US Medical Device Clearance Process

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Wade S. Smith, MD, PhD
Director UCSF Neurovascular Division
Professor and Vice Chair, UCSF Department of Neurology
wade.smith@ucsf.edu
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US Device Clearance Process

Objectives

• Be able to articulate the differences between drug approval and device clearance within the FDA

• Be able to explain how devices are cleared or approved

• Be able to explain the clinical research steps necessary for device clearance
FDA Mission

• **Protect the public health** by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation.

• **Advance the public health** to make medicines more effective, safer, and more affordable

• **Regulate the manufacturing**, marketing and distribution of **tobacco** products to protect the public health and to reduce tobacco use by minors.

• **Ensure the security of the food supply** and by fostering development of medical products to respond to deliberate and naturally emerging public health threats.
FDA Organization (partial)

- CDRH: Center for Devices and Radiological Health
- CDER: Center for Drug Evaluation and Research
To sell a drug in the US

• You need FDA drug approval for a specific indication through CEDR
  – Drug must safe and effective
  – Drug manufacturing and distribution is regulated
  – Exceptions (dietary supplements)
  – Companies cannot sell/market a drug that is not approved for the specific indication
To sell a drug in the US

- Drugs have a label that says what it is approved for and instructions on how to dose it
  - IV t-PA had a label change in 1996 for use in acute ischemic stroke for example
  - Off label use is at the discretion of the medical provider
  - Marketing off label use is illegal
To sell a drug in the US

• Orphan drug use
  – Approved for rare diseases
  – Barrier to approval is less, and therefore the expense is less
  – Some pharmaceutical companies specialize in orphan drugs
Device Clearance

• A medical device is cleared for use by a trained medical professional by CDRH
  – The device must be safe
  – It needs to effective in doing something, and something is not necessarily a clinical endpoint
  – the least burdensome rule

• The FDA cannot approve a medical professional
## Summary: Drugs vs. Devices

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approved</td>
<td>Cleared or Approved</td>
</tr>
<tr>
<td>2 randomized trials with clinical outcomes</td>
<td>Least burdensome rule of clearance: surrogate outcomes, randomized or registry, single trial okay</td>
</tr>
<tr>
<td>Little post-marketing interaction with prescriber (other than advertising)</td>
<td>Intimate manufacturer involvement post marketing (training and advertising)</td>
</tr>
<tr>
<td>The label may be ignored by prescribing physician</td>
<td>Training rules are consistent with IFU</td>
</tr>
<tr>
<td>Reimbursement may be linked to disease</td>
<td>Reimbursement becoming more linked to disease</td>
</tr>
</tbody>
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Device Approval or Clearance

- Follows 3 pathways
  - Premarket Approval (PMA)- Approval pathway
    - Used for new devices not yet tested in man
    - Reasonable assurance the device is safe
    - Higher risk devices
    - Longer, more expensive
  - Premarket Notification (510-K)- Clearance Pathway
    - The device seeking clearance must be substantially equivalent to something that is already cleared
    - May not need even need clinical data (in vitro data may be sufficient)
  - HDE (humanitarian device exemption)
Device Clearance

• Premarket Notification (510-K)
  – Applicant claims that the device is substantially equivalent in the 510-K application
  – If the FDA agrees, the device is cleared
  – The FDA may request a PMA
  – The FDA may decline and ask for further data
Non-Significant Risk Device

• Does not meet all of the following:
  – implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
  – Is for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject
  – Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject;
  – Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
Example of Cleared Devices

- PFO occlusion for stroke prevention
- MERCI retriever
- Simvisc
Example of Cleared Devices

- Simvisc
- Cleared as a medical device
Example of Cleared Devices

• PFO occlusion for stroke prevention
  – Label goal was stroke prevention
  – HDE path
  – Slow recruitment
  – HDE withdrawn
  – Trials finished quickly
  – Ineffective; now effective and cleared for stroke Oct 2016
MERCI Retriever Clearance

- Retriever was already approved as a foreign body retriever
- Clot removal was considered substantially equivalent to foreign body retrieval
- 510K process for clot retrieval undertaken with the MERCI retriever as the predicate
MERCI Retriever Clearance

- MERCI Trial
- Prospective, single arm intervention
- Outcome: recanalization

Outcome:
1°: Recanalization
2°: 90-Day mRS
MERCI Retriever Clearance

• Primary outcome met: 48% recan vs. 18% historical control
• Secondary: much better outcome if vessel opened

Outcome:
1°: Recanalization
2°: 90-Day mRS
MERCI Retriever Clearance

- Data presented to advisory panel
- Subsequent data led to clearance in 2004

Diagram:
- CTA or AG LVO
- Stroke
- IV t-PA
- Not allowed
- Consent

Device

Outcome:
1°: Recanalization
2°: 90-Day mRS
MERCI Retriever Clearance

• Second gen devices 510K clearance using MERCI as predicate
• TREVO/Solitaire randomized trials showed stent-trievers better

Outcome:
1°: Recanalization
2°: 90-Day mRS
Future

• Movement toward proving devices (in trained hands) are clinically effective
• CMS beginning to only reimburse for devices being used in a clinical trial of efficacy
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