PROCESS VALIDATION FOR AM

Daniel Porter, PhD

Division of Applied Mechanics

Office of Science and Engineering Laboratories

Center for Devices and Radiological Health

U.S. Food and Drug Administration

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Disclaimer

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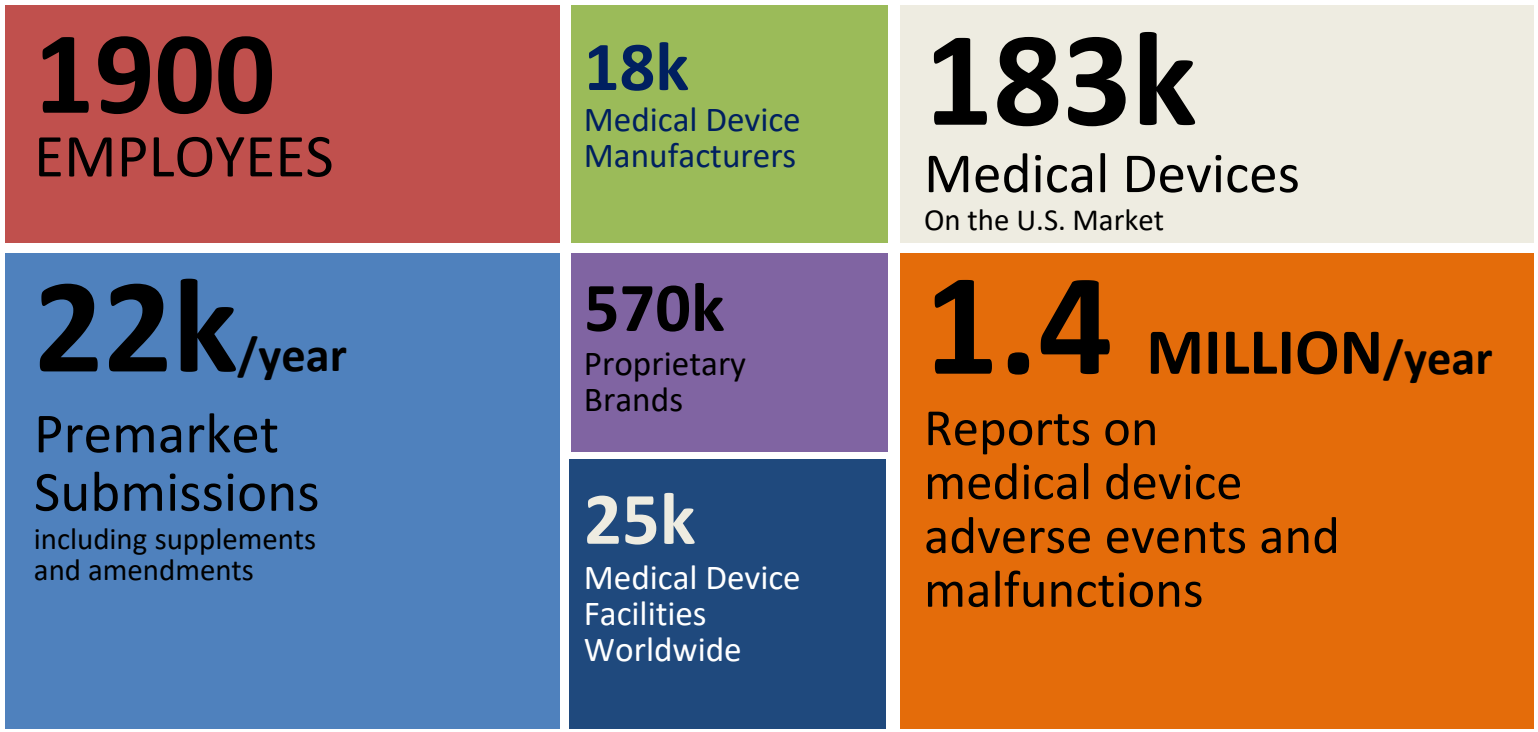
Speaker Bio

Dr. Daniel Porter currently is a Regulatory Scientist at the U.S. FDA's Division of Applied Mechanics researching the properties of additively manufactured (AM) lattice structures and AM facemask sealing efficacy. Dr. Porter also has experience as a Lead Reviewer in the Office of Orthopedic Devices (OHT6) within the Center of Devices and Radiological Health at the U.S. FDA. He holds a Bachelor and Master of Science in Mechanical Engineering from the University of Louisville (UofL). He completed nearly two years of internships at Sandia National Laboratories in New Mexico where he researched gas chromatography technologies for national security applications. Dr. Porter received his Ph.D. in Mechanical Engineering from UofL where he studied vibrational energy harvesting, MEMS technology, and AM. He completed his postdoctoral position at Southern Methodist University (SMU) in Dallas, Texas where he studied AM of ultraviolet industrial silicone and thermally curable medical grade silicone.

Overview of Presentation

- Introduction & Motivations
- Hypothetical Case Study Intro
- Device Design & Draft Labeling
- Process Workflow
- Software Workflow
- Material Control
- Post-Processing
- Monitoring Activities
- Worst-Case AM Selection
- Ending Remarks

CDRH Snapshot

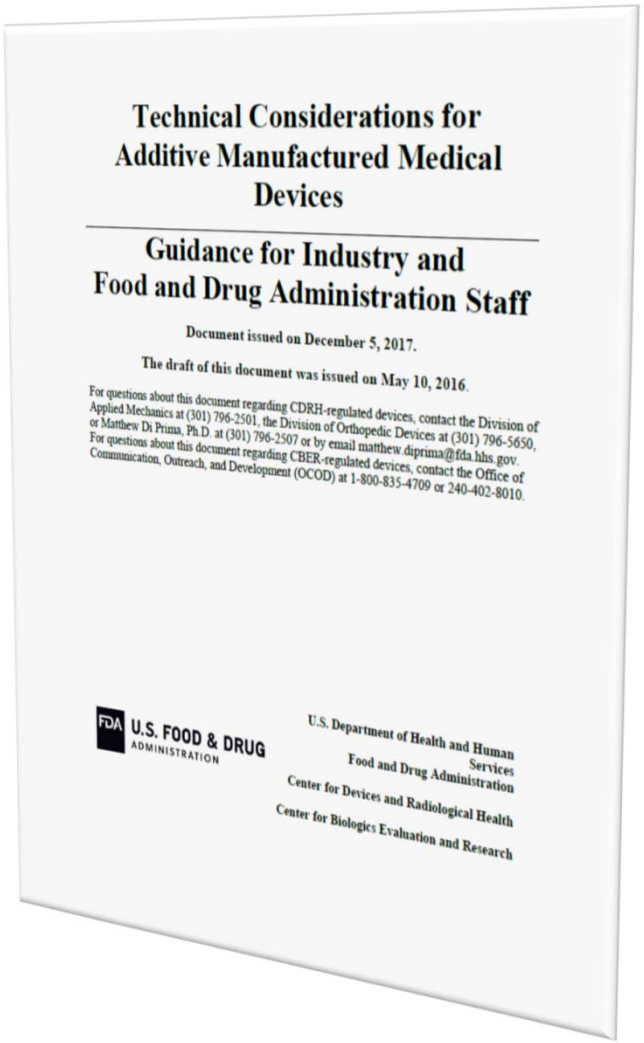


Introduction

- AM Guidance released December 5th, 2017.
- Intended to help stakeholders address AM aspects in regulatory submissions*.
- Gives a broad overview of considerations for AM.

*Does not include biological, cellular, or tissue-based products in AM.

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.



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.

For questions about this document regarding CDRH-regulated devices, contact the Division of Applied Mechanics at (301) 796-2501, the Division of Orthopedic Devices at (301) 796-5650, or Matthew Di Prima, Ph.D. at (301) 796-2507 or by email matthew.diprima@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

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FDA Guidance Documents

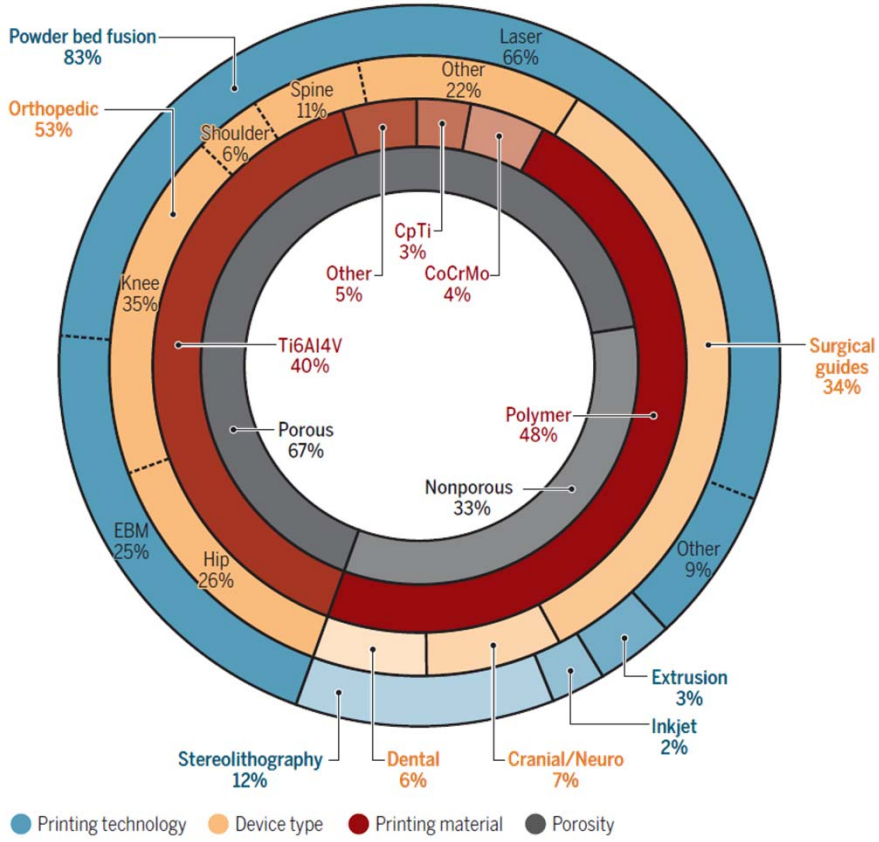
- Represent FDA's current thinking on a topic
- Do not create or confer any rights for or on any person
- Do not bind FDA or the public
- Allow you to use alternative approaches if the approach satisfies the requirements of the applicable statutes and regulations

Motivation

Up to ~2016

U.S. Submissions

- Submissions using AM appear to be increasing.
- More stakeholders new to AM technology.
- Powder Bed Fusion (PBF) appears to be dominant currently.
- <u>Would like to provide a hypothetical case study on one example of how to use the U.S. FDA AM Guidance.</u>



Ricles 2018. Regulating 3D-printed medical products. https://stm.sciencemag.org/content/10/461/eaan6521

Some Things to Keep in Mind

- Not all considerations are mentioned.
- Not stating what minimum activities/criteria are for submissions.
- No guarantee that this fictitious submission would be cleared.
  - Data is absent in this presentation.

Hypothetical Case Study

510(k) Submission

- Subject Submission: K19ABCD
- Sponsor: **Subject Company**
- Device: “Subject Bone Support System”
  - Patient Matched Bone Plate
  - Adults
  - Long Bones
- Product Code: HRS, 21 CFR 888.3030
- Technology: **Powder Bed Fusion**
  - Energy Source: Laser
  - Material: Ti-6Al-4V (ASTM F2924-14)

VS

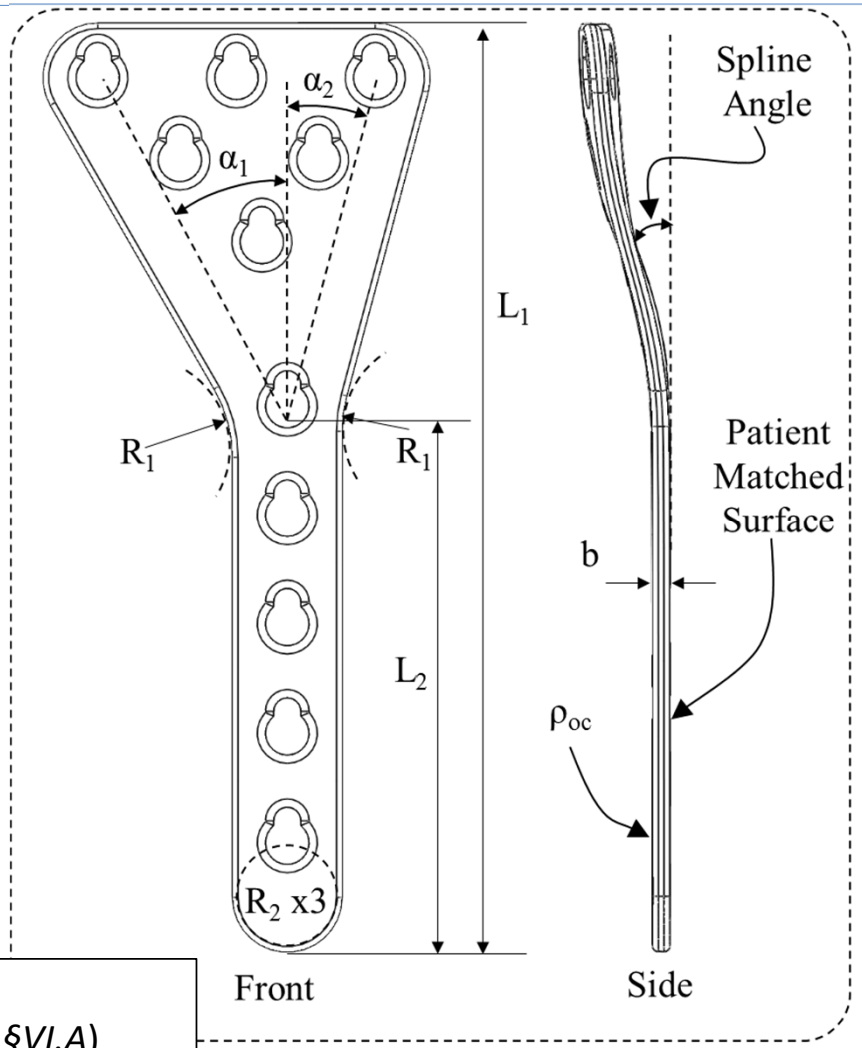
- Predicate Submission: K17EFGH
- Sponsor: **Predicate Company**
- Device: “Predicate Bone Support System”
  - Adults
  - Long Bones
- Product Code: HRS, 21 CFR 888.3030
- Technology: **Traditional Subtractive Manufacturing**
  - Material: Ti-6Al-4V ELI (ASTM F136)

Similar Indications for Use

Device Design

Patient matched bone plate

- Frontal angle α_1
- Anterior angle α_2
- Total length L_1
- Partial shaft length L_2
- Minimum plate thickness b
- Patient matched spline surface
- Radial curvature ρ_{oc}

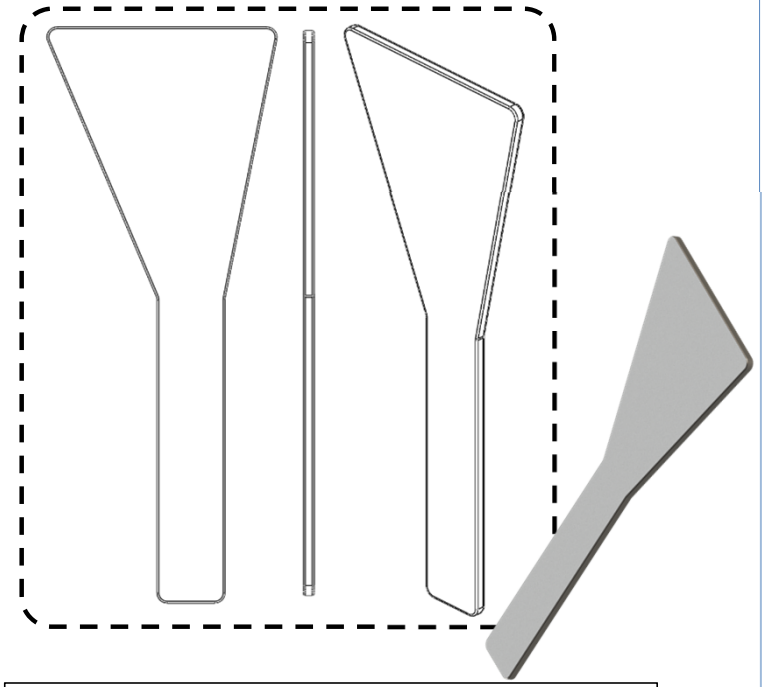


Minimum feature size ~=0.7 mm (*AM Guidance §V.A*)
Understand and describe critical features (*AM Guidance §VI.A*)
All input variables have validated limits (*AM Guidance §V.B*)
Understand allowable dimensional tolerances (*AM Guidance §VI.C*)

Short Configuration

Long Configuration

Representative "Sacrificial" Test Coupon

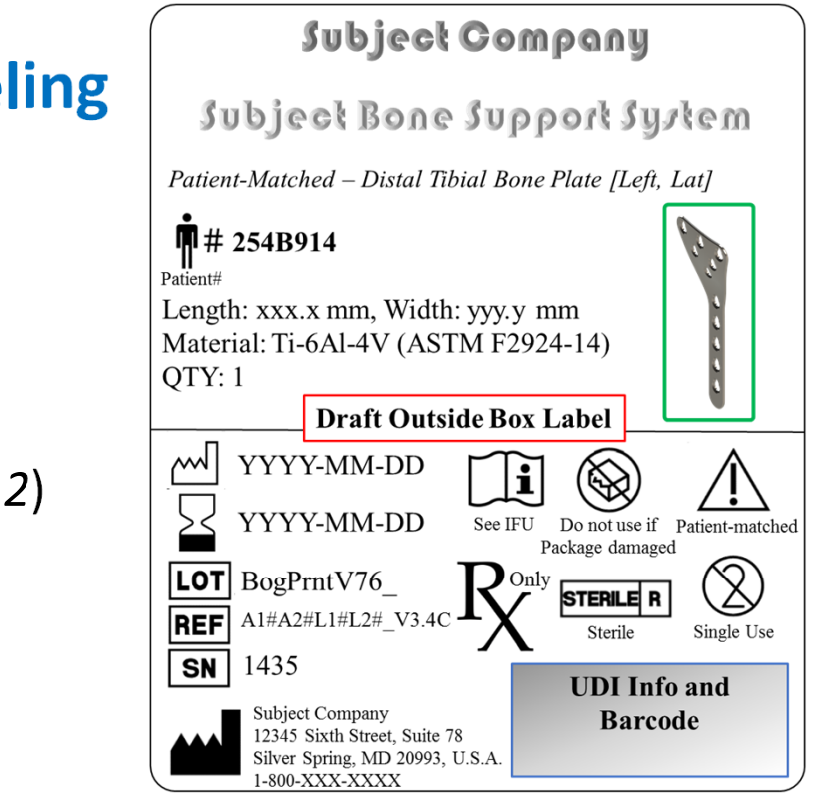


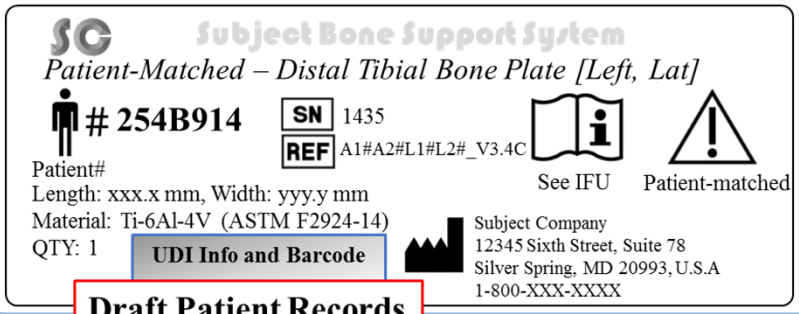
Subject Company presents data showing that Sacrificial coupons are representative of the final, finished device (*AM Guidance §VI.D.2*).

Draft Labeling

(*AM Guidance §VII*)

- Labeling indicates patient matched
- Patient identification number
- Design iteration number (*AM Guidance §V.B.2*)
- Patient's anatomy location
- Expiration date (*AM Guidance §V.B.1*)
- Other(s)





Process Workflow

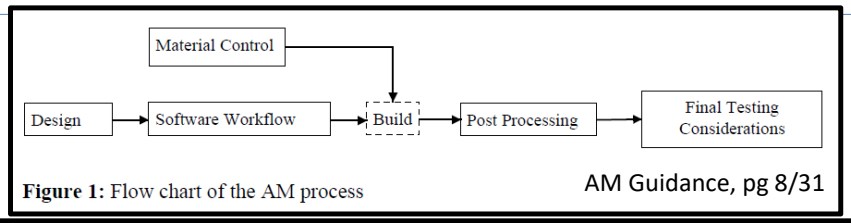
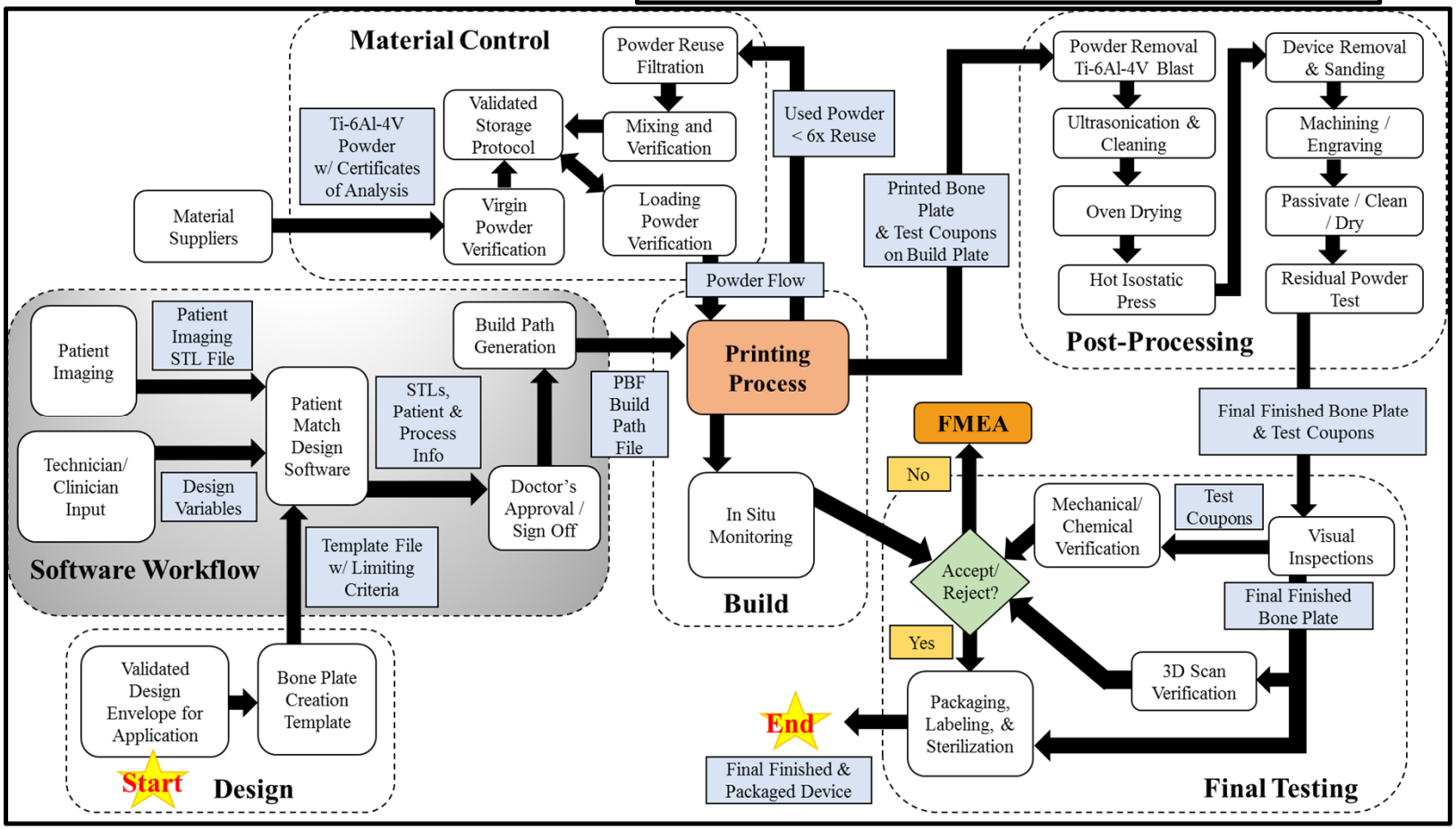
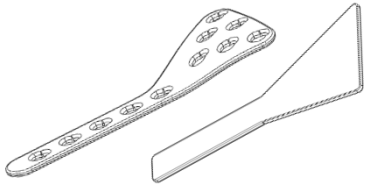


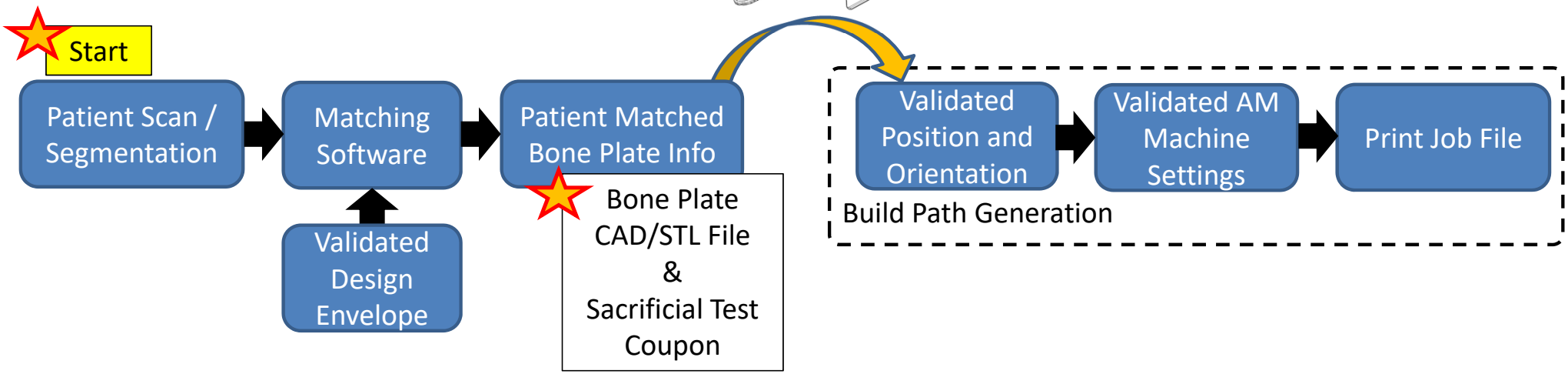
Figure 1: Flow chart of the AM process

AM Guidance, pg 8/31



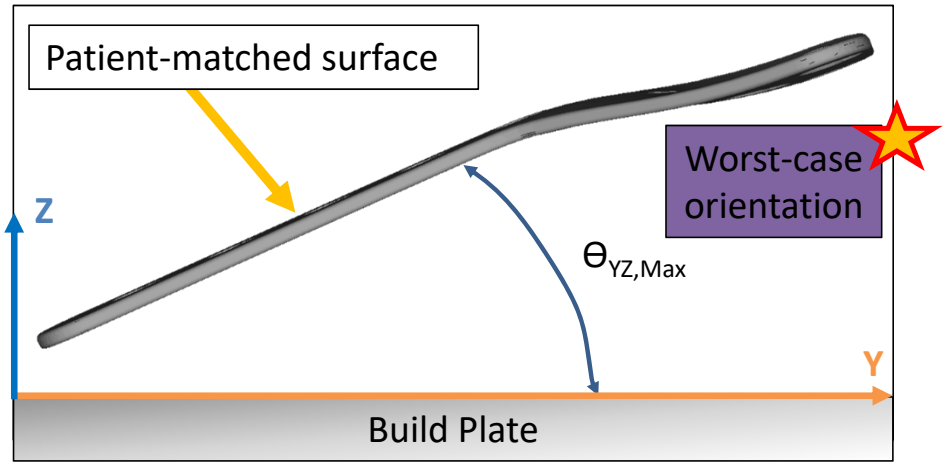
Software Workflow

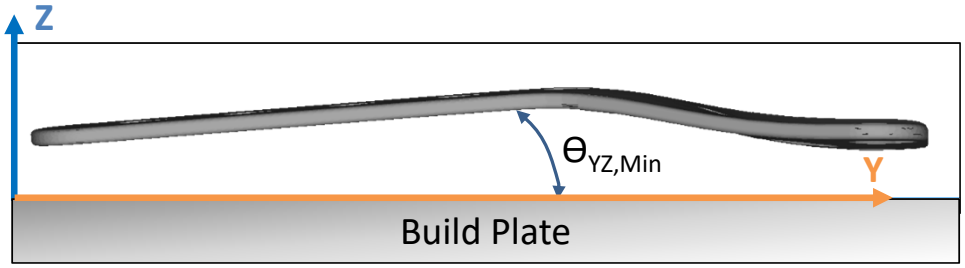


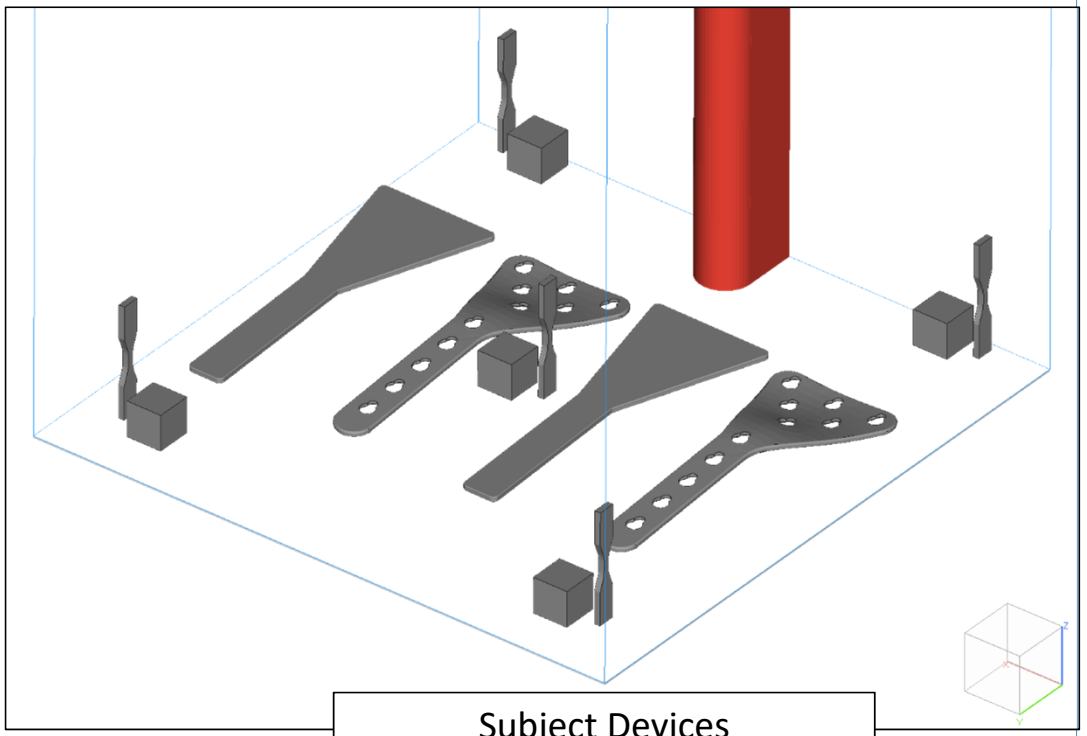


- Considers build volume placement, laser power, speed, path, etc. (*AM Guidance §V.C.2*).
- If new software/firmware or changes to software/firmware then the Subject Company understands:
  - Revalidation may be needed (*AM Guidance §V.F.2*) .
  - Consult "*When to Submit a 510(k) for a Change to an Existing Device*".

Position and Orientation







Subject Devices
&
Sacrificial Test Coupon

Validated Orientations (*AM Guidance §V.F.4*)

No worst-case position from OQ/PQ

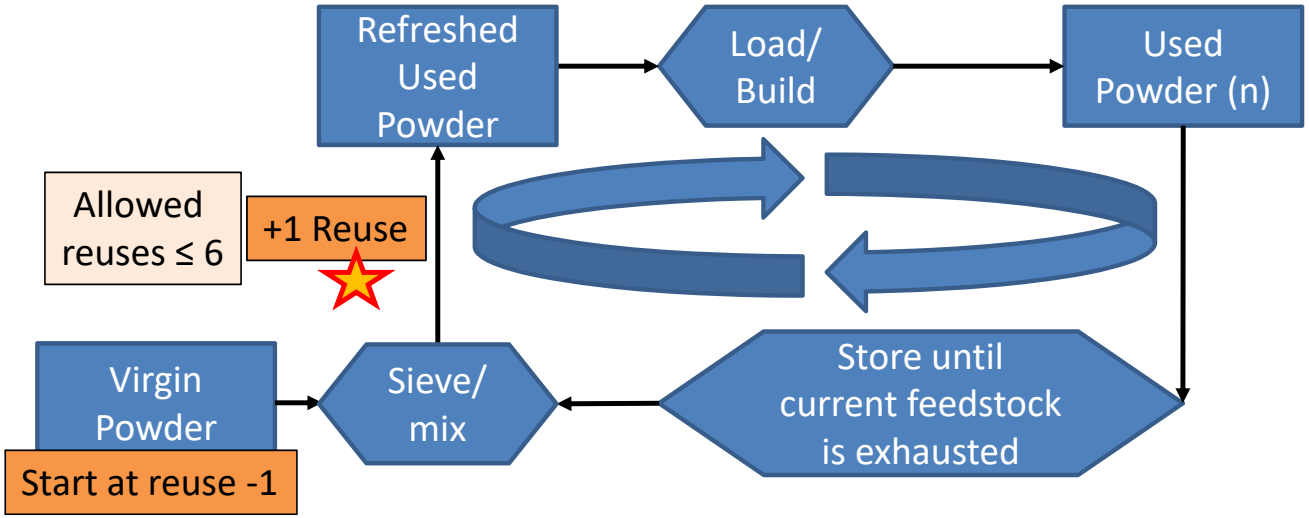
Build supports on non-patient matched face (*AM Guidance §V.C.2.ii*)

Material Control

- Virgin Ti-6Al-4V powder from supplier, with certificate of analysis.
- Subject Company verifies virgin powder (*AM Guidance §V.D.1*):
  - Particle size distribution.
  - Chemical constituency (ICP-AES, combustion, inert gas fusion).
- Mixes powder in ratio (used:virgin) 1:1.
- Validated storage protocol under inert gas (argon).
- OQ/PQ showed non-conformance to ASTM F2924-14 after **9** reuse/mixes (i.e. sieves).
  - Process is repeatable.
  - Safety factor -> Will only reuse/mix (i.e. sieve) powder **up to 6 times**.

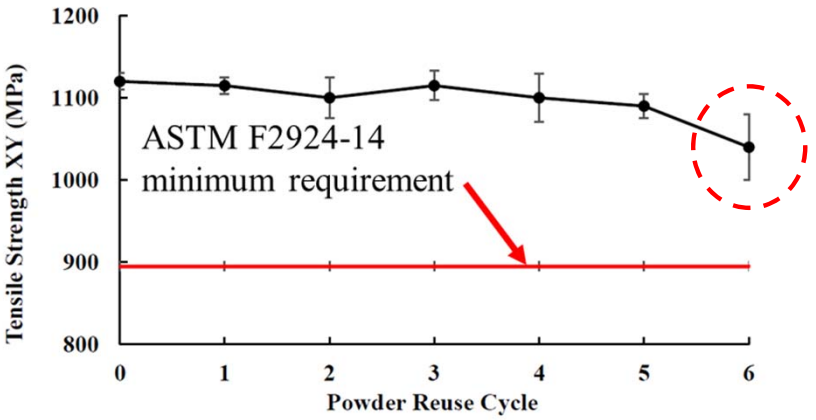
Material Control - Powder Reuse

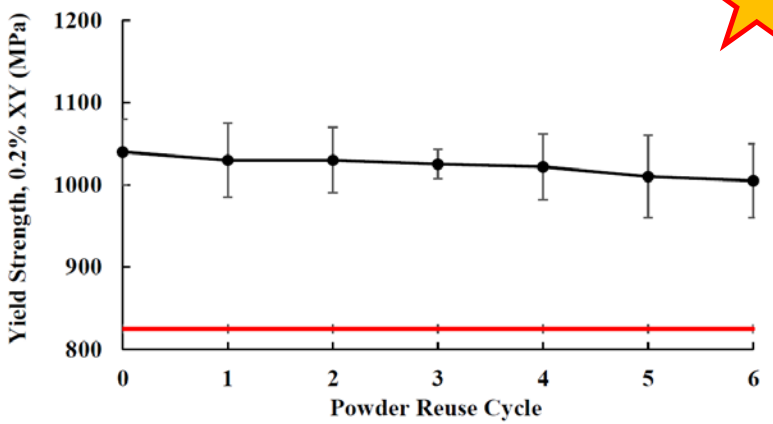
Subject Company's Powder Handling Routine

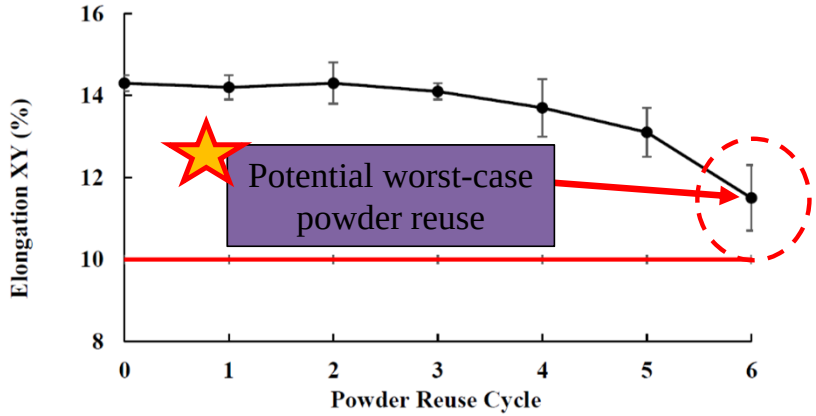


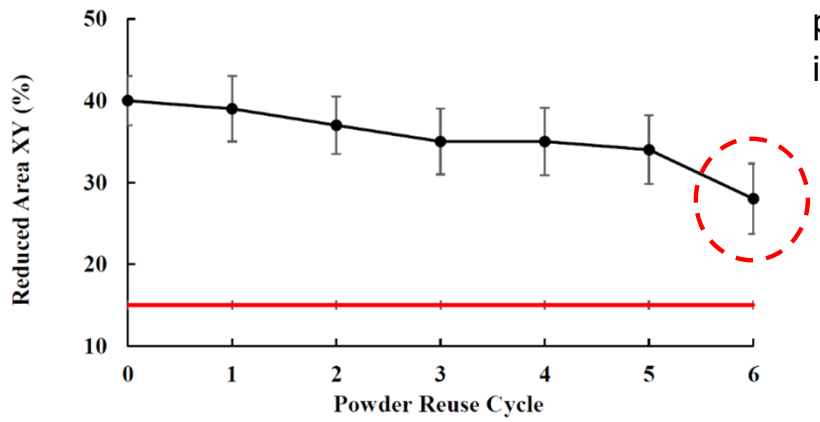
-Conveying the powder handling routine is important!
-Will not mix powder from differing lots.

Material Control - Powder Reuse







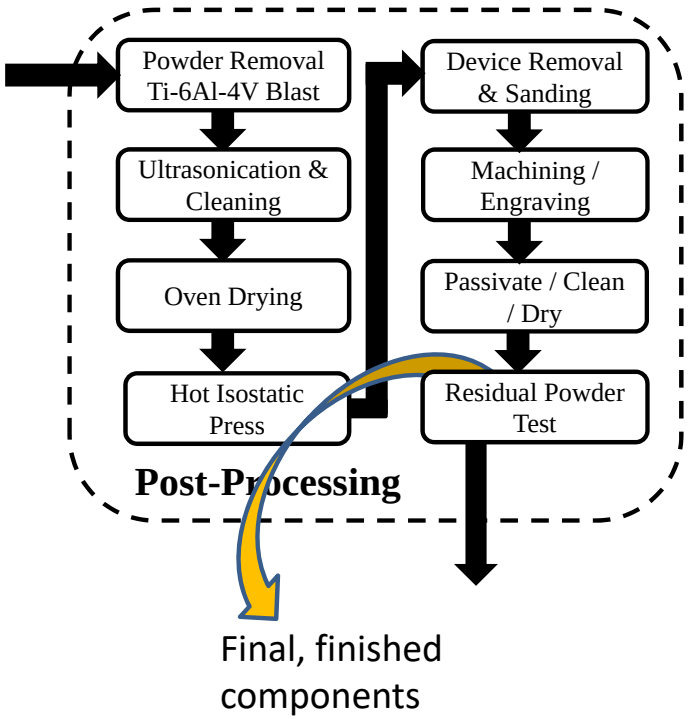


Hypothetical data from Subject Companies OQ/PQ E8 tensile coupons.

Chemical constituency charts as a function of powder reuse also important.

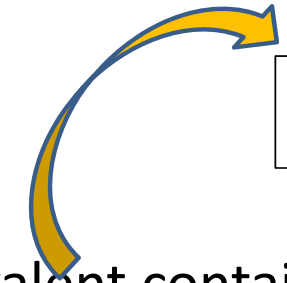
Post-Processing

- Devices and representative test coupons both go through post-processing.
- Subject Company decides to discuss the detrimental effect of the HIP process (*AM Guidance §V.E*).
- Residual powder test performed on final-finished devices (*AM Guidance §VI.E and §VI.F*).
  - Has specified acceptance criteria.



Residual Powder Analysis

- Subject company decides to use USP <788> to evaluate residual powder with 788's acceptance criteria.
- Uses Method 2, Microscopic Particle Count.
  - Particle size distribution
    - Size < 10 µm
    - 10 µm ≤ Size ≤ 25 µm
    - 25 µm ≤ Size
  - Morphology
- Acceptance criteria, assume 1 mL equivalent container volume.
  - 12 particles ≥ actual count (Size ≥ 10 µm)
  - 2 particles ≥ actual count (Size ≥ 25 µm)



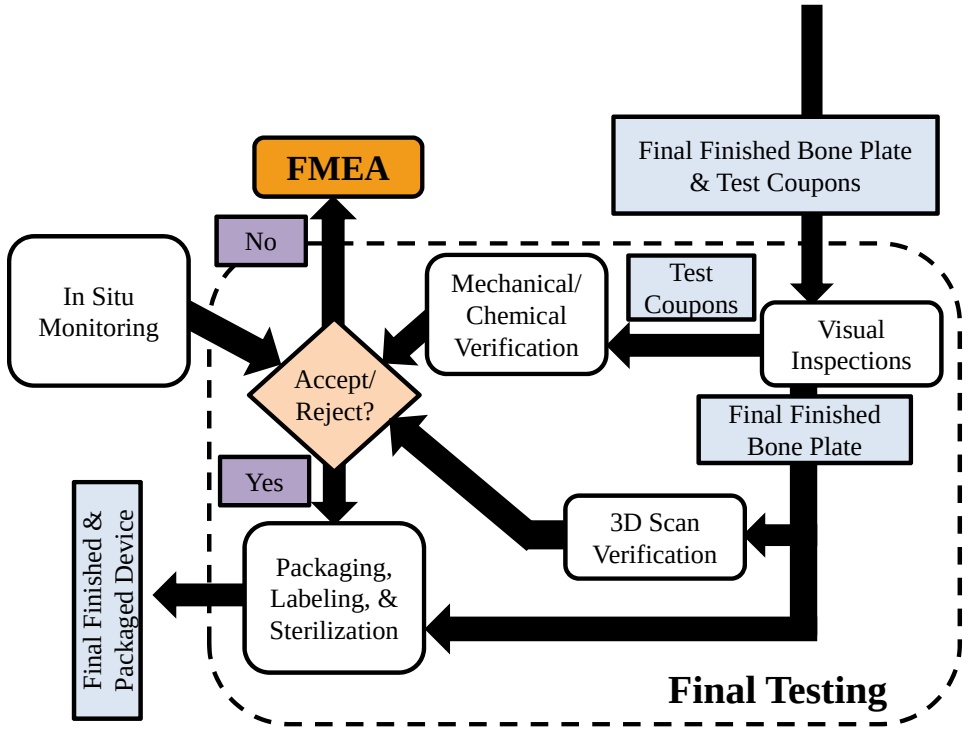
Substitute representative porous volume… if there was one.

-Device is not porous.
-Need better residual powder standards.

Monitoring (Verification) Activities

The Subject Company also does not want to create a new worst-case

- In situ monitoring (Oxygen sensors, etc.)
- Visual inspections
- 3D metrology scan – subject device
- 2x per build tensile specimens
- 1x density cubes
- Single cycle 4-point bend (ASTM F382-17) – sacrificial coupon
  - Verify load-displacement curve
- Chemical verification – sacrificial coupons
  - ICP-AES
  - Combustion
  - Inert Gas Fusion



Worst-Case Selection (AM)

Subject Company decides to also consider what is worst-case in regards to the AM process

- Build location dependence
  - Negligible
- Build orientation dependence
  - $\Theta_{YZ,Max}$
- Powder reuse/mixing (sieve) dependence
  - Reuse #6
- Laser power, speed, path dependence
  - Locked down. Tolerances known and monitored.
- Residual powder
  - None identified
- Other (device size selection, etc.)…

Worst-Case Selection w/Data and Robust Rationale

AM Component(s) to Performance Test

Ending Remarks

- Just **one** example of how to use the AM Guidance.
  - Many ways to address AM considerations for a pre-market submission.
- AM is a broad technology, and we **only look at L-PBF here**.
  - Potentially different considerations with other technologies.
- Should also defer to any device-specific Guidance Document(s) or special controls Guidance Document(s) for pre-market requirements.
- **High-level** overview.
- **No performance data presented** here for the subject or predicate device.

Thank You For Your Attention

Questions?

AdditiveManufacturing@fda.hhs.gov