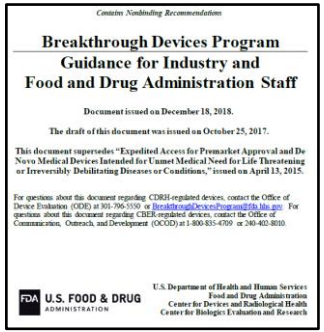
Regulatory Pathways for Innovative Products

Kenneth J. Cavanaugh Jr, Ph.D.
Deputy Director, Office of Cardiovascular Device
Center for Devices and Radiological Health
U.S. Food and Drug Administration

U.S. FDA Center for Devices and Radiological Health (CDRH)

- Ensure patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products
- Facilitates medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and assuring consumer confidence in devices marketed in the U.S.

Regulatory Pathways



Contains Nonbinding Recommendations

Breakthrough Devices Program
Guidance for Industry and Food and Drug Administration Staff

Document issued on December 18, 2018.

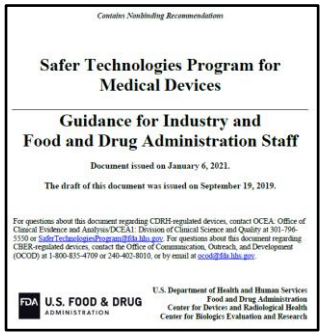
The draft of this document was issued on October 25, 2017.

This document supersedes "Expedited Access for Premarket Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions," issued on April 13, 2015.

For questions about this document regarding CDRH-regulated devices, contact the Office of Device Evaluation (ODE) at 301-796-5550 or BreakthroughDevicesProgram@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.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research



Contains Nonbinding Recommendations

Safer Technologies Program for Medical Devices
Guidance for Industry and Food and Drug Administration Staff

Document issued on January 6, 2021.

The draft of this document was issued on September 19, 2019.

For questions about this document regarding CDRH-regulated devices, contact OCEA: Office of Clinical Evidence and Analysis/DCEA1: Division of Clinical Science and Quality at 301-796-5550 or SafeTechnologiesProgram@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, or by email at ocod@fda.hhs.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

- Breakthrough Device Program (BD)
  - Devices providing more effective diagnosis/treatment of life-threatening/irreversibly debilitating disease as compared to available alternatives
- Safer Technologies Program (STeP)
  - Non-breakthrough devices offering safety advantages as compared to available alternatives

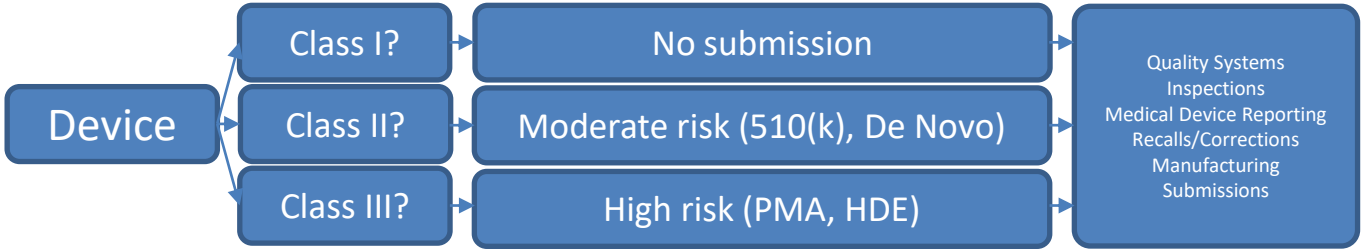
BD/STeP Features

- Increased opportunity for communication with CDRH
- Early engagement on data development plans
- Devices more likely to involve consideration of:
  - Benefit-risk assessment
  - Creative and flexible clinical study designs
  - Premarket-postmarket balance

How does CDRH promote innovation of digital health technologies?

Regulation of Digital Health

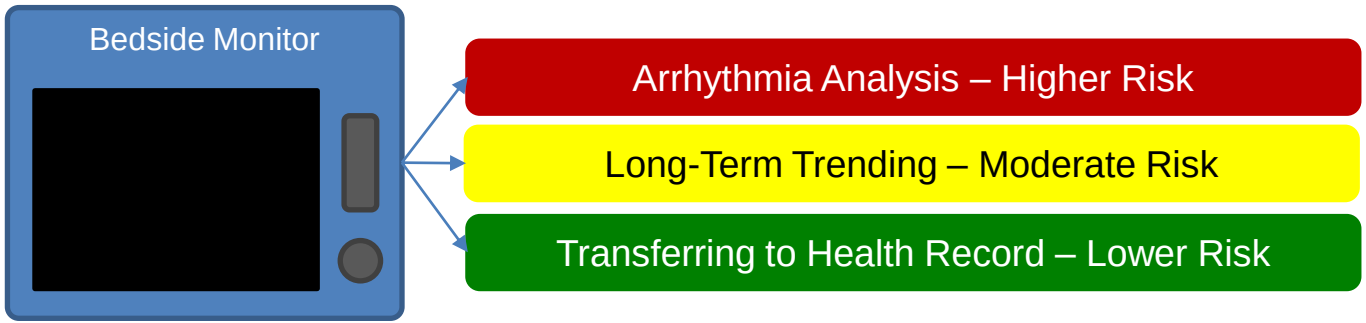
- DH technologies are regulated similarly to traditional devices



- However, some SaMD aspects involve more risk than others

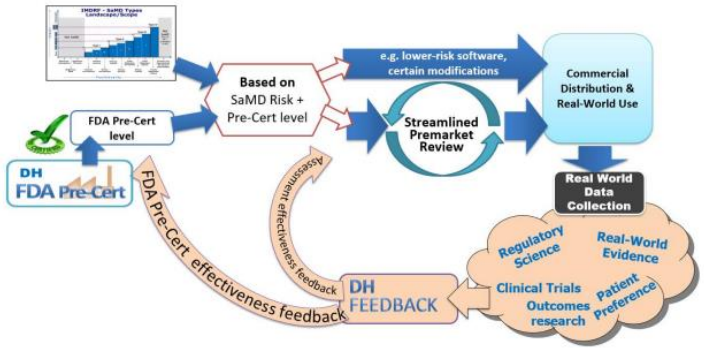
Software as a Medical Device (SaMD)

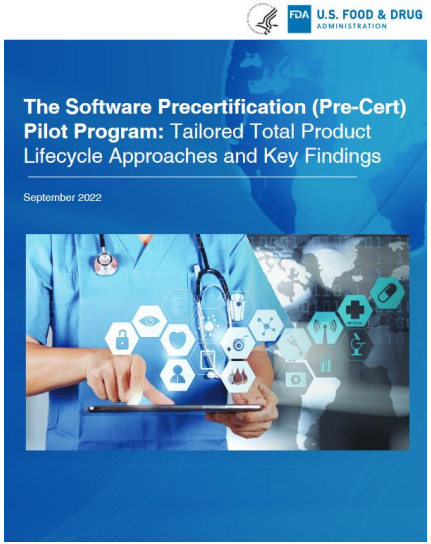
- Take “function-based” approach and regulate functions individually
  - Impact assessment
  - Some functions exempt by law or policy



Software Pre-Certification Pilot

Goal: Provide a streamlined path to market for innovative SaMD products





Completed September 2022

Artificial Intelligence / Machine Learning (AI/ML)

- Unique challenges associated with growth in AI/ML:
  - Datasets
  - “Black box” algorithms
  - Validation
  - Communicating with clinicians and patients
  - Facilitating innovation and iterative development

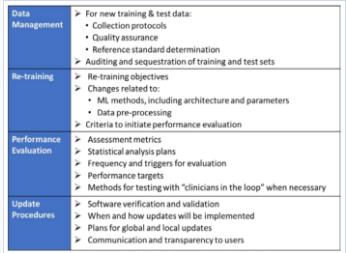
GMLP Guidelines

Goal: Facilitate development of Good Machine Learning Practices that address important AI/ML topics

Good Machine Learning Practice for Medical Device Development: Guiding Principles	
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices are Implemented
Clinical Study Participants and Data Sets are Representative of the Intended Population.	Training Data Sets are Independent of Test Sets
Selected Reference Datasets are Based Upon Best Available Methods	Model Design is Tailored to the Available Data and Reflects the Intended Use of the Device
Focus is Placed on the Performance of the Human-AI Team	Testing Demonstrates Device Performance during Clinically Relevant Conditions
Users are Provided Essential Information Clearly	Deployed Models are Monitored for Performance and Re-training Risks are Managed

Pre-Determined Change Control Plan (PCCP)

- Allows for iterative changes after devices receive marketing authorization
  - Signed into law in December 2022
  - Not limited to AI/ML devices

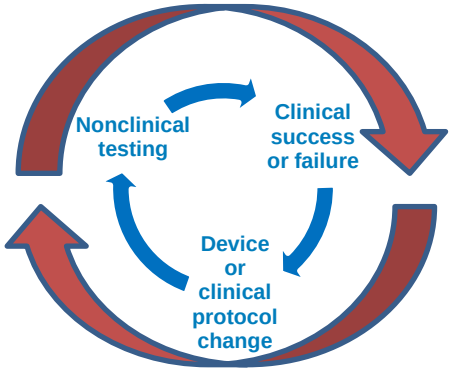
SaMD Pre-Specifications (SPS)	Algorithm Change Protocol (ACP)
Draws a region of potential changes around the initial specifications and labeling of the original device.	

What about scientific/clinical evaluation methods?

Early Feasibility Studies (EFS)

- Promote early-stage clinical research in U.S.
  - Small number of subjects
  - Device design not necessarily final
  - “Just-in-time” non-clinical testing

- Additional focus on streamlining non-regulatory processes
  - Site initiation
  - Reimbursement

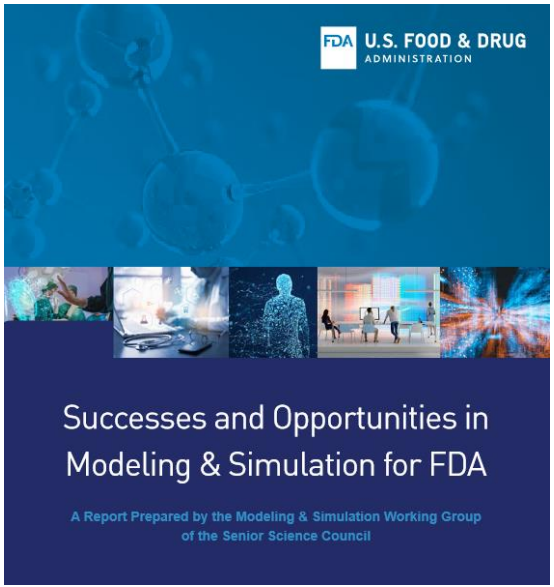


Novel Evaluation Methods

- Real-world evidence (RWE)
  - Regulatory application of clinical data from non-traditional sources
- Decentralized clinical trials
  - Alternative to site-based clinical studies
- Incorporating additional perspectives
  - Patients
  - Payers

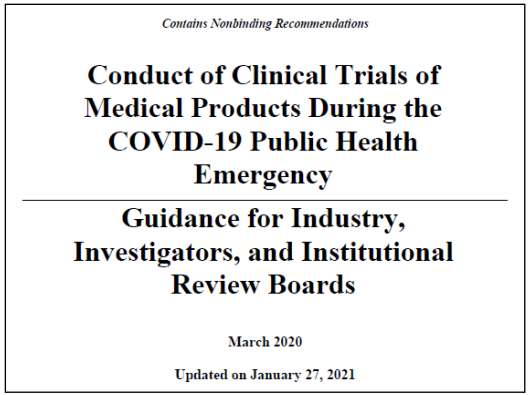
Modeling & Simulation

In silico approaches can provide a complement or alternative to traditional *in vitro* or *in vivo* approaches



Lessons From the COVID Pandemic

- Consider what pandemic-related changes can be adopted permanently
- Incorporate pragmatic approaches to clinical trial conduct and interpretation to minimize disruptions
- Harden the medical device supply chain



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Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on January 27, 2021

How do harmonization efforts promote innovation?

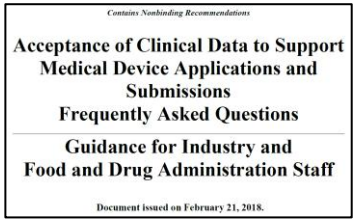
Global Innovation

Ongoing innovation of medical devices creates additional global value in:

- Aligning regulatory approaches
- Building platforms to better evaluate devices across their lifetimes
- Establishing networks

Facilitating Global Strategies

- Regulatory approaches
  - CDRH-Health Canada eSTAR pilot
  - Safety and performance-based 510(k) pathway
- Evaluation criteria
  - Developing essential principles
  - Recognized consensus standards
- Clinical study harmonization
  - Multi-national standardization of outcome measures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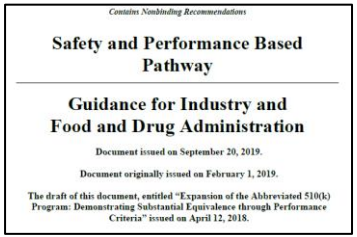
Acceptance of Clinical Data to Support Medical Device Applications and Submissions
Frequently Asked Questions

Guidance for Industry and Food and Drug Administration Staff

Document issued on February 21, 2018.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Safety and Performance Based Pathway

Guidance for Industry and Food and Drug Administration

Document issued on September 20, 2019.

Document originally issued on February 1, 2019.

The draft of this document, entitled "Expansion of the Abbreviated 510(k) Program: Demonstrating Substantial Equivalence through Performance Criteria" issued on April 12, 2018.

Additional Opportunities

- Proactive discussions with global partners can help align approaches and promote convergence
  - Regulator-industry
  - Regional
  - Outreach to other stakeholders

- **Shared goal:** Increase efficiency and reduce risk when developing a novel product for the global market

Thank you!

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