U.S. FOOD & DRUG ADMINISTRATION

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FDA/CDRH Webinar

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U.S. FOOD & DRUG ADMINISTRATION

Technical Considerations for Additive Manufactured Medical Devices

Additive Manufacturing Working Group
Center for Devices and Radiological Health

January 10, 2018

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- Office of Compliance
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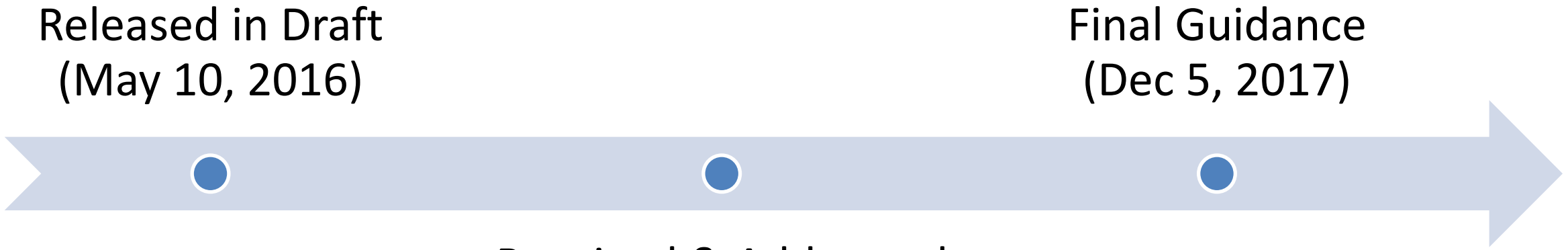
Guidance Documents

- Represent FDA's current thinking on a topic
- Do not create or confer any rights for or on any person
- Do not bind FDA or the public
- Allow you to use alternative approaches if the approach satisfies the requirements of the applicable statutes and regulations

This 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

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

Guidance Objectives

- **Supplement** device specific guidance or testing
  - Identify AM-specific concerns
  - Aid in determining a worst case conditions

- **Be a resource** for
  - The device portion of combination products
  - Stakeholders who are new to medical device manufacture or AM of medical devices

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

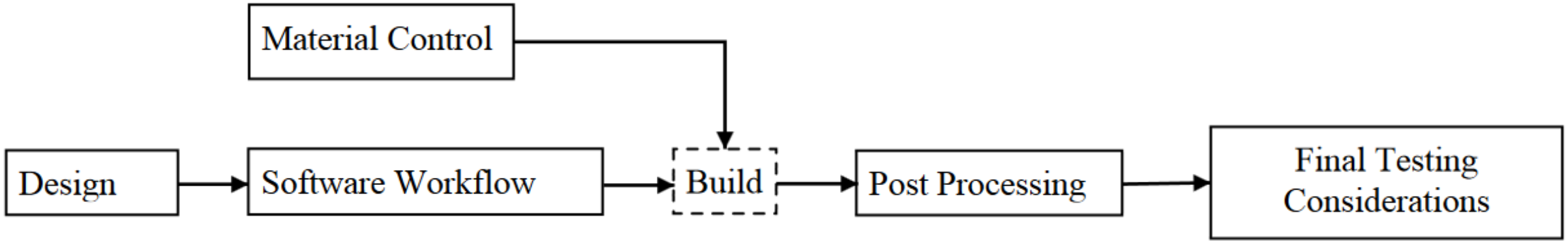
Out of Scope for this Guidance

- 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

Additive Manufacturing Process Simplified Flowchart



A Hypothetical Example Device

- Patient-matched cranial repair device
  - –Fit to patient anatomical imaging
  - –Uses patient-specific surgical guides
  - –Manufactured using
    - Powder bed fusion process
    - Ti-6Al-4V

DESIGN AND MANUFACTURING CONSIDERATIONS

Device Design

- –Additive manufacturing technologies have different design considerations
- –Patient matching is easier, accomplished through many methods

- Technical Consideration
  - –Device description includes
    - Description of additive manufacturing technology
    - Process flowchart
  - –For patient matching
    - Describe patient-matched features
    - Provide design envelope

Cranial device example:

- Brief description of the powder bed fusion technology & process flowchart
- Patient-matching design envelope
  - Curve of plate to match skull contours of the opposite side
  - Edges of plate to match cranial defect
  - Minimum allowable thickness = 2 mm
  - Sharpest corner = 3 mm radius
  - Maximum planar area = 25 mm^2

Software Workflow

- Software workflow is critical to Additive Manufacturing device design and production
- File conversions and translation from digital to printable forms
- Workflows often includes a human-in-the-loop

- Technical Consideration
  - Analyze workflow for effects on the Additive Manufacturing processes
    - Clearly describe analysis
  - How do any variations affect the final product

Cranial device example:

- Patient imaging using standard protocol
- Segmentation of patient anatomy from the imaging by trained users
  - Process validated to known image set
- Resolution
  - Printer: 100µm in powder bed plane
  - Printer: 50µm layer thickness
  - Image resolution = 250 μm^3

Material Controls

- Final material is produced *in situ*
- Quality and consistency of starting materials are very important
- Each technology, process, and even intended use may have different material requirements
- Material reuse can affect the final part

- Technical Consideration
  - Ensure starting material and mixture of re-used material (if applicable) will yield the appropriate physical and chemical properties

Cranial device example:

- Brief description of starting material requirements
  - meets ASTM F2924 chemistry requirements
  - powder size range from 10–40 µm
- Description and validation of powder reuse protocol
  - Powder is re-used a maximum of 5 times
  - Validation testing shows 5x re-used powder is similar to virgin, not a worst case test condition

Post-Processing

- Post-processing steps can affect
  - Final device performance
  - Material properties

- Technical Consideration
  - Describe any post-processing steps
  - Identify any detrimental effects on final device performance
  - Describe mitigations

Cranial device example:

- Post-Processing Steps:
  - Removal from powder bed
  - Cut from build plate
  - Annealed
  - CO_2 blasted
  - Final machining
  - Final cleaning
  - Gamma sterilized

Process Validation & Acceptance

- Device quality affected by numerous parameters
- Generally less experience in creating controlled Additive Manufacturing processes compared to traditional techniques.

- Technical Consideration
  - Evaluate how each step of the Additive Manufacturing process workflow affects the following steps.
  - Additive Manufacturing procedures may differ from other manufacturing techniques in
    - Process monitoring
    - Revalidation triggers
    - Acceptance testing criteria

Cranial device example:

- Extreme cranial curvature -> altered placement angle
  - Validate a range of placement angles for design envelope
- Individual cranial device size can alter thermal profile of build
  - Ensure that coupons are validated for worst case
  - Use an infrared camera to monitor bed temperature profile

DEVICE TESTING CONSIDERATIONS

Performance Testing

- Technology-specific concerns affecting performance of final finished device including
  - Orientation
  - Build location
  - Other parameters

- Technical Consideration
  - Part orientation and location should factor into worst case consideration for testing
  - Can leverage validation testing of system using representative coupons

Cranial device example:

- Validation of build space showed
  - Corners of build space had significantly poorer mechanical performance than rest of build space
  - Build orientation did not have a significant effect of mechanical performance

- Worst case selection consideration
  - No corners used, remaining space considered uniform
  - All devices printed same orientation,

Material Characterization

- Additive Manufacturing Technologies alter the starting material to create the final material during build
- Need to understand if the Additive Manufacturing process creates any material risks

- Technical Considerations
  - Investigate the effect the printing process has on your material
  - Specifics vary based on the material and Additive Manufacturing technology
  - Additional considerations for resorbable or other active materials

Cranial device example:

- Material Characterization
  - Virgin powder, 5x reused powder, and final part chemistry conform to ASTM F2924
  - Final part conforms to mechanical and microstructural requirements of ASTM F2924

Removing Manufacturing Residue, Device Cleaning and Sterilization

- Additive Manufacturing generally requires residue and support removal steps
- Complex geometries can make residue removal, cleaning, & sterilization a challenge

- Technical consideration
  - Describe your manufacturing residue removal process and validate
  - Should include worst case geometries (porosity/blind holes)
  - Placement of cleaning and sterilization test samples should be carefully considered

Cranial device example:

- Manufacturing removal process
  - Removed from powder bed
  - Blasted with CO2
  - Final Machining
- Validation/worst case
  - Solid part with no porosity/blind holes and machined to final size.
  - Little risk of residual powder on final finished part
- Cleaning and Sterilization
  - Validated cleaning cycle similar to non-AM devices with minimally complex or internal geometries
  - Gamma irradiated

Biocompatibility

- Ensure that Additive Manufacturing does not adversely affect biocompatibility

- Technical Consideration
  - ISO 10993 should be sufficient
  - Possible additional information/testing if
    - Known toxic substances (e.g. some photoinitiators)
    - Unknown long term effects
  - New FDA Guidance on Biocompatibility testing addresses use of ISO 10993

Cranial device example:

- Material has a long history in similar clinical applications
- Perform cytotoxicity testing for new cell types in this indication for use

ADDITIONAL LABELING CONSIDERATIONS

Additional Labeling Considerations

- Patient matched devices are not always easily identified by clinician

- Technical Consideration
  - Patient matched device should be labeled with
    - patient identifier
    - anatomical location (or identifier)
    - design iteration used to produce the device
    -
- **Note: These are safety considerations and do not intersect with or alter UDI requirements**

Cranial device example:
- Each printed device includes a tag with
  - Patient identifier
  - Anatomy identifier
  - Design designation

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Questions?

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http://www.fda.gov/training/cdrhlearn

Under the Heading: Specialty Technical Topics; subheading: Custom Devices