FDA Medical Device Programs: Premarket approval/clearance and Device Development Tools

Finn Donaldson, PhD

Division of Biomedical Physics
Office of Science and Engineering Laboratories
Center for Devices and Radiological Health
U.S. Food and Drug Administration

MeDe Innovation Annual Conference
Nottingham, UK
28th January, 2015

Center for Devices and Radiological Health
CDRH

Content

- Premarket review
- MDDT program

- Additive manufacturing
- Modeling & simulation

Center for Devices and Radiological Health









Mission:

"The mission of the Center for Devices and Radiological Health (CDRH) is to **protect and promote the public health**. […] We facilitate **medical device innovation by advancing regulatory science**, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and **assuring consumer confidence in devices marketed in the U.S.**"

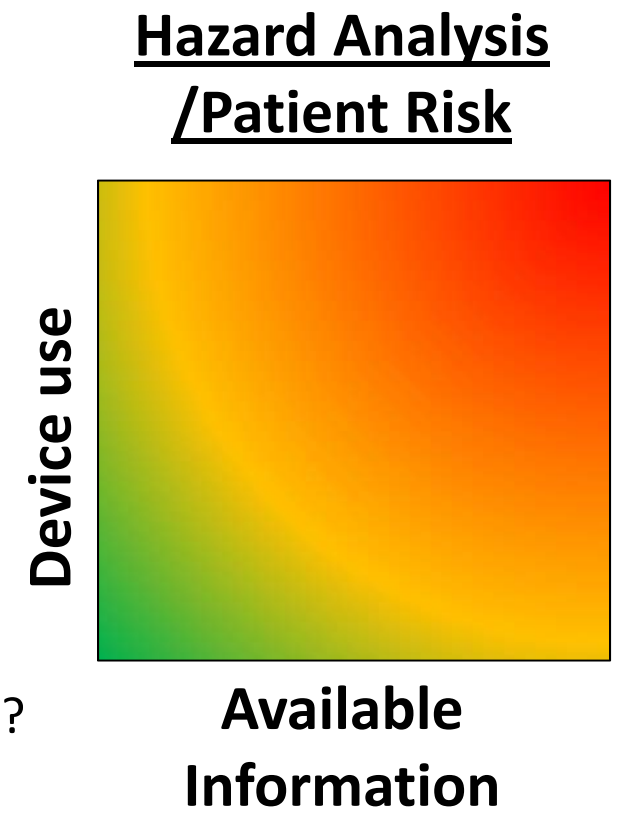


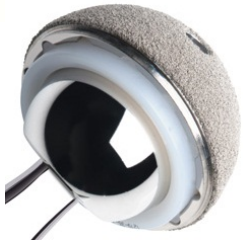


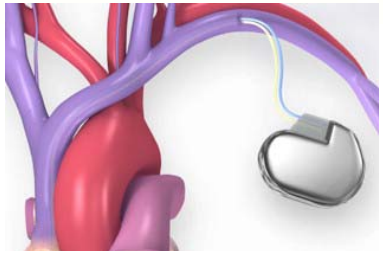
Premarket Review

Risk-based Classification

- Is there sufficient information to assure
  - » Equivalence?
  - » Effectiveness?
  - » Safety?
- Does it:
  - » Support or sustain human life?
  - » Prevent impairment?
  - » Pose unreasonable risk of illness or injury?







Device Class	Class I (exempt)	Class II	Class III
Risk	Low	Moderate	High
Premarket Submission	N/A	510(k)	PMA
Level of Evidence	N/A	Substantially equivalent to predicate	Demonstrate Safety and Effectiveness (e.g. Clinical trial)
Regulatory Controls	Registration and listing General Controls	General Controls Special Controls Devices-specific Guidance	General Controls PMA Device-specific Guidance
FDA decision if successful	N/A	Cleared	Approved

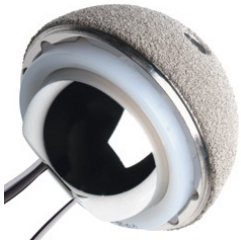
PM Image: http://www.heart.org/HEARTORG/Conditions/Arrhythmia/PreventionTreatmentofArrhythmia/Artificial-Pacemaker_UCM_448480_Article.jsp

Premarket Pathways I

510(k) – Premarket Notification = 60-80% of devices

Typically Class II devices - demonstrate "Substantial Equivalence" to a device already on the market (Predicate).

- **Q:** New indication? New Tech? Do **nonclinical studies (bench/animal/simulation)** support equivalence?
- ~10% require clinical data (for equivalence)
- 90 total FDA days to review



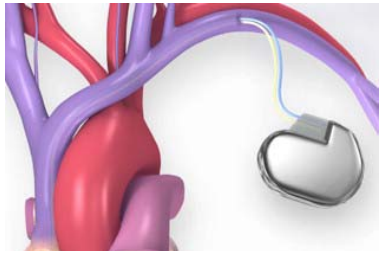
E.g. MoP Hip Replacement

http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm080243.pdf

PMA – Premarket Approval

Generally for Class III devices, requires a **clinical study** to demonstrate safety and effectiveness.

- **Q:** New indication? New Tech? Nonclinical data don't support equivalence?
- May require post-approval study requirements
- 320 total FDA days to review



E.g. Pace maker

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313368.pdf
http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm089767.pdf

Premarket Pathways II

How can you gather clinical data for a device that isn't legally marketable?

IDE – Investigational Device Exemption

Application to conduct a clinical study of an investigational device (usually supports a PMA)

- Early feasibility study
- Feasibility Study
- Pivotal Study

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm

Q-Sub – Pre-submission feedback

- Reach a mutual understanding of **nonclinical** and **clinical** questions/deficiencies to be answered in a submission.
- Necessary **content and endpoints** for studies (primarily clinical): Study Risk Determination to inform IDE design.
- Voluntary & can be requested at any time for any reasonable questions.

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

Medical Device Development Tools (MDDT)

Motivation for MDDT Program

- Innovative technologies often lack standard bench tests and trial designs
  - » Case-by-case tests agreed upon
  - » Sometimes results in 'reinventing the wheel' between submissions and sponsors
  - » Demonstrate the validity of the test each time
- Standards and validated tools aid device design and qualification
  - » Consensus standards
  - » **MDDTs**

Case-by-case

Standards and MDDT

What is an MDDT?

Three MDDT Categories

Clinical Outcome Assessments

e.g.
Subjective measure of clinical parameter:
Patient function or pain, Patient Reported Outcome

Biomarker Tests

e.g.
Objective measure of clinical parameter:
Glucose imaging with PET to identify tumors

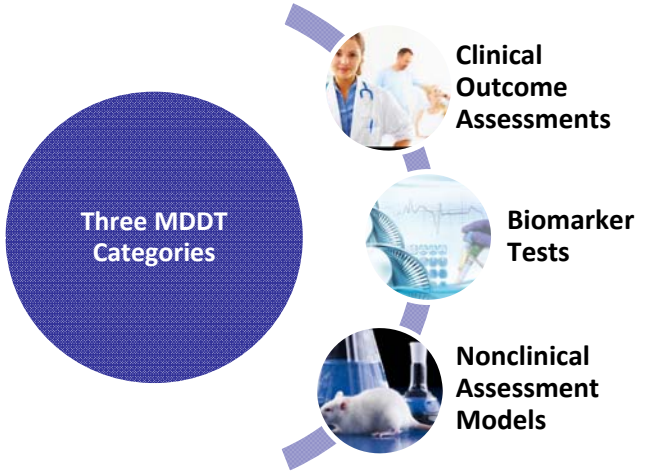
Nonclinical Assessment Models

e.g.
Computational fatigue simulation
Wear simulator protocol

https://www.federalregister.gov/articles/2014/08/15/2014-19360/pilot-program-for-qualification-of-medical-device-development-tools

What is an MDDT?

- A tool (COA, BT or NAM)
- **Voluntarily** developed by an interested party (e.g. industry sponsor, test lab, academia, FDA regulatory scientists)
- Enables the evaluation of regulatory questions in a submission, e.g.
  - » Diagnostic aid, patient selection, monitor treatment response, endpoints/midpoints ...in a clinical trial => Class III
  - » Bench/animal/modeling test that reduces test duration or sample size => Class II & III
- Qualified for use (or licensing) in subsequent pre-market submissions



Utility of a Qualified MDDT

- The results of an assessment can be relied upon for device development & evaluation, within a specified context of use
  - » Device industry need not reconfirm the suitability of a qualified MDDT
  - » Device industry users may need to demonstrate the tool is used according to the specified context of use
- Context of use ≈ boundaries within which evidence & justification supports tool use

Key Qualification Criteria

- *Description of MDDT* - Is the MDDT adequately described?
- *Context of use* - Is the clinical/regulatory context of use adequately and appropriately defined?
- ***Strength of evidence* - Tool validity, scientific plausibility, extent of prediction & capture.**
- *Advantages & disadvantages w.r.t other tools.*

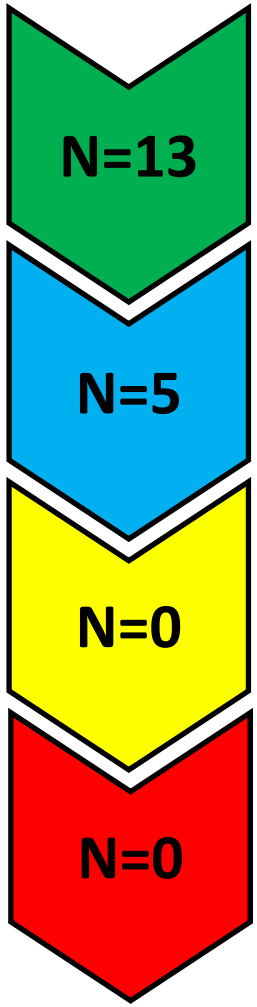
The strength of evidence needed to support qualification depends largely on the context of use.

MDDT Pilot and Timeline

- The FR Notice for the voluntary program was published on August 16, 2014. The aims of the pilot program are to
  - » Pressure test the process: logistics and decision making
  - » Inform changes to the program and guidance
  - » Qualify up to 10-15 pilot tools
- Pilot program will run until the draft guidance is finalized

https://www.federalregister.gov/articles/2014/08/15/2014-19360/pilot-program-for-qualification-of-medical-device-development-tools

MDDT Qualification Process – Pilot



Enrollment N's as of 01/15

Goal: 10-15 qualified

1. Proposal (no fee)

   Submitter enters 5-6 page proposal MDDT@fda.hhs.gov

   FDA Reviews, prioritizes and notifies if selected

2. Evidence plan

   Submitter provides a draft plan of evidence needed

   FDA consults and gives feedback on appropriateness

3. Gather evidence

   Submitter gathers evidence according to plan

   FDA gives interactive feedback upon request

4. Assessment

   Submitter provides qualification package

   FDA evaluates whether evidence supports tool in COU

If successful, description of MDDT is posted publicly

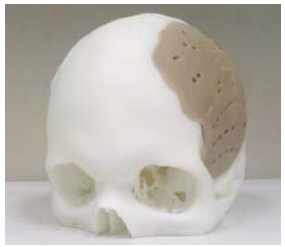
Summary of Benefits of MDDTs

- **For patients:** Innovative medical devices coming to market more quickly, increased adoption of outcome assessments with patient-centered treatment benefit
- **For tool developers:** Foster adoption of their tools & IP, collaboration to amplify evidence collection and reduce individual resource expenditure
- **For device industry:** More predictable product evaluation / reduced regulatory risk
- **For FDA product evaluators:** More efficient process / reduced review time by using established and validated assessments and end-points. Leverage FDA's and sponsor's efforts in creating the MDDT by applying them to multiple submissions.
- **For regulatory scientists:** Standing program to bridge advances in regulatory science into regulatory practice

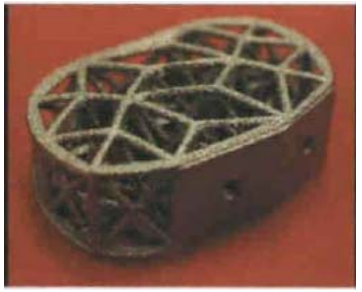
Additive Manufacturing

Types of Cleared Devices

- Patient matched implants
  - » Skull plates
  - » Image based devices

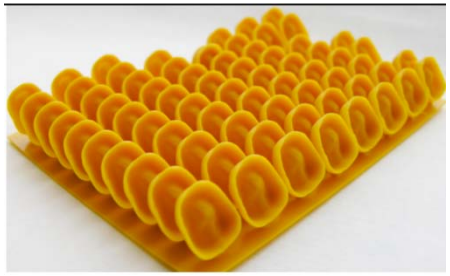


- Orthopaedic devices
  - » Hip Cups
  - » Spinal Cages
  - » Knee trays



- Patient matched surgical guides
  - » Craniofacial
  - » Knee
  - » Ankle

- Dental
  - » Temporary bridges
  - » Reconstructive surgery support

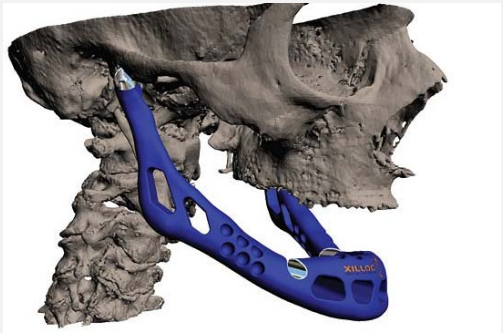


Considerations in a Submission

Imaging

- Type of imaging
- Accuracy and resolution
- Post-processing

Digital Design



- The base model
- Algorithm to fit device to patient
- Design limits
- Key features

Printing

- Print parameters
- Biocompatibility
- Finishing steps
- Cleaning/Sterility

Additive Manufacturing Summary

- Most devices to date are reviewed through existing regulatory pathways
- The agency is proactively gathering expertise and developing policy to address this technology
- Additive Manufacturing holds great promise for personalized medicine and innovative medical solutions

FDA Public Workshop held Oct 8-9 2014

- Slides and webcast available online http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm397324.htm
- Representatives from medical device manufacturers, OEMs, labs, universities, pharmaceuticals, and government
- Helped inform the FDA on the state of the industry and existing technical challenges

Modeling & Simulation

Modeling and Simulation

- ASME V&V40 - verification and validation for computational modeling of medical devices
- Parallel FDA guidance documents under development to cover
  - » Reporting of M&S studies
    - Draft was published in Jan 2014; final guidance being issued in FY2015
    - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm371016.htm
  - » Credibility V&V requirements
    - Draft to be published FY2015

FDA Regulatory Review Resources

- MDDT website and guidance

http://www.fda.gov/MedicalDevices/ScienceandResearch/MedicalDeviceDevelopmentToolsMDDT/default.htm
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm374427.htm

- CDRH Home Page

http://www.fda.gov/MedicalDevices/

- Division of Industry and Consumer Education (DICE) - *to ask general regulatory questions*

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ContactUs--DivisionofIndustryandConsumerEducation/default.htm

- Overview of Device Regulation

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview

- Standards Databases

http://www.fda.gov/medicaldevices/deviceregulationandguidance/standards/default.htm

Contact Information

Office of Science and Engineering Laboratories

Division of Biomedical Physics

Finn Donaldson, PhD
ORISE Fellow/Biomed. Engineer
Finn.Donaldson@fda.hhs.gov

Medical Device Development Tools
MDDT@fda.hhs.gov

Additive Manufacturing work group
AdditiveManufacturing@fda.hhs.gov

Acknowledgements

MeDe

FDA: James Coburn, Tina Morrison, Donna Lochner, Katie O'Callaghan, Gene Civillico