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

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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

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### Radiation Therapy Devices

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Device</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>892.5050</td>
<td>Medical charged-particle, radiation therapy system</td>
<td>II</td>
</tr>
<tr>
<td>892.5300</td>
<td>Medical neutron radiation therapy system</td>
<td>II</td>
</tr>
<tr>
<td>892.5850</td>
<td>Manual radionuclide applicator system</td>
<td>I exempt</td>
</tr>
<tr>
<td>892.5700</td>
<td>Remote controlled radionuclide applicator system</td>
<td>II</td>
</tr>
<tr>
<td>892.5710</td>
<td>Radiation therapy beam shaping block</td>
<td>II</td>
</tr>
<tr>
<td>892.5730</td>
<td>Radionuclide brachytherapy source</td>
<td>II</td>
</tr>
<tr>
<td>892.5740</td>
<td>Radionuclide teletherapy source</td>
<td>I exempt</td>
</tr>
<tr>
<td>892.5750</td>
<td>Radionuclide radiation therapy system</td>
<td>II</td>
</tr>
<tr>
<td>892.5770</td>
<td>Powered radiation therapy patient support assembly</td>
<td>II</td>
</tr>
<tr>
<td>892.5780</td>
<td>Light beam patient position indicator</td>
<td>I</td>
</tr>
<tr>
<td>892.5840</td>
<td>Radiation therapy simulator system</td>
<td>II</td>
</tr>
<tr>
<td>892.5900</td>
<td>X-ray radiation therapy system</td>
<td>II</td>
</tr>
<tr>
<td>892.5930</td>
<td>Therapeutic x-ray tube housing assembly</td>
<td>II</td>
</tr>
</tbody>
</table>

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### 892.5050 Medical Charged-Particle Radiation Therapy System

<table>
<thead>
<tr>
<th>Product Code</th>
<th>Device</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>IYE</td>
<td>Accelerator, linear, medical</td>
<td>II</td>
</tr>
<tr>
<td>MWW</td>
<td>Accessory, film dosimetry system</td>
<td>II</td>
</tr>
<tr>
<td>IYG</td>
<td>Betatron, medical</td>
<td>II</td>
</tr>
<tr>
<td>JW</td>
<td>Cyclotron, medical</td>
<td>II</td>
</tr>
<tr>
<td>NZT</td>
<td>Dosimeter, ionizing radiation, implanted</td>
<td>II</td>
</tr>
<tr>
<td>JAE</td>
<td>Microtron, medical</td>
<td>II</td>
</tr>
<tr>
<td>WM</td>
<td>Linear accelerator, medical</td>
<td>II</td>
</tr>
<tr>
<td>LHN</td>
<td>System, radiation therapy, charged-particle</td>
<td>II</td>
</tr>
<tr>
<td>MUI</td>
<td>System, planning radiation therapy treatment</td>
<td>II</td>
</tr>
</tbody>
</table>
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.
  - Accelerator beam output characteristics compared to the predicate

Standards Used for Linear Accelerators

- IEC 60601-1-3:2005 (FDA Consensus Standard 12-13), Medical electrical equipment – Part 1-3: Particular requirements for the safety of x-ray equipment in the range 1 MEV to 50 MEV
- 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. 2.3
- IEC 60825-1 Ed. 2.0-2007, FDA Consensus Standard 12-149, Medical equipment – Collateral standard: Safety requirements for laser products – Part 1: Equipment classification and requirements (Radiology)
- IEC 62137:2006 (FDA Consensus Standard 12-100), Medical equipment – Coordinates, movements, and scales Consolidated Edition 1-2
- IEC 62276:2005 (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 12-59), 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

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

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

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

<table>
<thead>
<tr>
<th>Components</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications for use</td>
<td>Principles of operation</td>
</tr>
<tr>
<td>Device description</td>
<td>Methods of manufacture</td>
</tr>
<tr>
<td>Marketing history</td>
<td>Reference to performance standards</td>
</tr>
<tr>
<td>Summary of non-clinical results</td>
<td>Proposed labeling</td>
</tr>
<tr>
<td>Summary of clinical results</td>
<td>Bibliography of published reports</td>
</tr>
</tbody>
</table>

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