:1988 +A1:1991 + A2:1995 (FDA Consensus Standard 5-4); Medical Electrical Equipment – Part 1: General Requirements for Safety, 1988; Amendment 1, 1991-11, Amendment 2; 1995
- IEC 60601-1-1:2000 (RDA Consensus Standard 5-27), Medical electrical equipment – Part 1-1: General requirements for safety – Collateral standard: Safety requirements for medical electrical systems (General)
- IEC60601-1-2:2014: (FDA Consensus Standard 5-34), Medical Electrical equipment – Part 1-2: General Requirements for Safety – Collateral Standard: Electromagnetic Compatibility – Requirements and tests
- IEC60601-1-3: 1994 (FDA Consensus Standard 12-199), Medical Electrical Equipment – Part 1-3: General Requirements for Basic Safety and Essential Performance – Collateral Standard: Radiation protection in diagnostic x-ray equipment – (Radiology)
- IEC 60601-1-3 : (FDA Consensus Standard 5-41)Medical electrical equipment – Part 1: General requirements for safety – 4- Collateral standard: Programmable electrical medical systems edition 1.1.
- IEC 60601-2-1:1998 +A1:2002 (FDA Consensus Standard 12-152), Medical electrical equipment – Part 2-1:Particular requirements for the safety of electron accelerators in the range 1 MeV to 50 MeV
- IEC 60601-2-32: 1994 (FDA Consensus Standard 12-127), Medical Electrical Equipment – Part 2: Particular requirements for the safety of associated equipment of X-ray equipment – Ed. 1.0.
- IEC 60601-2-44: 20002 (FDA Consensus Standard 12-120). Medical electrical equipment – Part 2-44: Particular requirements for the safety of x-ray equipment for computed tomography – Ed 2.1.
- IEC 60825-1 Ed. 2.0 2007, FDA Consensus Standard 12-168), Safety of laser products – Part 1: Equipment classification and requirements (Radiology)
- IEC 61217: 2008 (FDA Consensus Standard 12-190), Radiotherapy equipment – Coordinates, movements, and scales Consolidated Edition 1-2.
- IEC 62274: 2005 (FDA Consensus Standard 12-241), Medical Electrical equipment – Safety of radiotherapy record and verify systems.
- IEC 62336-1 ED. 2.0: 2007, (FDA Consensus Standard 5-50), Medical devices – Application of usability engineering to medical devices. (Radiology).
- AAMI RT2: 2017 Radiation Therapy Readiness Check

Pros/Cons for 510(K) For Radiation Therapy Devices

Pros	Impact
As safe / as effective as predicate	Still being reviewed as substantially equivalent
Tool claim still compared to predicate	FDA review accuracy/precision, depth dose profile
Dependence on standards	Increase FDA review confidence, faster review
Time to market	30-90 days, new device available to use
Feature creep	Devices change over time

Cons	Impact
Minimal clinical data reviewed during 510(K)	Specific tumors or locations may need post-market clinical or performance testing
Tool claim not really testing all new indications for use	Some indications not called out in 510(K) may need IDE testing or meta analysis or new 510(K)
Tool claim not easy for marketing	Some claims need clinical data
Broad tool claims	Encourage practice of medicine testing

Regulatory Authority

- FDA was given the authority to begin regulating all medical devices on May 28, 1976 when the President signed the Medical Device Amendments Act.
- The Radiation Control provisions (originally enacted as the Radiation Control for Health and Safety Act of 1968) are located in Sections 531 through 542 of the Act. They apply to any "electronic product" which is defined as: any manufactured or assembled product (or component, part, or accessory of such product) which, when in operation,
  - (i) contains or acts as part of an electronic circuit and
  - (ii) emits (or in the absence of effective shielding or other controls would emit) electronic product radiation.

  "Electronic product radiation" is defined as:
  - (A) any ionizing or non-ionizing electromagnetic or particulate radiation, or
  - (B) any sonic, infrasonic, or ultrasonic wave, which is emitted from an electronic product as the result of the operation of an electronic circuit in such product.

Code Federal of Regulations

- Medical Device Regulations (21 CFR 892)
  - Charged-particle therapy, Neutron therapy, Brachytherapy, Teletherapy, X-ray therapy
- Electronic Product Radiation Control (21 CFR 1000)
  - Any manufactured or assembled product which, when in operation: contains or acts as part of an electronic circuit and emits (or in the absence of effective shielding or other controls would emit) electronic product radiation
  - Electronic product radiation means any ionizing or nonionizing electromagnetic or particulate radiation or any sonic, infrasonic or ultrasonic wave emitted from an electronic product

Pre-Market Approval of Medical Devices

- A new device is automatically in Class III (PMA) and must undergo premarket approval or reclassification before it can be marketed unless
  - it was in commercial distribution prior to May 28, 1976 and is substantially equivalent (SE) to another such device (510(K)) or
  - it is within a type of device introduced after May 28, 1976 that has been reclassified into Class I or II (510(K)) and is SE to another device within such classification or
  - it has successfully gone through the *de Novo* classification process.

PMA

- Class III medical devices (Radioactive microspheres)
- Safety and effectiveness has to be demonstrated
- Submission includes data and information and/or information incorporated by reference
  - IDE or master files
- Important components

Components	
Indications for use	Principles of operation
Device description	Methods of manufacture
Marketing history	Reference to performance standards
Summary of non-clinical results	Proposed labeling
Summary of clinical results	Bibliography of published reports

Conclusion

- PMA – directly reviews safety and effectiveness of unproven technology
  - Only one device right now – radioactive microspheres
- 510(K) – reviews safety and effectiveness compared to a substantially equivalent predicate
- Most medical devices get to market by the 510(K) process
- 510(K) devices have a faster time to market and faster availability for clinical use and testing
- Tool claims encourage clinical testing of specific intended uses not called out an Indication for use

CDRH Database Links

- CDRH's Product Classification: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm
- Searchable List of Recognized Standards by Product Code: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm