US Medical Device Clearance Process

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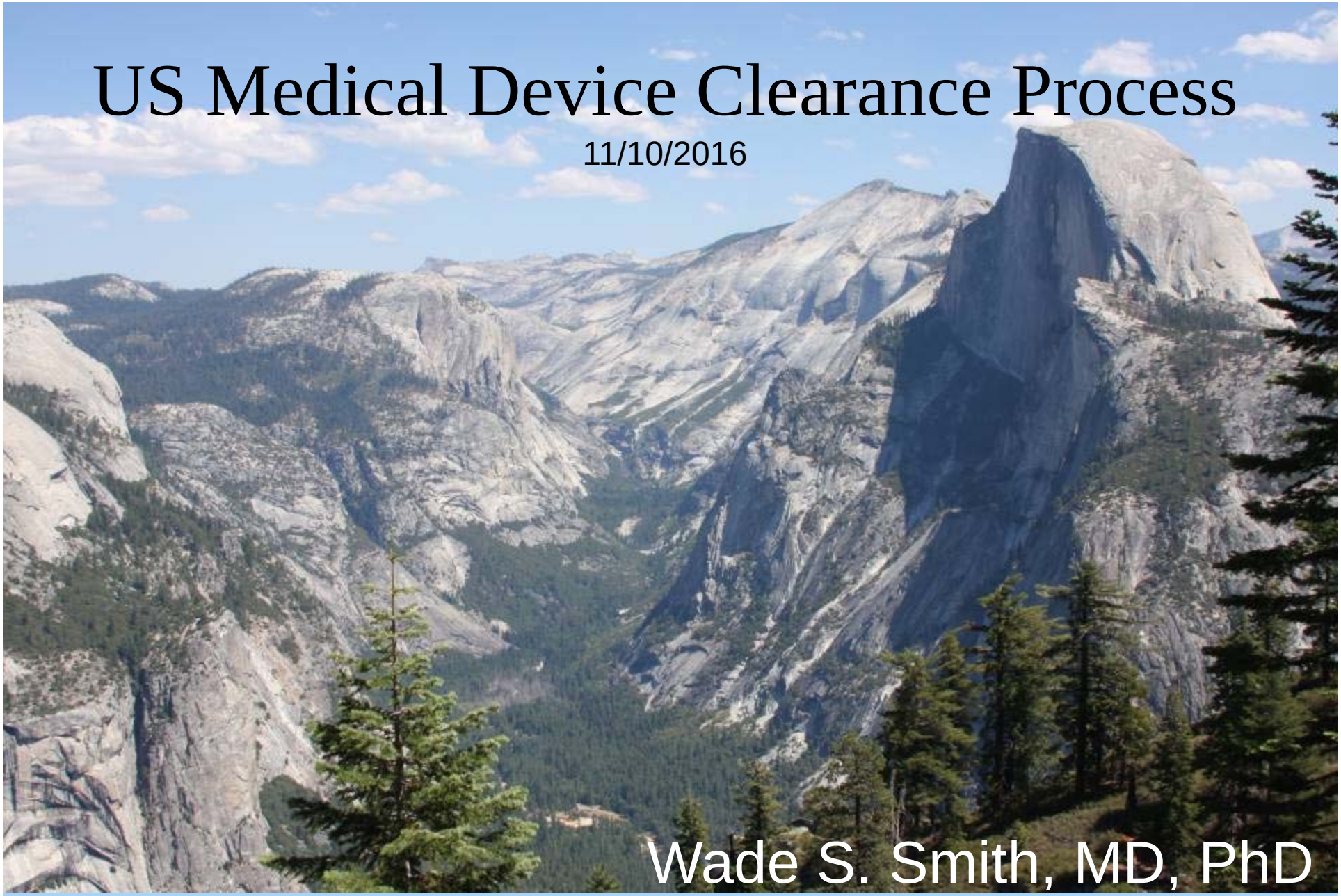

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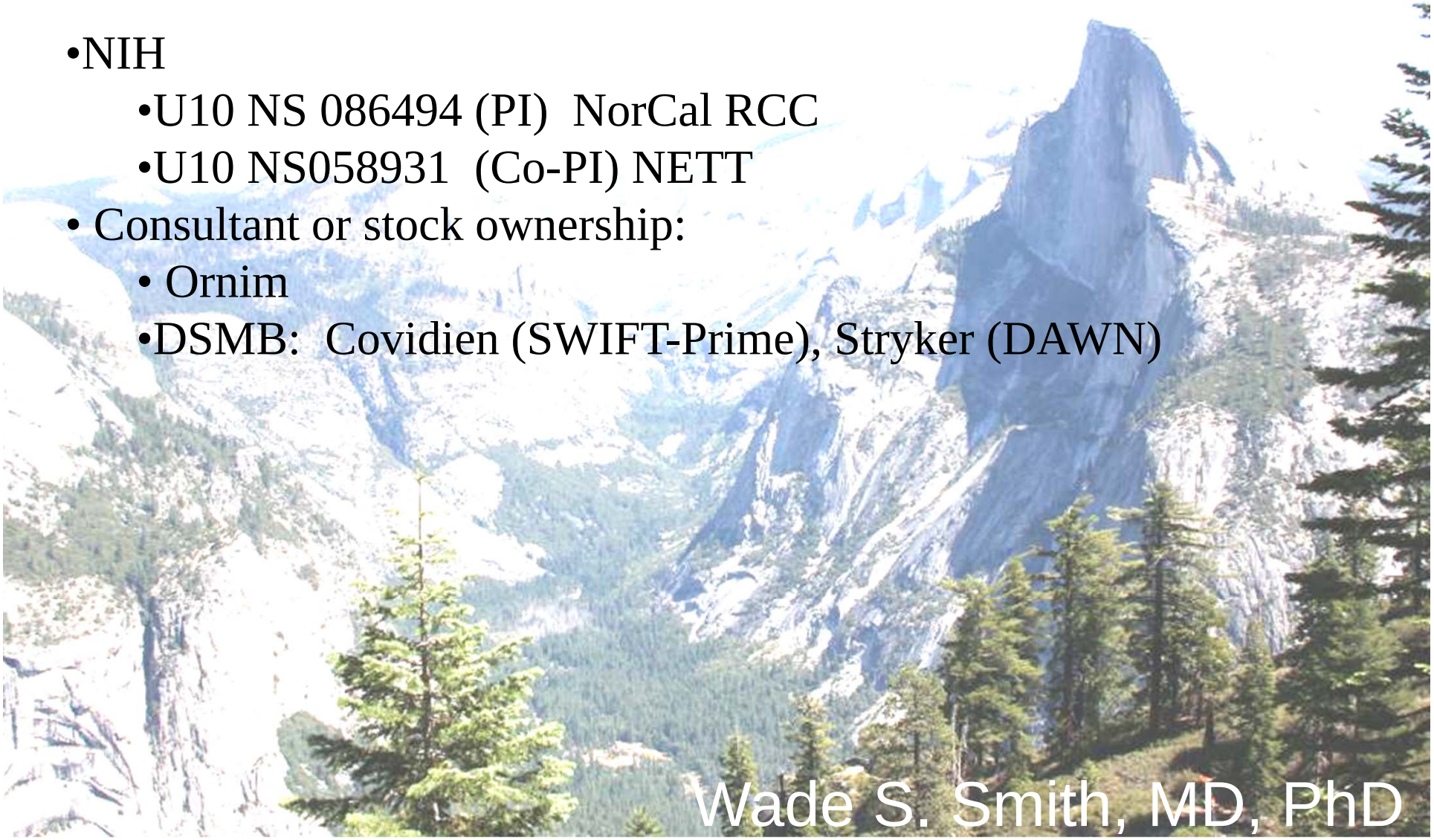
Disclosures



- NIH
  - U10 NS 086494 (PI) NorCal RCC
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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

Drugs

- Approved
- 2 randomized trials with clinical outcomes
- Little post-marketing interaction with prescriber (other than advertising)
- The label may be ignored by prescribing physician
- Reimbursement may be linked to disease

Device

- Cleared or Approved
- Least burdensome rule of clearance: surrogate outcomes, randomized or registry, single trial okay
- Intimate manufacturer involvement post marketing (training and advertising)
- Training rules are consistent with IFU
- Reimbursement becoming more linked to disease

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

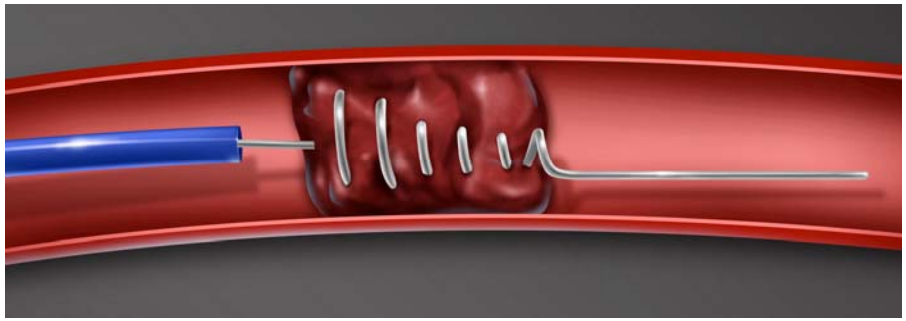
- Premarket Notification (510-K)
  - Applicant claims that the device is substantially equivalent in the 510-K application
  - If the FDA agrees, the device is cleared
  - The FDA may request a PMA
  - The FDA may decline and ask for further data

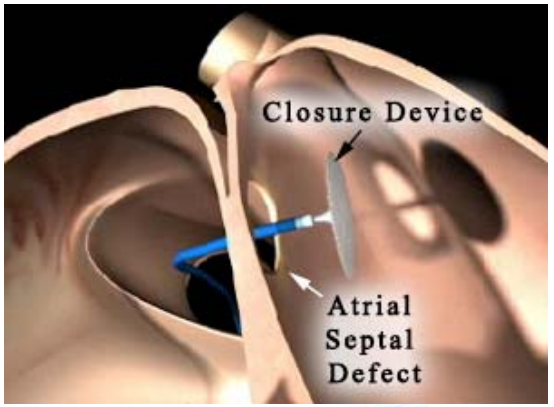
Non-Significant Risk Device

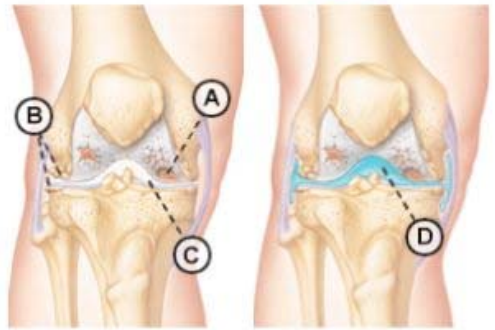
- Does not meet all of the following:
  - implant and presents a *potential for serious risk to the health, safety, or welfare of a subject*;
  - Is for use supporting or sustaining human life and presents a *potential for serious risk to the health, safety, or welfare of a subject*
  - Is for a use 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



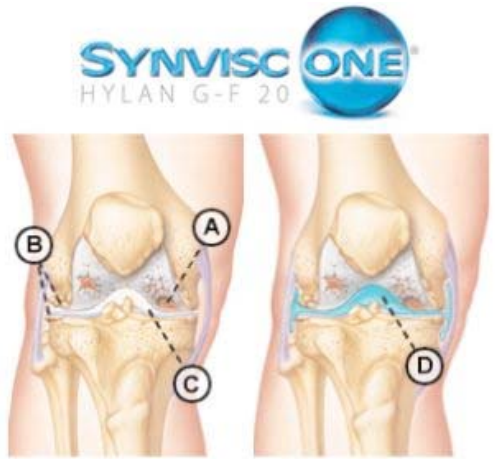




A. Cartilage wears away
B. Bone spurs may develop
C. Joint fluid breaks down
D. Synvisc-One

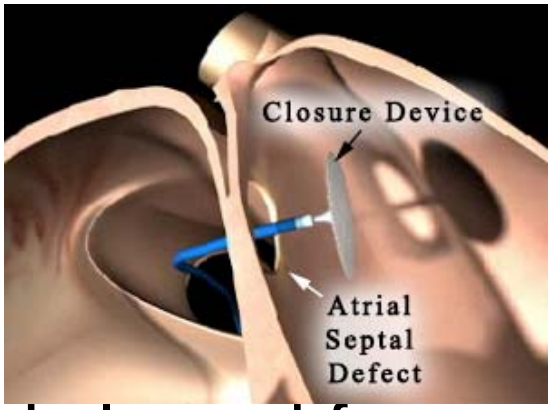
Example of Cleared Devices

- 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

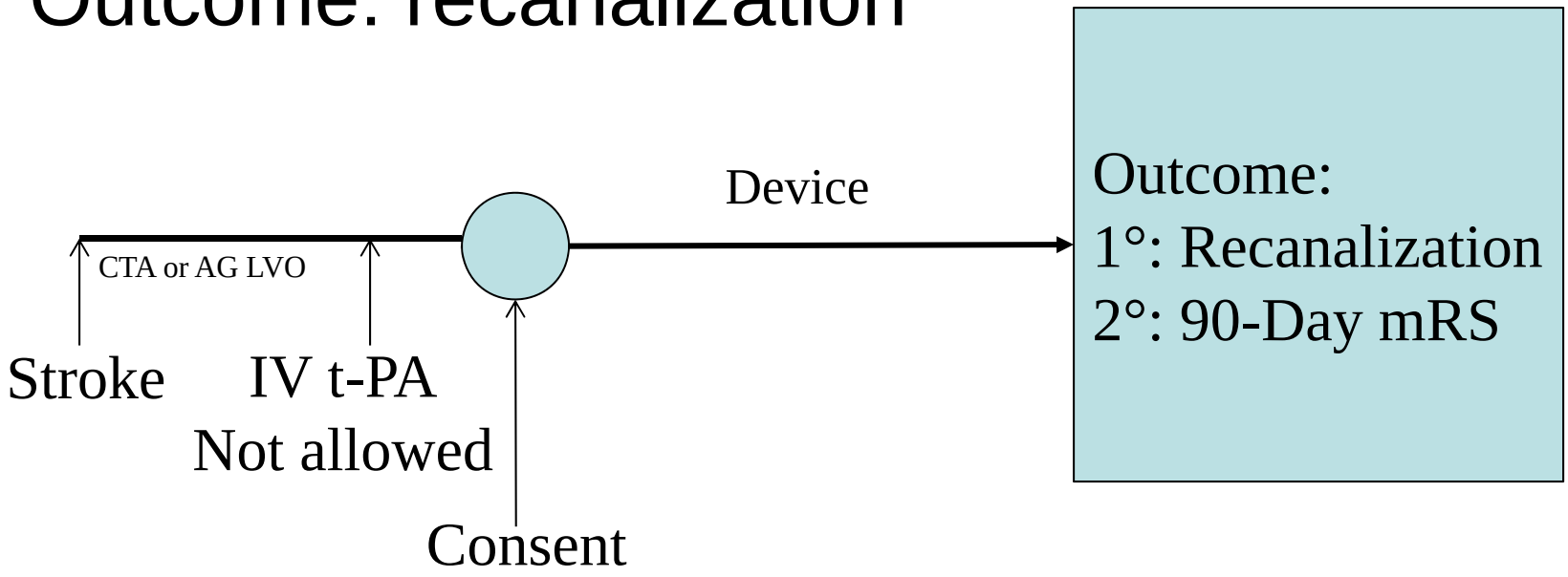


MERCI Retriever Clearance

- 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

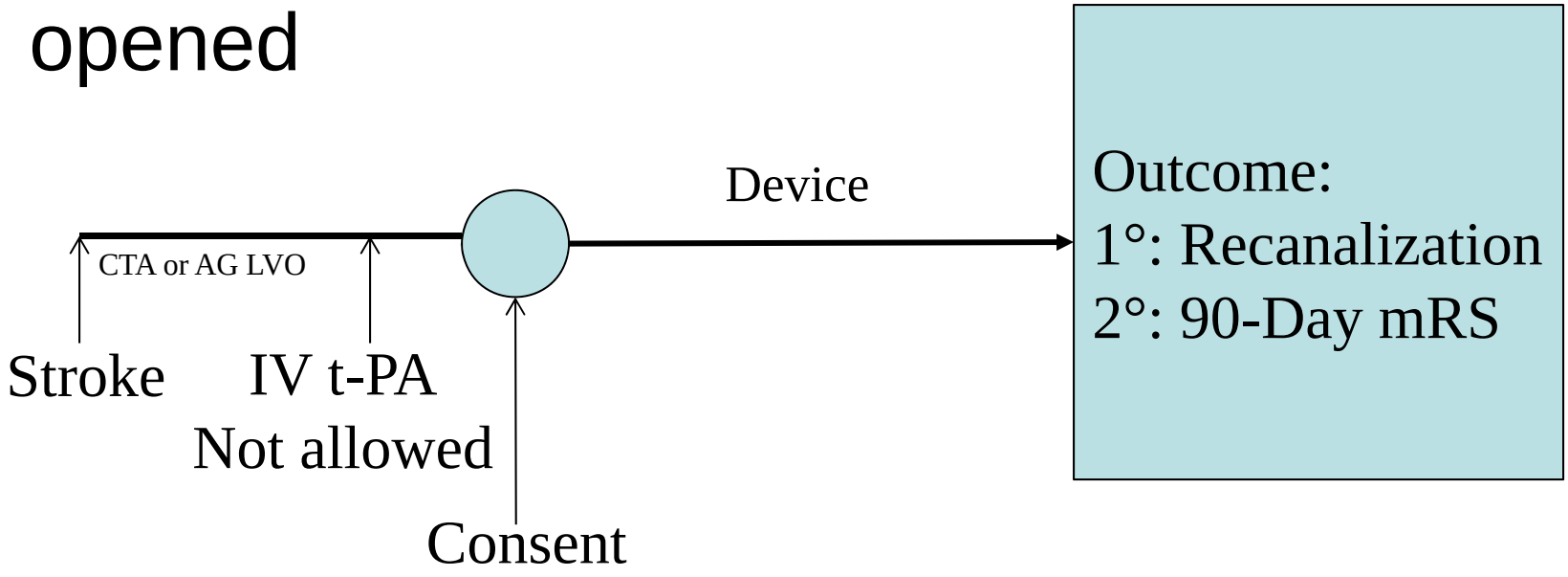
MERCI Retriever Clearance

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



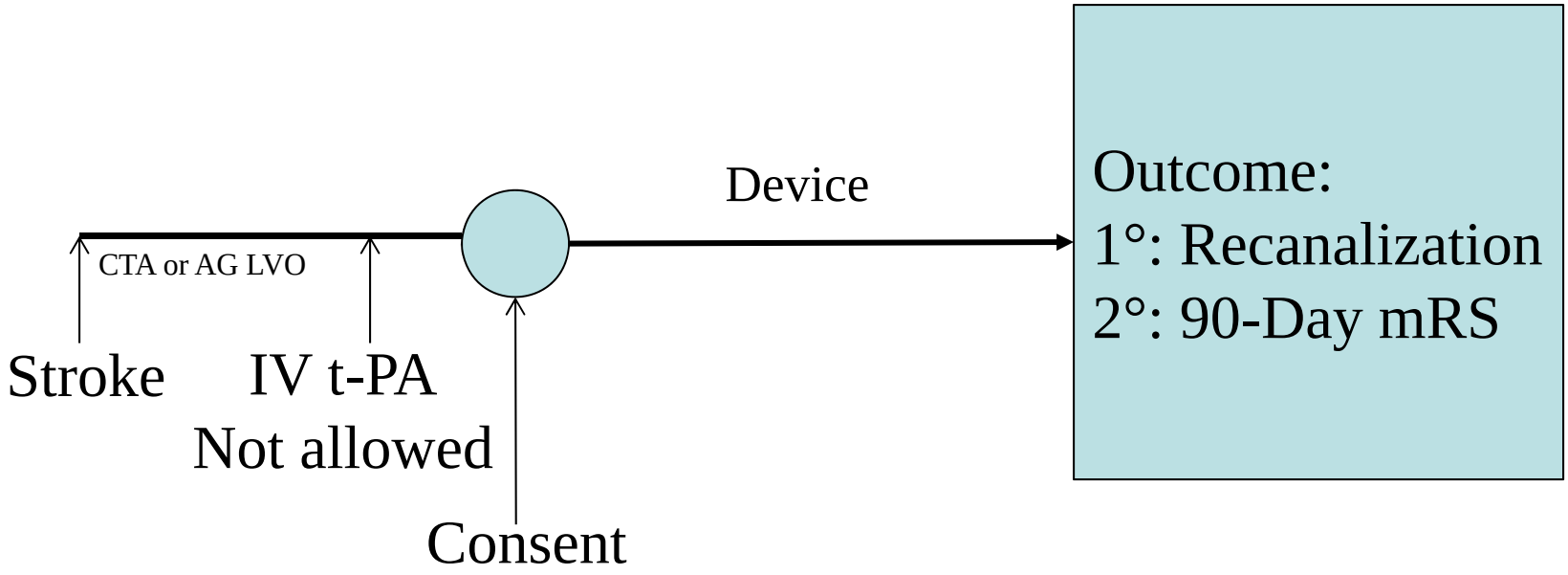
MERCI Retriever Clearance

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



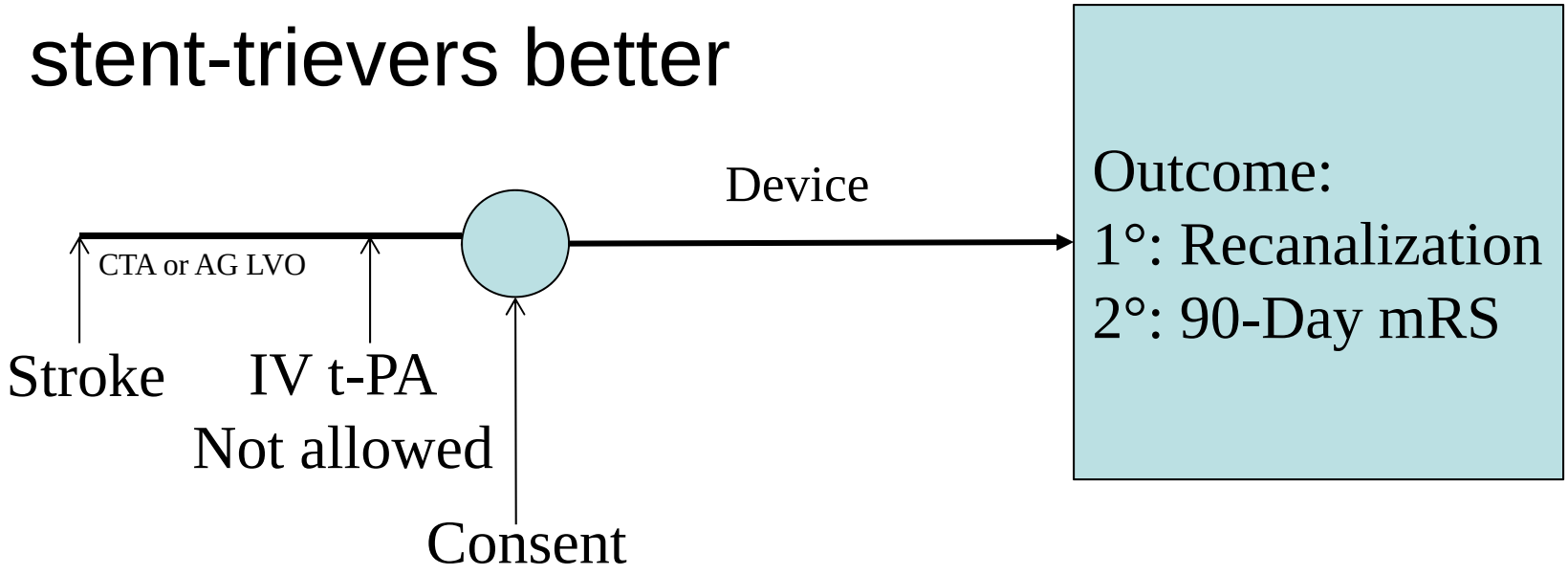
MERCI Retriever Clearance

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



MERCI Retriever Clearance

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



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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