Update on Regulating 3D-Printed Medical Products

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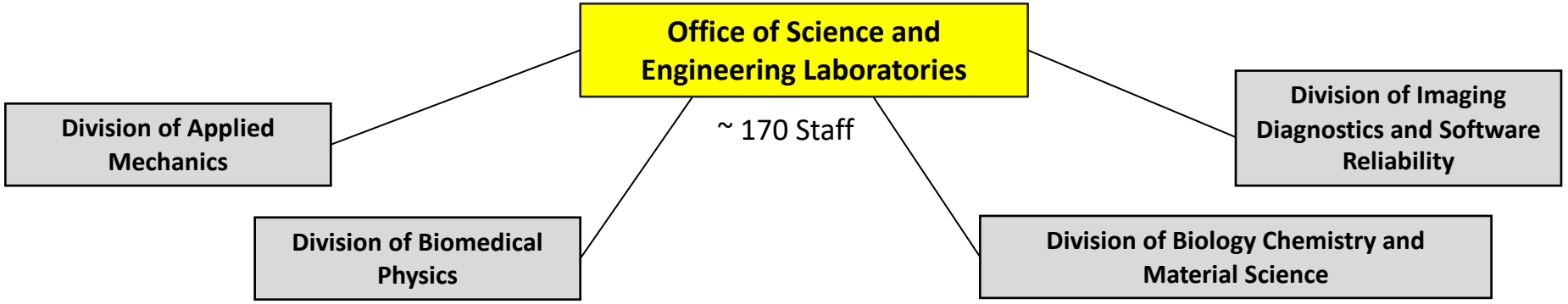
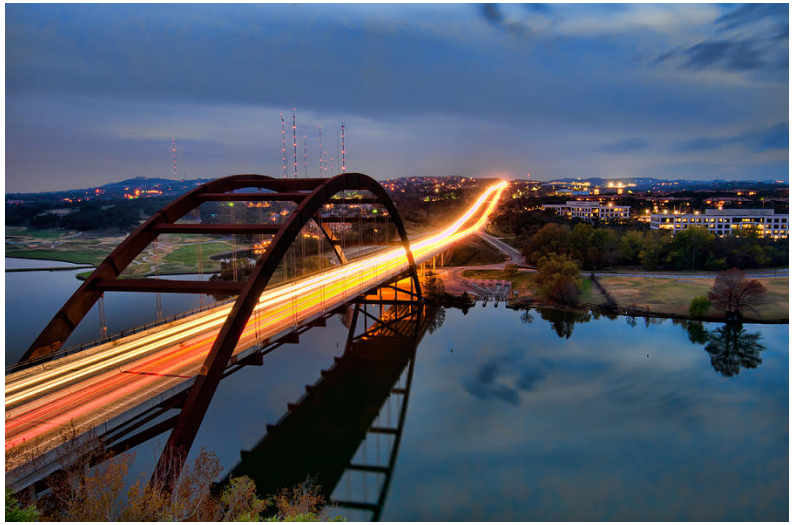


Office of Science and Engineering Laboratories Mission:

- Ensure readiness for emerging and innovative medical technologies
- Develop appropriate evaluation strategies and testing standards
- Create accessible and understandable public health information
- Deliver timely and accurate decisions for products across their life cycle

[1]https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhoffices/ucm115989.htm

Predictable and Efficient Pathways



- Medical Device Development Tools
  - FDA validated methods that can be used for device approval and clearance
- Standards: ISO, IEC, ASTMi
  - Publically accessible recognized standards
- Guidance Documents
- Scientific Dissemination

Outline

- Final AM Technical Guidance
- Analysis of 510(k) Cleared Devices from 2010 – 2016 made using AM
- 3D Printing of Anatomical Models

Technical Considerations for Additive Manufactured Medical Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 5, 2017.

The draft of this document was issued on May 10, 2016.

FINAL AM TECHNICAL GUIDANCE

In Scope for this Guidance

- **Design and Manufacturing** Considerations
  - Provides technical considerations that should be addressed as part of QS requirements
  - QS requirements determined by existing regulatory classification/regulations

- **Device Testing** Considerations
  - Describes what AM specific information should be included in a premarket submission
  - Type of premarket submission is determined by regulatory classification

Out of Scope for this Guidance

- Regulatory policy
  - Point of care/hospital printing
  - Device specific regulations
- Direct printing of cells/tissues
- Specific device/policy questions should be addressed through the pre-submission process:
  http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

Guidance Objectives

- Broadly address considerations for AM medical devices
  - Identify important aspects of the technologies and workflows
  - Provide a framework for evaluating processes using AM

- ***Not all considerations apply*** to every AM technology, material, or device

Sponsors should apply individual considerations based on their specific situation

From Draft to Final Guidance

- 294 comments from 29 commenters
- Multiple stakeholder interactions
  - Scientific and industry meetings
  - Standards Committees

Significant Changes

- **Added** a brief section (V.B.4) on cybersecurity and personally identifiable information (PPI)
  - Points to existing guidance
  - Does not present new guidance

- **Updated** Labeling (VII)
  - Now consistent with other guidance documents
  - Clarified to apply only to patient matched devices

Significant Changes

- **Replaced** most instances of “cleaning” with “removing manufacturing material residue” in Cleaning and Sterilization (VI.E)
  - Harmonize with the regulatory language in CFR 820.3
  - Does not refer to removing biological soil
  - Does not reflect a change in technical considerations

Patient matching considerations

- **Not custom devices**
  - See §V.E of Custom Device Exemption Guidance
- Treated as a specified design envelope
  - Requires validation
  - Show Substantial Equivalence of worst case(s)
- Addresses patient matching in conjunction with AM
  - Does not address ***all*** concerns with patient matched devices

SCIENCE TRANSLATIONAL MEDICINE | PERSPECTIVE

REGULATORY SCIENCE

Regulating 3D-printed medical products

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Additive manufacturing [also known as three-dimensional (3D) printing] is the layer-wise deposition of material to produce a 3D object. This rapidly emerging technology has the potential to produce new medical products with unprecedented structural and functional designs. Here, we describe the U.S. regulatory landscape of additive manufactured (3D-printed) medical devices and biologics and highlight key challenges and considerations.

ANALYSIS OF 510(K) CLEARED PRODUCT MADE VIA 3D-PRINTING (2010 – 2016)

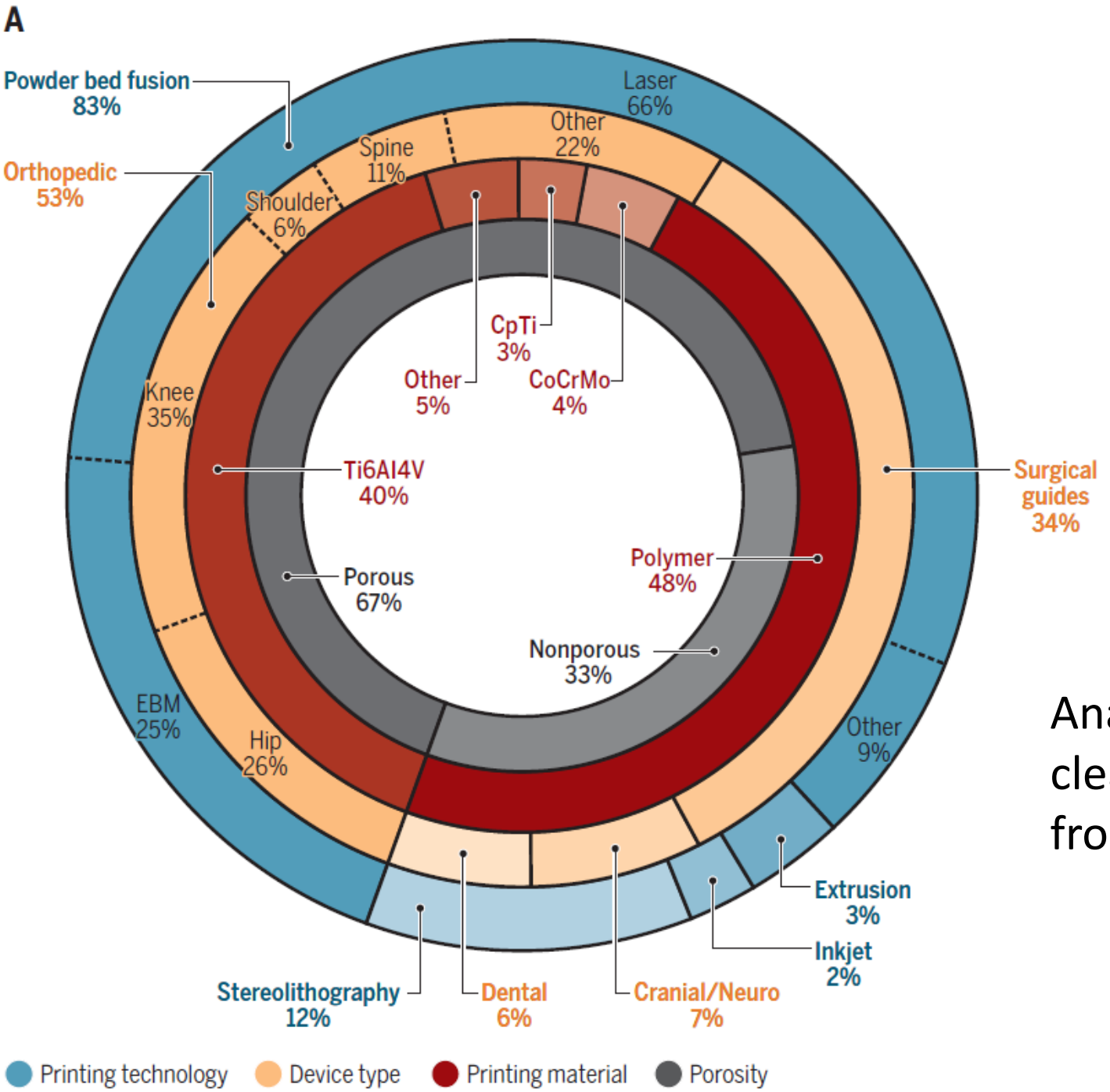
Methodology

Clearance

- Searched FDA database from 2010 – 2016 for the terms:
  - Additive manufacturing
  - 3D Printing
  - Rapid manufacturing
  - Additive fabrication
  - Electron beam melting
  - Selective laser sintering
- Manually verified and filtered
- Data de-identified and aggregated

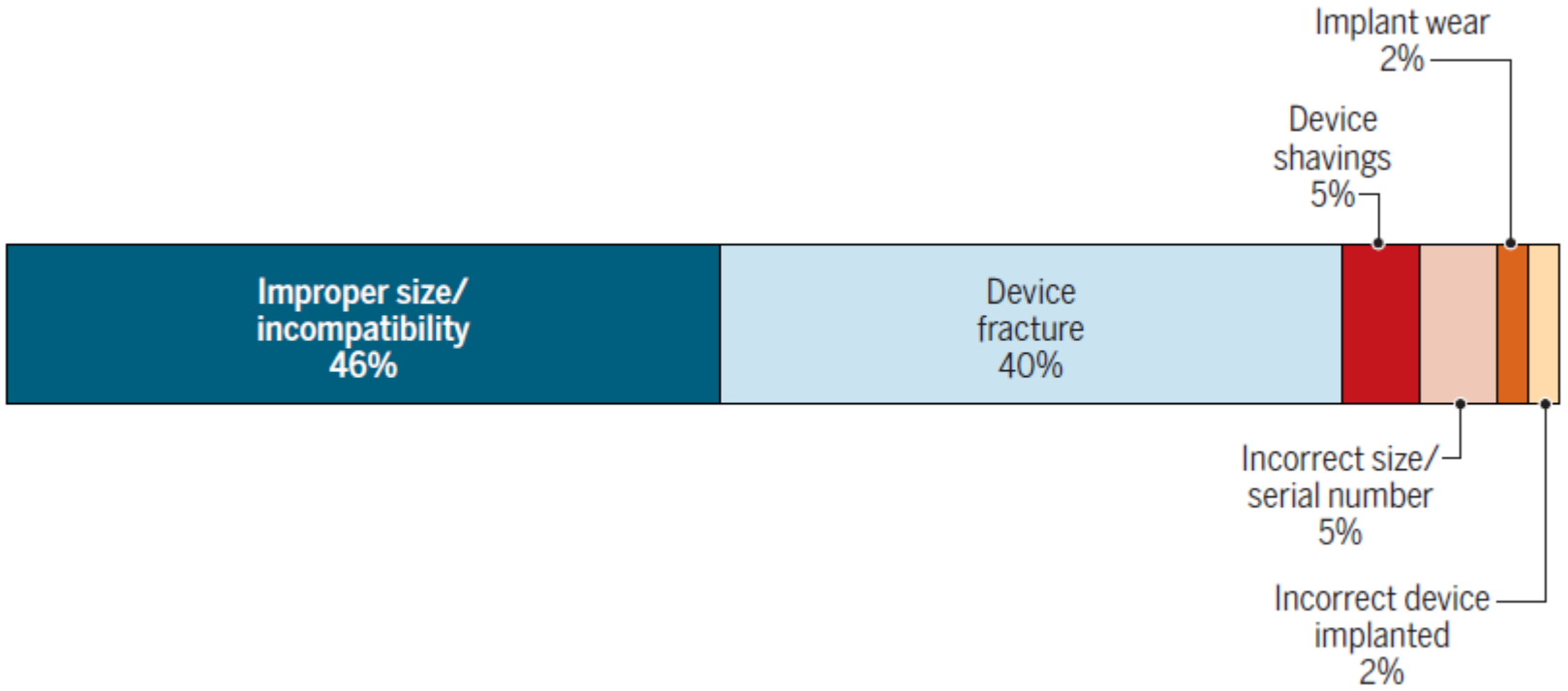
MDR

- Search of FDA Manufacturer and User Facility Device Experience Database for adverse reports for device identified in clearance search
- Snap shot of 2014 (most recent year with complete MDR data at time of analysis)
- Initial 836 reports screened for issues related to:
  - Product error
  - Use error
  - Therapeutic failures



Analysis of 510(k) cleared AM devices from 2010 - 2015

2014 MDR Findings



ANATOMICAL MODELS

Are 3D Printed Anatomic Models Medical Devices?

Answer: It depends on the intended use of the 3D printed anatomic model.

> *FDA defines a **medical device** as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:*
>
> *"… intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man …"*

If 3D printed anatomic models are being marketed for **diagnostic use**, then they are considered a medical device.

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How are 3D Printed Anatomic Models Classified?

- Classified based on intended use, risk, and predicate device existence

- Diagnostic Intended Use – Class II
  - Intended for adjunctive use along with radiological images (MRI, CT, US, etc.) for diagnosis, patient management, and/or treatment selection.
  - Inaccurate models could mislead the physician resulting in a misdiagnosis, delayed treatment, or patient mismanagement.
  - Models may be found substantially equivalent to software generated 3D models/segmentation of anatomy for image analysis and measurement which can be achieved with performance testing

- Not a Medical Device
  - Not intended for diagnostic use
  - Not subject to general controls (registration and listing, GMP, etc.)
  - No risk to patient; use does not impact diagnosis or patient management

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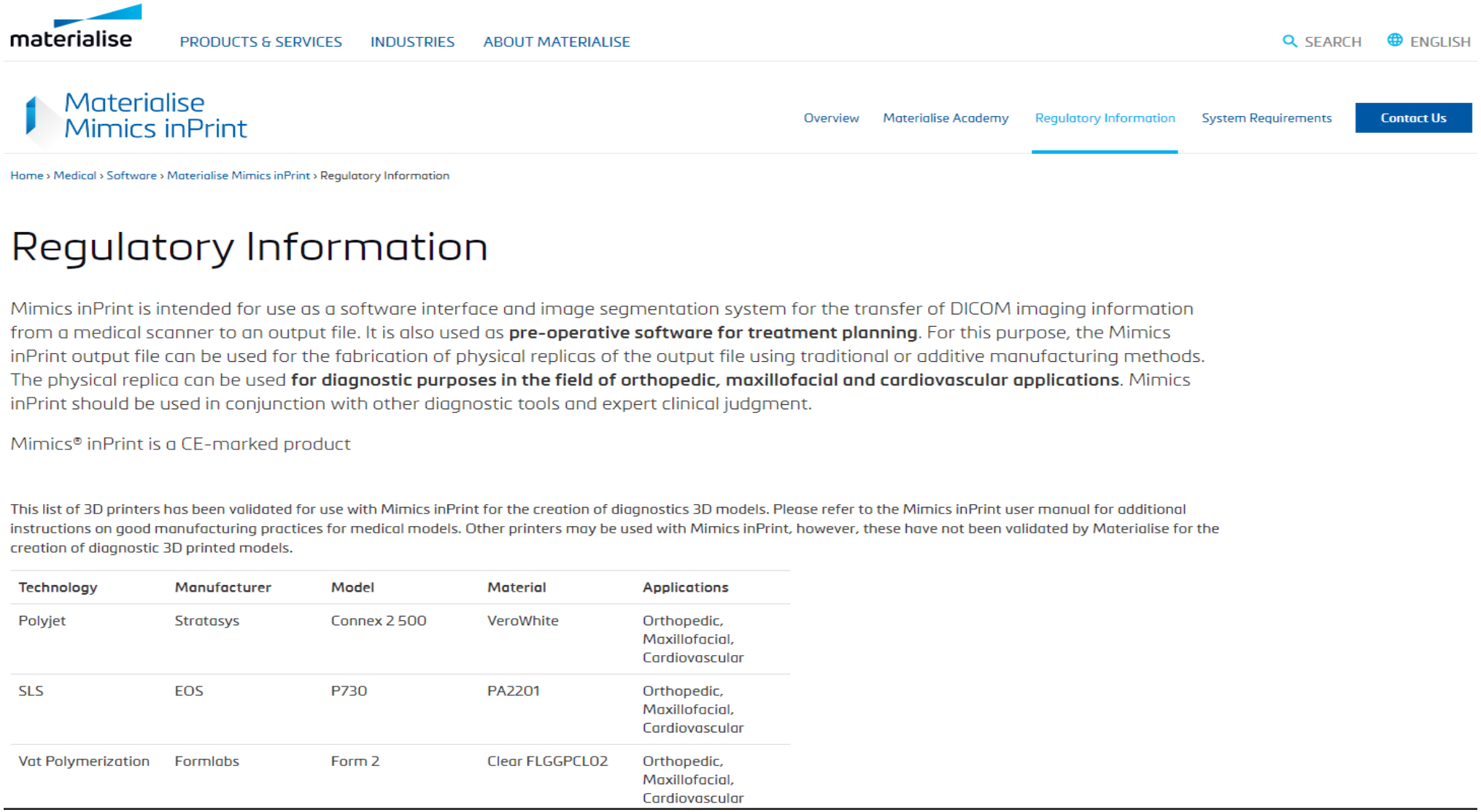
Materialise Mimics InPrint



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Materialise Mimics inPrint

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Regulatory Information

Mimics inPrint is intended for use as a software interface and image segmentation system for the transfer of DICOM imaging information from a medical scanner to an output file. It is also used as **pre-operative software for treatment planning**. For this purpose, the Mimics inPrint output file can be used for the fabrication of physical replicas of the output file using traditional or additive manufacturing methods. The physical replica can be used **for diagnostic purposes in the field of orthopedic, maxillofacial and cardiovascular applications**. Mimics inPrint should be used in conjunction with other diagnostic tools and expert clinical judgment.

Mimics® inPrint is a CE-marked product

This list of 3D printers has been validated for use with Mimics inPrint for the creation of diagnostics 3D models. Please refer to the Mimics inPrint user manual for additional instructions on good manufacturing practices for medical models. Other printers may be used with Mimics inPrint, however, these have not been validated by Materialise for the creation of diagnostic 3D printed models.

Technology	Manufacturer	Model	Material	Applications
Polyjet	Stratasys	Connex 2 500	VeroWhite	Orthopedic, Maxillofacial, Cardiovascular
SLS	EOS	P730	PA2201	Orthopedic, Maxillofacial, Cardiovascular
Vat Polymerization	Formlabs	Form 2	Clear FLGGPCL02	Orthopedic, Maxillofacial, Cardiovascular

U.S. FOOD & DRUG ADMINISTRATION

Questions?

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www.fda.gov/3DPrinting

Postgraduate Research Opportunity - Polymer Scientist/Chemist

FDA - Center for Devices and Radiological Health (CDRH)

Perform laboratory research studies that will include conducting 1) oxidative aging studies of polymeric materials, and 2) chemical analysis which includes polymer extraction following oxidation

- B.S. (1-2 years experience) or M.S. in chemistry, polymer science, chemical/polymer engineering or related field
- Hands-on experience in chemical analysis (e.g. LC/MS, GC/MS, ICP/MS, FTIR) and/or polymer analysis (e.g. DSC, TGA, GPC)
- Submit cover letter, resume/CV, and contact information for 3 references to David Simon PhD, david.simon@fda.hhs.gov