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Technical Considerations for Additive Manufactured Medical Devices

Additive Manufacturing Working Group
Center for Devices and Radiological Health

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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

- Released in Draft (May 10, 2016)
- Final Guidance (Dec 5, 2017)
- Received & Addressed Comments

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

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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

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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

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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

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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:
Additive Manufacturing
Process Simplified Flowchart

Design → Software Workflow → Build → Post Processing → Final Testing Considerations → Material Control
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

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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 mm²

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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 µm³

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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

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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
  • CO2 blasted
  • Final machining
  • Final cleaning
  • Gamma sterilized

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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

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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 and final part chemistry conform to ASTM F2924
• Final part conforms to mechanical and microstructural requirements of ASTM F2924

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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

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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

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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
Questions?

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