PROPOSED REGULATORY FRAMEWORK FOR MODIFICATIONS TO ARTIFICIAL INTELLIGENCE/MACHINE LEARNING (AI/ML)-BASED SOFTWARE AS A MEDICAL DEVICE (SAMD)

Matthew Diamond, MD, PhD
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Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

Discussion Paper and Request for Feedback

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Evolving Digital Health Device World …

**“Traditional” Device World**

**Product Development Timeline**
- Months to years +
- Less frequent modifications

**Postmarket Data**
- Limited availability and access to real world data (522, PAS, MDRs, MedSun)

**FDA Premarket Program Volume**:
- Stable (~3,500 510(k) submissions / 2200 pre-submissions)

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**Evolving Digital Health Device World**

**Weeks to months** + (incremental, iterative) and potentially frequent modifications

**Potential for high availability and access to rich real world data (benefits and risks)**

**Potential for exponential increase in volume of submissions**

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The Need for a Tailored Approach
Examples of AI/ML-Based SaMD

FDA News Release

FDA Permits Marketing of Artificial Intelligence-Based Device to Detect Certain Diabetes-Related Eye Problems

April 11, 2018

FDA News Release

FDAAuthorizes Marketing of First Cardiac Ultrasound Software That Uses Artificial Intelligence to Guide User

February 7, 2020
AI/ML-Based Medical Devices

- Ability of AI/ML systems to learn from the wealth of real world data and improve their performance
- Development of novel AI/ML devices in all medical fields
- Fundamentally transform the delivery of healthcare
  - Earlier disease detection
  - More accurate diagnosis
  - New insights into human physiology
  - Personalized diagnostics and therapeutics
Tailoring a Regulatory Framework for AI/ML-Based SaMD

- Enhance patient access to high quality digital medical products
- Maintain a reasonable assurance of safety and effectiveness
- Enable manufacturers to rapidly improve software products with minor changes
- Minimally burdensome
Continuous Learning for Software as a Medical Device

Medical software manufacturers are encouraged to leverage the software technology’s capability of capturing real world performance data to understand user interactions with the SaMD, and to conduct ongoing monitoring of analytical and technical performance to support future intended uses.

Adapted from “Software as a Medical Device (SaMD): Clinical Evaluation,” www.imdrl.org
Continuous Learning for Software as a Medical Device

“Locked” Algorithm with Discrete Updates

Spectrum of AI/ML-Based Algorithms

Updates less frequent and performed by human

Updates more frequent and performed by computer

Continuously Adaptive Algorithm
Continuous Learning for Software as a Medical Device

If adaptations are pre-specified, and the methods for determining an appropriate adaptation clearly delineated, then a decision-making framework, as described here, may be similarly applied for both locked and adaptive algorithms.
Data selection and management

Model training and tuning

Model validation
  - Performance evaluation
  - Clinical evaluation

Data for re-training

1. Culture of Quality and Organizational Excellence
2. Review of SPS (SaMD Pre-Specifications) & ACP (Algorithm Change Protocol)
3. Real-World Performance Monitoring
4. Model monitoring
  - Log and track
  - Evaluate performance

Legend
- AI Model Development
- AI Production Model
- AI Device Modifications
- Proposed TPLC Approach

Good Machine Learning Practices
SPS & ACP: A Pre-Determined Change Control Plan

**SPS = SaMD Pre-Specifications:**
- **WHAT** are the proposed types of changes to the SaMD the sponsor intends to achieve?
- Draws a virtual “region of potential changes” around the initial specifications and labeling of the device.

**ACP = Algorithm Change Protocol:**
- **HOW** will the changes (pre-specified in the SPS) be performed and validated?
- Step-by-step delineation of the procedures to be followed for a specific device and type of change
SPS & ACP: A Pre-Determined Change Control Plan

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**Types of Pre-Specifications:**
1) Retraining for performance improvement
2) New data acquisition system
3) Change related to intended use
### SPS & ACP: A Pre-Determined Change Control Plan

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<table>
<thead>
<tr>
<th><strong>ACP Components:</strong></th>
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<tr>
<td><strong>Data Management</strong></td>
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| - For new training & test data:  
  - Collection protocols  
  - Quality assurance  
  - Reference standard determination  
  - Auditing and sequestration of training and test sets |
| **Re-training** |
| - Re-training objectives  
- Changes related to:  
  - ML methods, including architecture and parameters  
  - Data pre-processing  
- Criteria to initiate performance evaluation |
| **Performance Evaluation** |
| - Assessment metrics  
- Statistical analysis plans  
- Frequency and triggers for evaluation  
- Performance targets  
- Methods for testing with “clinicians in the loop” |
| **Update Procedures** |
| - Software verification and validation  
- When and how updates will be implemented  
- Plans for global and local updates  
- Communication and transparency to users |
Good Machine Learning Practices (GMLP)

GMLP = Good Machine Learning Practices

- Accepted practices in ML/AI algorithm design, development, training, and testing that facilitate the quality development and assessment of ML/AI-based algorithms
- Based on concepts from quality systems, software reliability, machine learning, and data analysis, etc
Approach to Modifications Utilizing SPS + ACP

*This flowchart should only be considered in conjunction with the accompanying text in the AI/ML discussion paper.
Further Questions or Feedback

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