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Precision in Practice: Navigating Regulatory Requirements for Patient-Specific Implants & Surgical Planning Software

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Dave is a seasoned regulatory expert with extensive proficiency in U.S. medical device regulations. His regulatory career began in 2009 at the FDA where he dedicated 7 years to the premarket orthopedic devices branch. Dave held pivotal roles including acting branch chief of the orthopedics branch and senior premarket lead reviewer. Departing the FDA in March 2016, Dave transitioned to MCRA, where his regulatory has been further strengthened working with novel and innovative technologies and companies. Since joining MCRA, Dave has spearheaded a multitude of regulatory projects, focusing primarily on U.S. regulatory affairs with a specialized emphasis on orthopedic joint arthroplasty, trauma, sports medicine, navigation, robotics, wound management, and plastic and reconstructive devices.

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Dr. Akhlaghi is a former FDA lead reviewer for medical devices as part of Radiological Health, with extensive knowledge of regulatory requirements in the medical device and digital health fields. He is an electrical and computer engineer with expertise in AI, machine learning, data analytics, signal/image processing, and study design. His work focuses on Software as a Medical Device (SaMD), AI/ML-enabled devices, image optimization guided by AI, presurgical planning software, PCCP, computer-aided SaMD, and ultrasound imaging.

What We Offer

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Healthcare Compliance • Outsourced Chief Compliance Officer • Digital Health

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Due Diligence

Market Research • Regulatory Compliance • Risk Assessment • Clinical Data Evaluation

AI & Imaging Center

Regulatory Support • Clinical Study Design & Execution • Data Collection & Sourcing • Imaging Operations & Network of Experts • Project & Data Management • Statistical Analysis

MCRA Therapy Specializations.

- Neurology
- Orthopedics & Spine
- Cardiovascular
- In-Vitro Diagnostic
- Wound Care
- Anesthesia & Critical Care
- Digital Health
- General Surgery
- Plastics & Reconstructive Surgery
- Cell & Gene Therapy
- Radiological Health
- Biologics & Combination Devices

Agenda

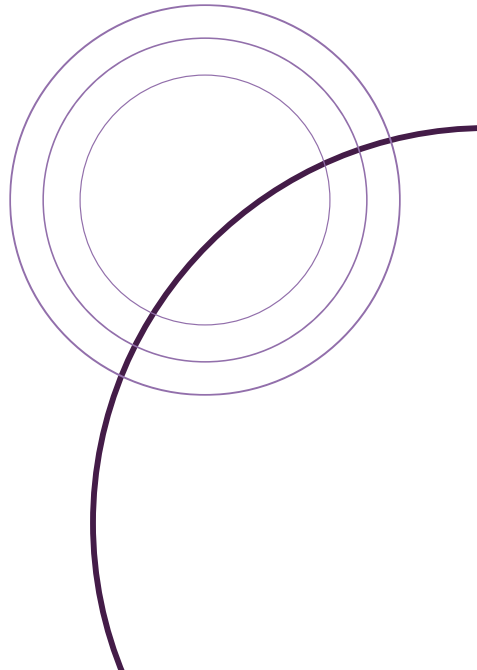
- Introduction
- Review testing & validation requirements – implants + software + AI/ML
- Understand key regulatory pathways for orthopedic patient-specific implants and software
- Discuss FDA expectations and recent guidance
- Compare integrated vs. SaMD submissions
- Share practical tips and real-world trends

Why Focus on Patient-Specific Devices & Software Now?

- Surge in personalization: implants tailored to anatomy, workflow
- Complex cases can be addressed
- Reduction in inventory
- Proliferation of software: planning tools, AI decision support
- Complex submissions: FDA evaluating hardware + software together
- Regulatory landscape is evolving – fast
- Opportunity to improve outcomes and streamline clearance

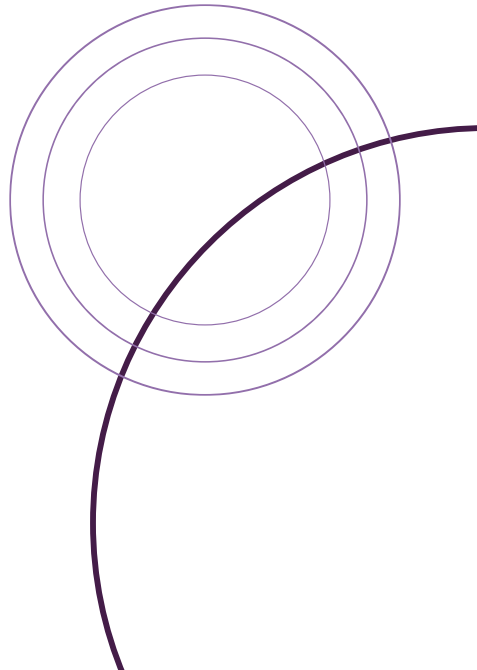
What is Software as a medical device (SaMD)

- Software intended for medical purposes **without** being part of a hardware medical device
- Includes tools for patient-specific surgical planning and implant assessment
- Subject to FDA oversight as a medical device
- Examples: AI-powered pre-op planning tools for orthopedic implants



SaMD vs. Non-SaMD: Regulatory Definitions

- SaMD: Software intended for medical purposes without being part of a hardware medical device
- Defined by IMDRF & adopted by FDA
- Examples:
  - ✓ AI tool for implant planning (SaMD)
  - ✗ Software embedded in robotic arm (not SaMD)
  - ✗ Software planning to develop a Patient Specific Implant (not SaMD)
- FDA Guidance: "Clinical Decision Support" & SaMD Evaluation



Purpose of software in patient specific implants:

- **Implant assessment:**
  - Automated or semi-automated analysis of radiographic images
  - Automated or semi-automated anatomical measurements
  - Implant type and size recommendations aligned with clinical guidelines
  - Custom implant design

- **Pre-surgical planning:**
  - Segmentation and 3D rendering of patient anatomy
  - Annotation of anatomical landmarks and relevant measurements
  - Overlay of FDA-cleared implants on patient-specific models for surgical planning
  - Generation of a visualized surgical plan outlining procedural steps

Types/Examples of Surgical Planning Software

Presurgical planning → General assessment tools (Includes AI/ML-based tools):

- Visualization/measurement:
- Segmentation and 3D modeling
- Virtual implant sizing & positioning
- Bone cutting guides or robotic trajectories
- AR/VR – based presurgical planning
  - Visualization
  - Guidance

Presurgical planning for patient-specific implant design/fabrication (Includes AI/ML-based tools):

- Visualization/measurement
- Segmentation and 3D modeling
- Customized implant design and modifications
- Bone cutting guides or surgical trajectories

Presurgical planning workflows

→Surgical planning

Image acquisition

Image analysis

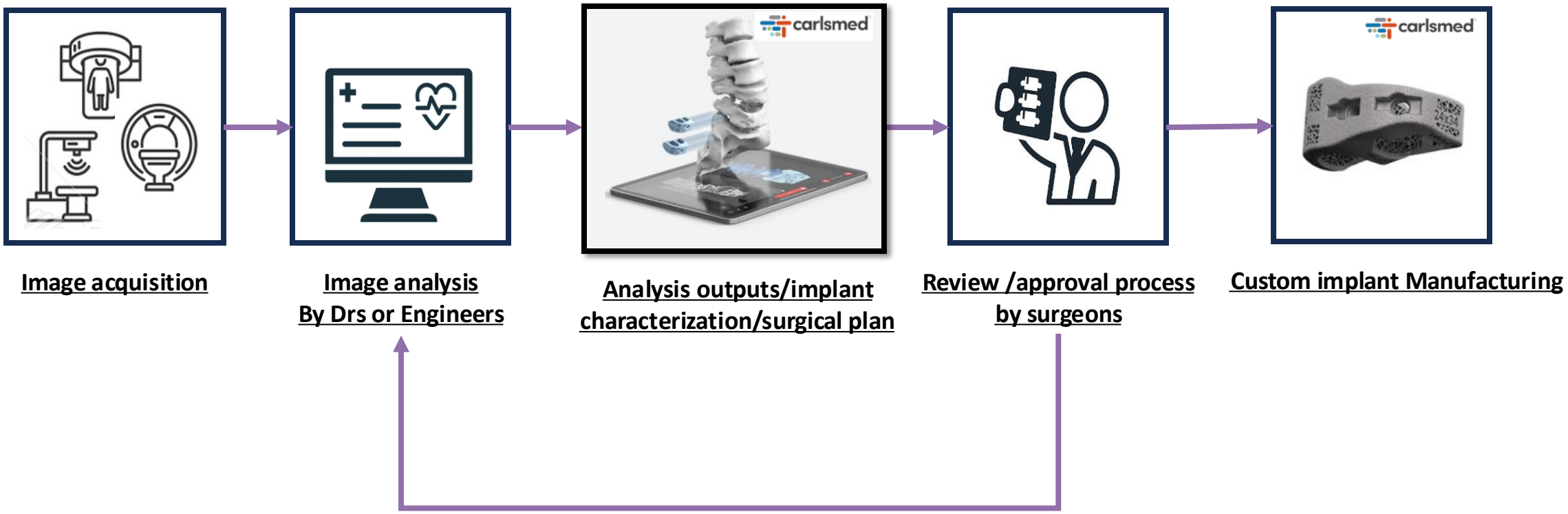
Analysis outputs/surgical plan

Review /approval process by surgeons

https://www.formus.com/

Presurgical planning workflows

→Patient specific Implant



https://carlsmed.com/

Regulatory Pathways for Surgical Planning Software

- Standalone SaMD often cleared via 510(k)
    - Dependent on features and claims
- De Novo possible for novel AI/ML tools
- Integrated software submitted with implant or robot
    - Generally, has taken on the classification of the implant
- Key FDA references:
    - CDS Guidance
    - SaMD Clinical Evaluation (IMDRF)
    - AI/ML Framework (2023 draft)

Most of SaMD are process under quantitative imaging regulation (21 CFR 892.2050) as they mostly focused on

- Segmentation of anatomical land-marks
- Standard automated/semi-automated measurements of anatomical landmark (mostly derived from segmentations)
- Recommendation of implant size based on derived measurements and clinical guidelines (look-up table)

Quantitative imaging regulation:

21 CFR 892.2050: Medical Image Management and Processing System

- **Definition:**

  A device that provides capabilities for the review and digital processing of medical images to assist in disease detection, diagnosis, or patient management

- **Functions Include:**
  - Image manipulation, enhancement, or quantification
  - Advanced image processing such as segmentation, multimodality image registration, or 3D visualization
  - Complex quantitative functions like semi-automated measurements or time-series analyses

- **Classification:**

  Class II (General control)

- **Standards:**
  - Digital Imaging and Communications in Medicine (DICOM)
  - Joint Photographic Experts Group (JPEG)

Quantitative imaging regulation:

Key product codes and definition

- **LLZ: System, Image Processing, Radiological**
  - Devices that provide capabilities for the review and digital processing of medical images for interpretation by a trained practitioner
  - Functions may include image manipulation, enhancement, or quantification intended for use in disease detection, diagnosis, or patient management

- **QIH: Automated Radiological Image Processing Software**
  - Software that automates the processing of radiological images
  - Functions may include image segmentation, multimodality image registration, or 3D visualization, intended for use in interpretation and analysis of medical images
  - Mostly used for AI/ML enabled devices

Quantitative imaging regulation:

Key requirements: Documentation and performance tastings

- **Function Description**
  - Detailed technical description of the quantitative imaging function(s), including inputs, outputs, and user interaction levels

- **Technical Performance Assessment**
  - Detailed performance specifications that correspond to the claims and uncertainty associated with the quantitative imaging function
  - Key components:
    - Bias and Precision: Assess the accuracy and repeatability of measurements when compare against gold/reference standard
    - Limits of Detection and Quantitation: Determine the smallest detectable and quantifiable measurements
    - Sensitivity and Specificity: Measure the ability to correctly identify/recommend appropriate type, size and location
    - Uncertainty Analysis: Quantify the degree of variability in measurements
    - Generalizability: Assess the generalizability of device output across intended patient population (age, gender, race, ethnicity) and compatible imaging devices.

- **Labeling (User instruction)**
  - Clear instructions for image acceptance or quality assurance activities to be performed by the user
  - Key components:
    - Quality Assurance Protocols: Instructions on characteristics to test, test methods, and metric calculations.
    - Actions for Quality Assurance Failures: Guidance on steps to take when quality assurance fails.
    - Purpose: To ensure users can obtain, understand, and interpret the values provided by the quantitative imaging function

AI/ML enabled devices:

- **Key characterization:**
  - AI/ML-enabled quantitative imaging devices are software-driven radiological tools that use artificial intelligence or machine learning algorithms to extract and quantify features from medical images (e.g., CT, MRI, X-ray) to support clinical decisions, such as surgical planning in orthopedics.

- **Key Capabilities:**
  - Automated anatomical segmentation (e.g., bone or joint structures)
  - 3D reconstruction for surgical planning
  - Quantification of volumes, angles, or distances
  - Pattern recognition for disease detection or treatment outcomes

- **Challenges in FDA Review:**
  - Performance must be demonstrated across diverse patient datasets
  - Algorithm transparency, validation, and explainability
  - Reproducibility and robustness in clinical environments

AI/ML enabled devices:

Good Machine Learning Practice (GMLP)

➢ What is GMLP:

- GMLP provides guiding principles for developing medical devices that incorporate AI/ML. It ensures safe, effective, and high-quality algorithm development throughout the total product lifecycle.

➢ Key Principles

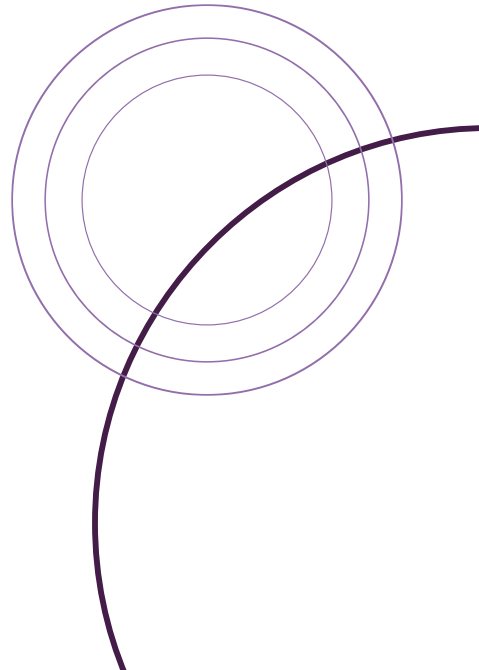
- Multidisciplinary Expertise:
  - Involvement of clinicians, data scientists, and regulatory experts from the start.
- Data Quality & Integrity:
  - Use of curated, representative datasets with clear data provenance.
- Training/Testing Best Practices:
  - **Use independent training and validation datasets**.
  - Evaluation on relevant clinical endpoints.
- Algorithm Transparency:
  - Clear documentation of model architecture, input data, and decision logic.
- Monitoring & Re-training:
- Plan for continuous learning systems with ongoing performance monitoring post-deployment.

What Are Patient-Specific Implants?

- Designed based on patient-specific imaging (e.g., CT/MRI)
- Use a *design envelope* to standardize testing
- Common in orthopedics: joints, spine, trauma
- Distinct from:
    - Standard implants: off-the-shelf
    - Custom devices: under Custom Device Exemption or Compassionate Use

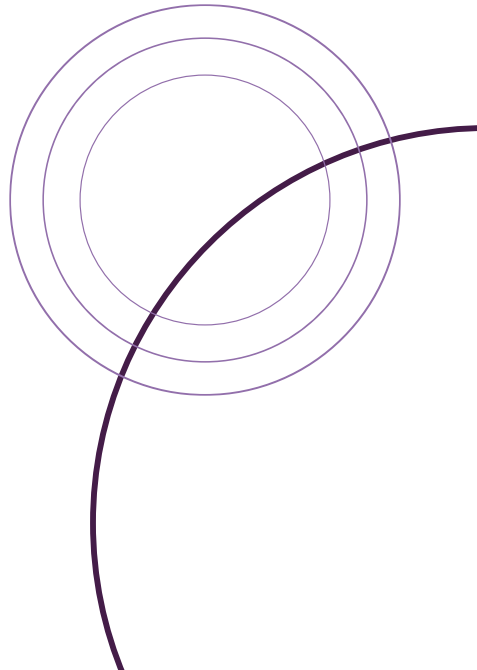
Regulatory Pathways for Patient-Specific Implants

- Most follow the 510(k) pathway
    - Risk and bail out options important!
    - What does the surgeon do if the device does not fit
- Design envelope needed to justify worst-case testing
- Custom Device Exemption (CDE) – rarely applicable
- Include:
    - 3D models of anatomical fit
    - Process validation for manufacturing



When to Use a Design Envelope?

- **Always!**
- Defines range of variation including
  - Design: dimensions, geometry
  - Patient conditions: correction, disease states, margins, etc.
- Enables representative mechanical testing
- Justify worst-case for:
  - Strength
  - Wear
  - Fatigue
- Crucial to group devices under a single clearance



Mechanical Testing: How to Address Patient-Specificity

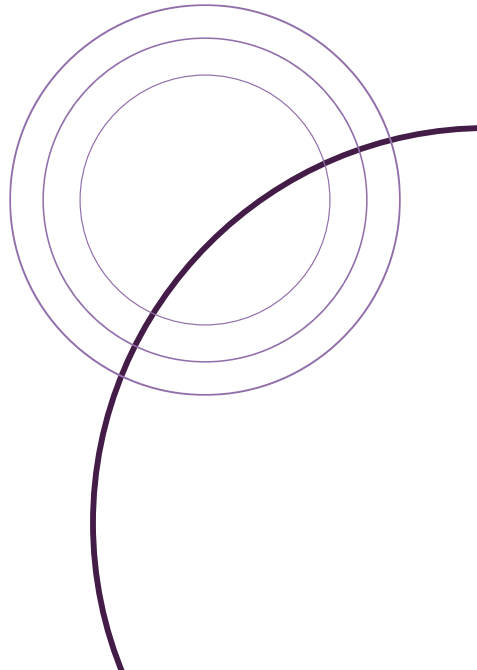
- Identify worst-case geometry using design envelope
    - Often edge cases of the design envelope
    - Are there multiple worst cases options?
- Test:
    - Static & fatigue strength
    - Wear (for articulating joints)
- Consider 3D printing variability and FDA guidance
- May need multiple builds or locations to support consistency

Cadaver Studies: When and Why to Use Them

- Used to validate:
  - Surgical workflow
  - Patient Specific implant fit & positioning
  - Software-guided tools (e.g., robotic trajectories, guides)
- Minimum: 3 surgeons of varying experience (novice, intermediate, expert) x 3 cadavers
  - FDA now asks about surgeon experience and conflicts
- Acceptance criteria (e.g. surgeon feedback, alignment)
- Statistical justification
- Pre-sub may be useful

Biocompatibility, Cleaning, & Sterilization

- ISO 10993 risk assessment and testing is essential
- Often rely on material characterization + manufacturing rationales + limited testing
- Confirm:
    - Manufacturing residues
    - Additive materials (3D printing powders, supports)
- Cleaning validation and supportive powder residues
- Sterilization validation must cover full range of geometries



Human Factors & Usability

- Especially important for software used in the OR
- Usability testing should match user profile (surgeons, techs)
- Validate key tasks:
    - Image review
    - Implant planning
    - Error recovery
- Include known use errors and mitigations
- Might be able to rationalize not performing full HF on PS implants but will require cadaver validation

FDA Questions, Feedback, & Tips

- Risk to patient & bailout plan in the OR
  - Inaccurate cuts
  - Multiple sizes
- Design envelope falls outside the predicate
- Repeatability of builds to validation work
- Accuracy of cuts (indication specific)
- Timing of imaging to surgery
- HF creeping into requests
- PS instruments need separate validation considerations
  - Patient-Matched Guides to Orthopedic Implants (FDA draft guidance)

SaMD or Integrated Submission?

- SaMD: Standalone software submitted separately (own 510(k))
- Integrated: Submitted as part of system (implant + software + accessories)
- FDA evaluates intended use, dependencies, and workflow integration

Strategic Trade-Offs: SaMD vs Integrated Submissions

Separate SaMD

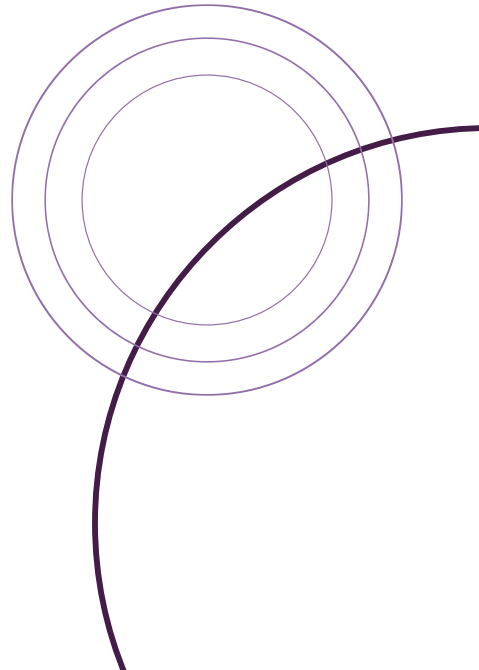
- Faster iteration and updates
- Better for platform technologies
- Potential for broader use with other systems
- Requires own risk assessment & labeling
- Additional submissions to FDA often in series
- Interacting with different FDA review teams

Integrated Submission

- Simpler for “locked” systems (robot + software + implant)
- One FDA review group
- May reduce burden of standalone V&V
- Tied to device/hardware/anatomy

How Companies Are Approaching It Today

- Trend: Early-stage companies prefer bundling
    - Minimizes cross-review between FDA OHTs
- Established platforms often separate software
    - Modular updates, new indications
- Consider your:
    - Product roadmap
    - Regulatory history
    - Software independence



Staying Ahead: Updated FDA Guidance & What's Next

- FDA Software Guidance:
  - Updated SaMD & CDS requirements
- AI/ML Framework:
  - Draft and evolving expectations
- Design Envelope & Testing:
  - Clarifications on worst-case assessments
- Future Trends:
  - Integration with digital health ecosystems

Future Trends in Orthopedic Innovation & Regulation

- Increasing personalization with 3D printing and digital planning
- Growing role of AI/ML—both as a decision support tool and in predictive analytics
- Expansion of software updates post-clearance (modular approaches)
- Interoperability with broader digital health systems
- Greater regulatory focus on cybersecurity & human factors

Key Takeaways for Regulatory Success

- Define Your Product Clearly:
  - Patient-specific implants, integrated systems, or standalone SaMD
- Use Design Envelopes Effectively:
  - Justify mechanical testing and worst-case scenarios
- Testing & Validation:
  - Align mechanical, biocompatibility, and software V&V to FDA expectations
- Regulatory Strategy:
  - Early FDA interactions can clarify requirements—use pre-subs when needed
- Stay Informed:
  - Monitor evolving FDA guidances and market trends

Question?

Thank you!