Regulatory Pathways for Innovative Products

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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

- **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

- Device
  - Class I?
    - No submission
  - Class II?
    - Moderate risk (510(k), De Novo)
  - Class III?
    - High risk (PMA, HDE)
  - Quality Systems
    - Inspections
    - Medical Device Reporting
    - Recalls/Corrections
    - Manufacturing Submissions

• However, some SaMD aspects involve more risk than others
Software as a Medical Device (SaMD)

• Take “function-based” approach and regulated 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
October 2021

<table>
<thead>
<tr>
<th>Good Machine Learning Practice for Medical Device Development: Guiding Principles</th>
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<tbody>
<tr>
<td>Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle</td>
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<td>Clinical Study Participants and Data Sets are Representative of the Intended Population</td>
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<td>Selected Reference Datasets are Based Upon Best Available Methods</td>
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<td>Focus is Placed on the Performance of the Human-AI Team</td>
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<td>Users are Provided Essential Information Clearly</td>
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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

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<tr>
<th>SaMD Pre-Specifications (SPS)</th>
<th>Algorithm Change Protocol (ACP)</th>
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<td>Draws a region of potential changes around the initial specifications and labeling of the original device.</td>
<td>For new training &amp; test data:</td>
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<td>Collection procedure</td>
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<td>Qualification</td>
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<td>Performance standard and determination</td>
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<td>Auditing and resubmission of training and test sets</td>
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**Data Management**
- For new training & test data:
  - Collection & processing
  - Qualification
  - Performance standard and determination
  - Auditing and resubmission of training and test sets

**Retraining**
- Changes to training sets:
  - ML methods, including architecture and parameters
  - Data & preprocessing
  - Criteria for reference performance evaluation

**Performance Evaluation**
- Assessment metrics:
  - Statistical analysis plans
  - Analysis and results for evaluation
  - Performance targets
  - Methods for slicing and "tolerance in the loop" when necessary

**Update Procedures**
- Software verification and validation
  - When and how updates will be implemented
  - Plans for global and local updates
  - Communication and transparency to users
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
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
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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