FDA Regulatory Approach for Additive Manufacturing

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Speaker Bio

Dr. Matthew Di Prima is a Materials Scientist in the US Food and Drug Administration's Office of Science and Engineering Laboratories, housed in the Center for Devices and Radiological Health. His areas of research are investigating how the additive manufacturing process can alter material properties, the interplay between corrosion and durability testing, and explant analysis. Along with his research duties, he is the head of the Additive Manufacturing Working Group which is spearheading efforts across the Agency to address how this technology affects medical devices and other regulate medical products

Outline

- FDA and Medical Device Regulations
  - Device Classification
  - Regulatory Controls
  - Submission Types
- How this is applied to AM
  - Cleared AM Medical Devices
  - Patient Matched Devices
  - Anatomical Models

FDA's Mission

- Protecting the public health by assuring that foods (except for meat from livestock, poultry and some egg products which are regulated by the U.S. Department of Agriculture) are safe, wholesome, sanitary and properly labeled; ensuring that human and veterinary drugs, and vaccines and other biological products and medical devices intended for human use are safe and effective
- Protecting the public from electronic product radiation
- Assuring cosmetics and dietary supplements are safe and properly labeled
- Regulating tobacco products
- Advancing the public health by helping to speed product innovations

This equals ~25% of consumer spending in the US

www.fda.gov/AboutFDA/Transparency/Basics/ucm194877.htm

CDRH's Role

- Regulates medical devices and radiation-emitting products
- Evaluate safety and effectiveness of medical devices
  - Before and after reaching market
- Assure patients and providers have timely, continued access to safe, effective, and high-quality medical devices

CDRH Snapshot

1900
EMPLOYEES

18k
Medical Device Manufacturers

183k
Medical Devices
On the U.S. Market

22k/year
Premarket Submissions
including supplements and amendments

570k
Proprietary Brands

25k
Medical Device Facilities Worldwide

1.4 MILLION/year
Reports on medical device adverse events and malfunctions

Medical Device, defined

- Instrument, apparatus, machine, implant, in vitro reagent, including component, part, or accessory
- Diagnoses, cures, mitigates, treats, or prevents disease or condition
- Affects structure or function of body
- Doesn’t achieve purpose as a drug
- Excludes certain software functions
  - data storage, administrative support, electronic patient records

Section 201(h) of FD&C Act

Device Regulations

- 21 Code of Federal Regulations (CFR): Parts 800-1050
  - 800-861: cross-cutting device requirements
    - Example: 812 - Investigational Device Exemption
  - 862-1050: device-specific requirements
    - Example: 876 - Gastroenterology and Urology Devices

- 21 CFR: Parts 1-99
  - general medical requirements that also apply to medical devices

Device Classification

- Based on device description and intended use
- Determines extent of regulatory control
- Class I, II, or III
  - increases with degree of risk
- Product Codes: three-letter coding to group similar devices and intended use

How to determine classification

- Classification is defined under Code of Federal Regulations (e.g. 21 CFR 888.3350)

  (a) Identification: A hip joint metal/polymer semi-constrained cemented prosthesis is a device intended to be implanted to replace a hip joint. The device limits translation and rotation in one or more planes via the geometry of its articulating surfaces. It has no linkage across-the-joint. This generic type of device includes prostheses that have a femoral component made of alloys, such as cobalt-chromium-molybdenum, and an acetabular resurfacing component made of ultra-high molecular weight polyethylene and is limited to those prostheses intended for use with bone cement (888.3027).

  (b)Classification. Class II.

- This language is specific, slight changes in device design/function can change the regulation and therefore the classification
- If your device is not in the CFR, you have to request a designation and classification from the FDA, 513(g)

Classes of Medical Devices

Class	Risk	Controls	Submission
I	Lowest	General	• Exempt* • 510(k)
II	Moderate	General and Special (if available)	• 510(k)* • Exempt
III	Highest	General and PMA	• PMA

*** More common submission requirement of this Class**

General Controls: Examples

Control	Regulation (21 CFR Part)	Brief Description
Labeling	801	provide information for users
Medical Device Reporting	803	report device-related injuries and deaths
Establishment Registration	807	register business with FDA
Device Listing	807	identify devices
Quality System	820	ensure safe, effective finished devices
Adulteration	FD&C Act 501	provide device not proper for use
Misbranding	FD&C Act 502	provide false or misleading labeling

FD&C Act = Federal Food Drug, and Cosmetic Act

Special Control

- Specific to Class II devices
- Usually for well-established device types
- Found in "(b) *Classification*" of regulation
  - example: 21 CFR 876.5860(b)

21 CFR 876.5860 High permeability hemodialysis system

- (a) Identification. A high permeability hemodialysis system is a device intended for use as an artificial kidney system for the treatment of patients with renal failure, ...

- (b) Classification. Class II. The special controls for this device are FDA's:

  - (1) "Use of International Standard ISO 10993 'Biological Evaluation of Medical Device - Part I: Evaluation and Testing,' "
  - (2) "Guidance for the Content of 510(k)s for Conventional and High Permeability Hemodialyzers,"
  - (3) "Guidance for Industry and CDRH Reviewers on the Content of Premarket Notifications for Hemodialysis Delivery Systems,"
  - (4) "Guidance for the Content of Premarket Notifications for Water Purification Components and Systems for Hemodialysis," and
  - (5) "Guidance for Hemodialyzer Reuse Labeling."

Special Controls: Examples

- Design, Characteristics or Specifications
- Testing
- Special Labeling
- Guidance Documents

Premarket Submission Types

- Investigational Device Exemption (IDE)
- Premarket Notification (510(k))
- Premarket Approval Application (PMA)
- De Novo
- Humanitarian Device Exemption (HDE)

AM and Device Manufacturing

- Generally, manufacturing method does not change regulatory classification or regulatory controls
- This allows AM products to use existing regulatory pathways
  - The majority of AM devices have been cleared through the 510(k) pathway to date
  - Predicate devices can be AM or non-AM
  - Generally, we don't expect the "technological characteristics of the devices [to] raise different questions of safety and effectiveness"[1]
  - I.E., a spine cage is a spine cage and a bone plate is a bone plate

[1] FDA Guidance "Benefit Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics"

AM 510(k) Submissions

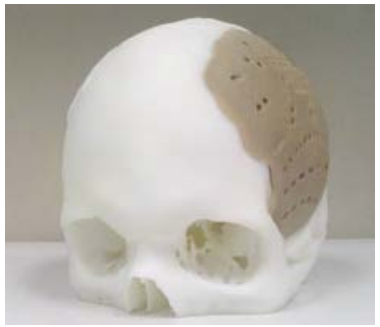
- FDA Guidance "Technical Considerations for Additively Manufactured Medical Devices" details pre-market submission expectations
- For a 510(k) submission, we are looking for the worst case AM condition to be determined in order to ensure subject device performance is substantially equivalent to the predicate
- This is different from most non-AM submissions as material performance can be assessed separately from the manufacturing process
  - In most cases purchasing controls and an understanding of tooling/post-processing effects **are** sufficient to address material performance
  - For AM controlling only the feedstock and understanding the tooling/post-processing effects **are not** generally sufficient to address material performance

AM 510(k) Submissions – Establishing Worst Case Build Conditions

- Build location
  - Establish the worst case build location or that all build locations have comparable mechanical properties
- Build orientation
  - If multiple build orientations are used, which will have the worst mechanical properties
- Feedstock re-use
  - For AM processes that re-use feedstock, what is the re-use scheme and is there a worst-case feedstock condition in terms of performance and variability
- Residual feedstock in lattice/porous structures
  - How residual feedstock material is removed from lattice/porous structures and what is the worst case for residual feedstock in final device

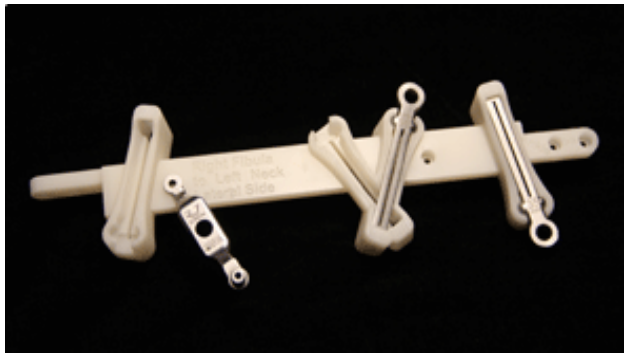
Evidence of this working: 510(k) Cleared 3D Printed Devices

- Patient matched implants
  - Skull plate
  - Maxillofacial implants



K121818
OsteoFab by OPM
http://www.accessdata.fda.gov/cdrh_docs/pdf12/K121818.pdf

- Patient matched surgical guides
  - Craniofacial
  - Knee
  - Ankle

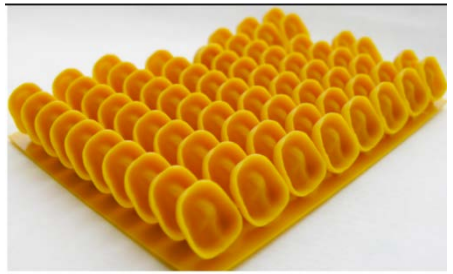


K120956
VSP® by Medical Modeling
http://www.accessdata.fda.gov/cdrh_docs/pdf12/K120956.pdf

- Orthopedic devices
  - Hip Cups
  - Spinal Cages
  - Knee trays

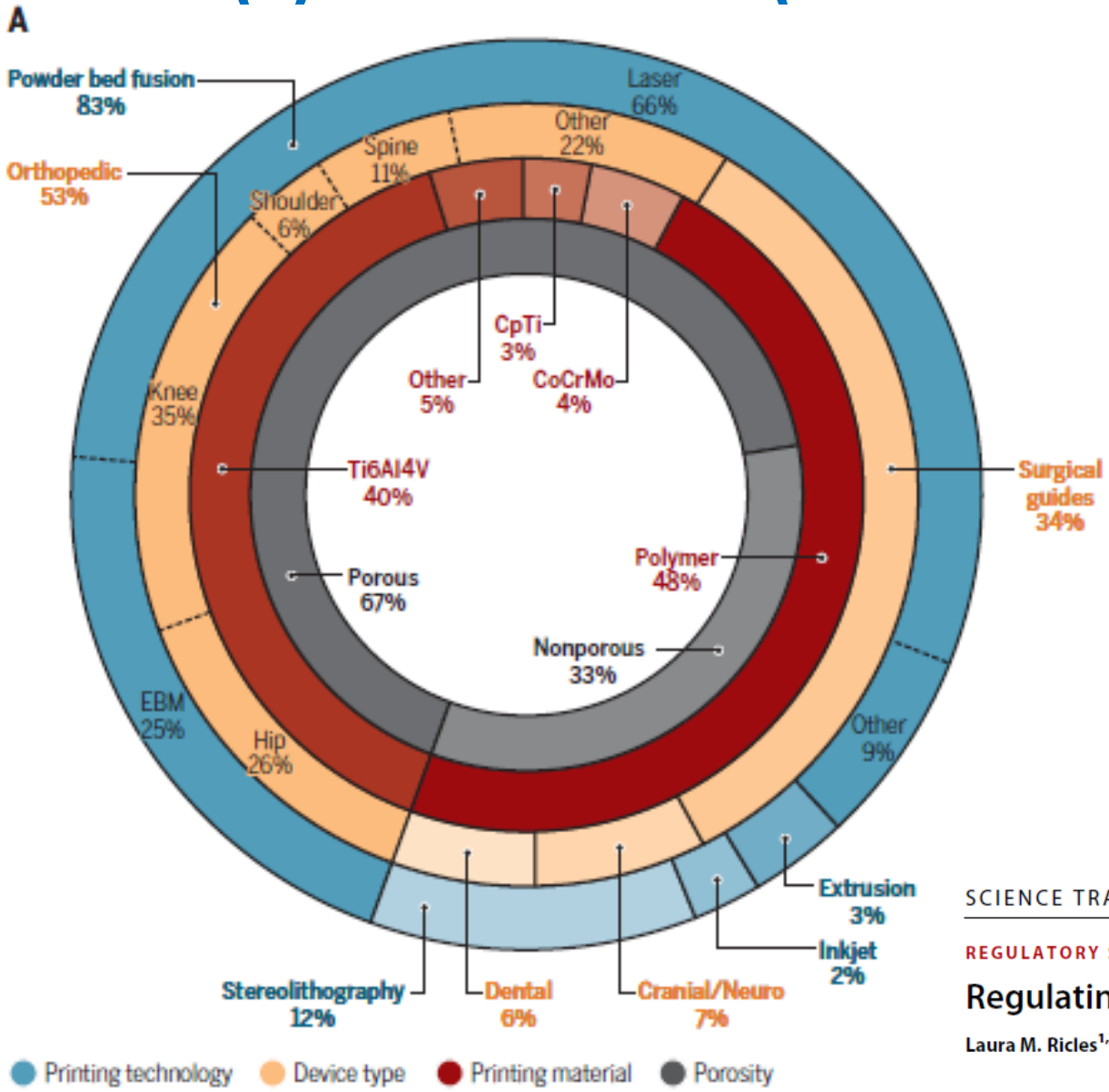
K102975
Novation Crown by Exatech
http://www.accessdata.fda.gov/cdrh_docs/pdf10/K102975.pdf

- Dental
  - Temporary bridges
  - Reconstructive surgery support



K102776
e-DENT Temporary Resin by DeltaMed GmbH
http://www.accessdata.fda.gov/cdrh_docs/pdf10/K102776.pdf

Cleared 510(k) AM Products (2010 – 2016)



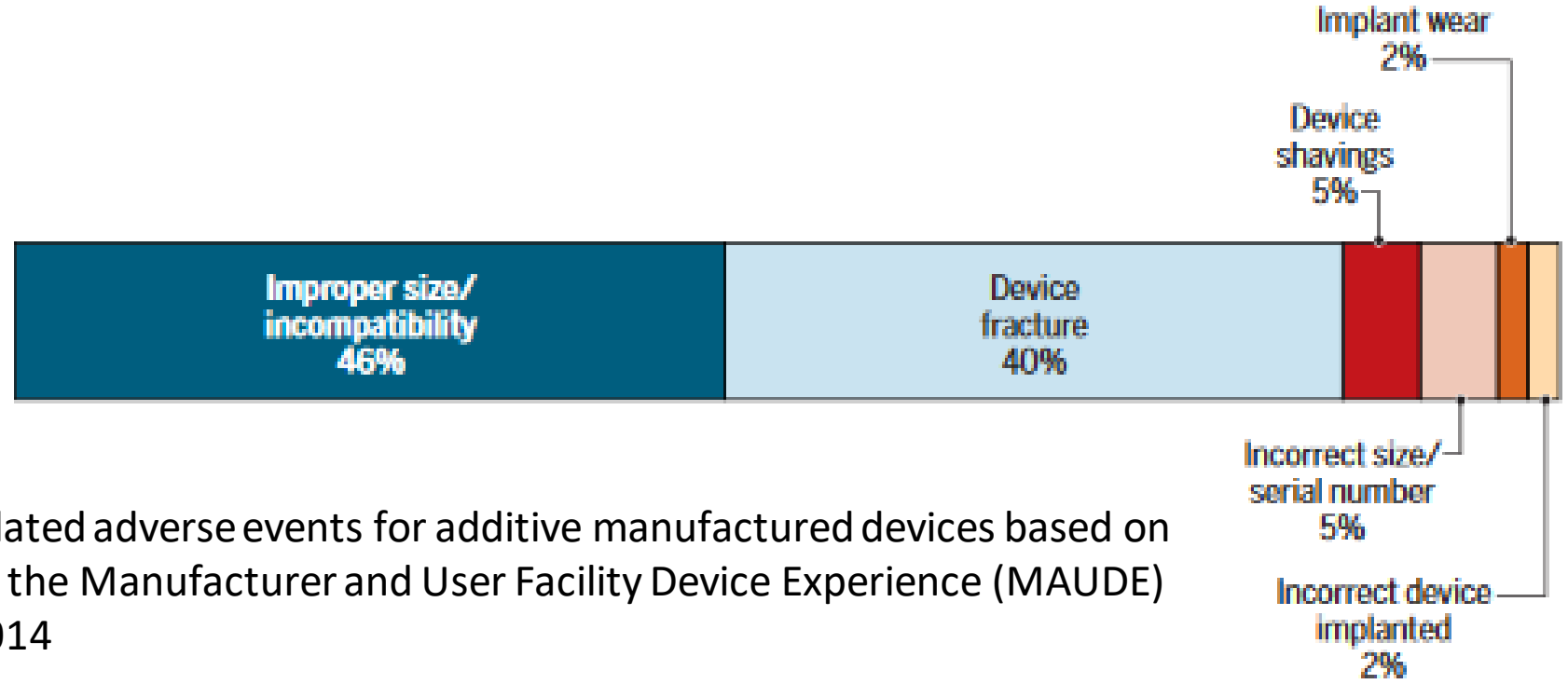
SCIENCE TRANSLATIONAL MEDICINE | PERSPECTIVE

REGULATORY SCIENCE

Regulating 3D-printed medical products

Laura M. Ricles[1,2], James C. Coburn[3], Matthew Di Prima[3], Steven S. Oh[1]*

AM Device Adverse Events 2014



59 product-related adverse events for additive manufactured devices based on 836 reports to the Manufacturer and User Facility Device Experience (MAUDE) database in 2014

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Patient Matched Devices

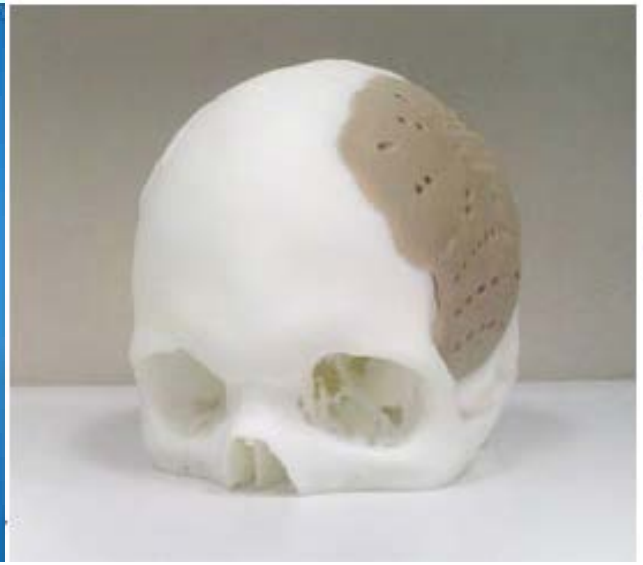
- Pairing 3D imaging (CT, MRI, optical scanning) with AM printing for personalized medical devices
  - Implants
  - Anatomical models
- Incorporating virtual surgical software allows for personalized cutting guide and tools
- Regulatory challenge is that there is no longer a discrete device to assess, instead we are looking at a design envelope

Examples of Patient Matched Devices

K133809:

http://www.oxfordpm.com/news/article/2014-08-19_oxford_performance_materials_receives_fda_clearance_for_3d_printed_osteofab_patient-specific_facial_device.php

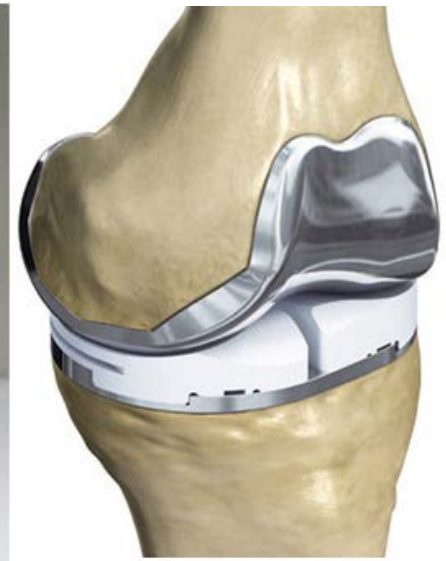
http://www.accessdata.fda.gov/cdrh_docs/pdf13/K133809.pdf



K121818:

http://www.oxfordpm.com/news/article/2013-02-18_osteofab_patient_specific_cranial_device_receives_510k_approval_-_osteofab_implants_ready_for_us_market_and_beyond.php

http://www.accessdata.fda.gov/cdrh_docs/pdf12/K121818.pdf



K122870:

http://www.conformis.com/customized-knee-implants/products/itotal/

http://www.accessdata.fda.gov/cdrh_docs/pdf12/K122870.pdf

Patient Matched Regulatory Approach

- Not Custom Devices
  - Devices meeting the regulatory definition of “custom devices” are exempt from pre-market review
  - §V.E of FDA “Custom Device Exemption Guidance” explains why patient matched device generally don’t meet the custom device requirements
- Treating the design envelope as the device design requirements
  - Design envelope needs to be validated for the intended use
  - For 510(k)-eligible devices, substantial equivalence needs to be shown for the worst cases

AM Anatomic Models

- Intended Use of the Anatomic model is key to determine if they are considered medical devices
- Diagnostic Use makes a model a medical device (i.e., the model will affect diagnosis, patient management, or patient treatment)
  - Models used to make a diagnosis based on examination or a physical measurement of structural changes from the 3D model
  - Using the model to size and/or select a device or surgical instrument based on a comparison, fitting, or measurements with the model
  - Using the model to determine whether a specific surgical procedure may be viable

AM Anatomic Model Regulatory Approach

- A 3D printed patient-specific anatomic model that is intended for diagnostic use is, in essence, a physical representation of a digital 3D model that is produced by medical image analysis software.

- The software used to generate the 3D printed models based on medical images, will be regulated. There needs to be evidence that the 3D printed models are of equivalent accuracy to the digital 3D models (segmented volumes).

- The goal is not to have to clear every individual 3D printed model, or the 3D printers. Instead, FDA will clear software capable of generating diagnostic quality 3D printed anatomic models that has been tested and validated on a set of 3D printers based on the performance needed for the intended use and anatomy (i.e., orthopedic, cardiovascular, neurological, etc.).

Summary of AM Regulatory Approach

- Existing FDA regulatory pathways and controls have been sufficient to handle the AM medical devices that we have reviewed
- Existing product performance requirements/predicate comparisons have generally been sufficient to ensure safety and efficacy
  - One product specific test standards has been developed to address fatigue concerns in AM acetabular (hip) cups
  - Ongoing research to evaluate adequacy of lattice/porous standards for AM Products
- Currently working to develop a framework to handle the adoption of AM technologies by hospitals and other points of care.

Thank You For Your Attention

Questions?

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