REGULATORY GUIDANCE AND EVIDENTIARY PRINCIPLES FOR DIGITAL HEALTH TECHNOLOGY DEVELOPMENT

PRESENTED BY BAKUL PATEL, DIRECTOR OF DIGITAL HEALTH @ FDA/CDRH

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Our mission at CDRH is to protect and promote the public health.

We provide oversight for Medical Devices and Radiation-Emitting Products.

1. We assure that patients and providers have timely and continued access to safe, effective, and high-quality devices.

2. **We provide consumers, patients, their caregivers, and providers with understandable and accessible science-based information about the products we oversee.**

3. We facilitate 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.
FDAs Definition of a Device

*Per Section 201(h) of the Food, Drug, and Cosmetic Act, a device is:*

An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

1. recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,

2. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

3. intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o).
Examples of Medical Devices

- Software for intracranial hemorrhage diagnosis and treatment
- Mobile app to determine the presence of atrial fibrillation
- Tongue depressors
- Bedpans
- Pacemakers
- Closed loop artificial pancreas systems
- Blood glucose meters
Medical Device Class and Regulatory Controls

Increasing Risk
Classification determines extent of regulatory control (Risk Based)

Class I
- General controls

Class II
- General controls
- Special controls

Class III
- General controls
- Premarket approval (PMA)
FDA Recognizes Increasing Digitization Across the Healthcare Continuum

Moving healthcare from the clinic to the patient.

Understanding patient’s behavior and physiology “in the wild.”

Focusing on prevention for early/smaller interventions.

Leveraging computing power, sensors, connectivity, and software.
Digital health technology is the convergence of computing power, connectivity, sensors, and software used in healthcare.

- Used as a medical product;
- Incorporated into a medical product (include a pharmacologic product);
- Used to develop a medical product;
- Used to study a medical product;
- Used as a companion or adjunct to a medical product, including diagnostics and therapeutics.
Embracing Digital Health Innovation

- Digital tools can provide consumers with valuable health information.
- Consumers who are better informed about health make better decisions.

What qualifies as a digital health product?

What digital health technologies need regulation?
# Therapeutic Domains Explored Today

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Domain</th>
<th>Sub-Domain</th>
<th>Domain</th>
<th>Sub-Domain</th>
<th>Domain</th>
<th>Sub-Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phobias / PTSD</td>
<td>Stress Management</td>
<td>Management / Relaxation</td>
<td>Surgical</td>
<td>Training / Planning</td>
<td>Physical</td>
<td>Rehabilitation</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Planning</td>
<td></td>
<td>Procedure</td>
<td>Management</td>
</tr>
<tr>
<td>Exercise</td>
<td>Cognitive</td>
<td>Rehabilitation</td>
<td>Optical</td>
<td>Rehabilitation</td>
<td>Addictions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Training</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Cognitive Training</td>
<td>Sports</td>
<td>Wellness</td>
<td>Disability</td>
<td>Solutions</td>
<td>Speech</td>
<td>Therapy</td>
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<tr>
<td>Wellness</td>
<td>Training</td>
<td></td>
<td></td>
<td></td>
<td>Therapy</td>
<td></td>
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<tr>
<td>Mood Disorders</td>
<td>Patient</td>
<td>Education</td>
<td>Preventative</td>
<td>Health</td>
<td>ADHD</td>
<td></td>
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<tr>
<td></td>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td>Senior</td>
<td>Care</td>
</tr>
</tbody>
</table>

Adapted from Walter Greenleaf’s (@waltergreenleaf) presentation at Life Sciences Forum 2018 – CINDE @Costa Rica
Noninvasive Treatment Mechanism

- Mobile apps
  *e.g., screen interaction, messaging*
- Immersive
  *e.g., AR, VR, Gaming*
- Sound
- Motion/Haptic feedback
- Avatar-based interaction

Picture Adapted from Walter Greenleaf’s (@waltergreenleaf) presentation at Life Sciences Forum 2018 -- CINDE @Costa Rica
Digital Biomarkers

“Digital biomarkers are defined as objective, quantifiable physiological and behavioral data that are collected and measured by means of digital devices such as portables, wearables, implantables or digestibles. The data collected is typically used to explain, influence and/or predict health-related outcomes.” - www.karger.com/DIB
# Uses of Digital Tools in Behavioral Health

## HEALTH AND WELLNESS
- Improve Cognitive Function
- Promote Exercise & Weight Management
- Stress Management
- Mood and Resilience
- Disability Solutions
- Addressing Isolation
- Grief Counseling

## DIGITAL DIAGNOSTICS (DDx)
- Neuropsychological Assessment
- Activities of Daily Living Assessment
- Physical Medicine – OT / PT
- Behavioral Medicine – psychology, psychiatry

## DIGITAL THERAPEUTICS (DTx)
- Post-Traumatic Stress Disorder
- Generalized Anxiety Disorder
- Depression
- Mild Cognitive Impairment
- Autism Spectrum Disorder
- ADHD

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Adapted from Walter Greenleaf’s (@waltergreenleaf) presentation at Life Sciences Forum 2018-- CINDE @Costa Rica
“Software as a Medical Device” (SaMD) is defined as software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.\(^5\)
A Rapidly Evolving Situation …

Current 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)

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
IMDRF Global Convergence in Characterizing SaMD

2013 - Foundational vocabulary

2014 - Risk framework based on impact to patients

2015 - QMS control ➔ Translating Software development practices to regulatory QMS

2017 - SaMD Clinical Evaluation ➔ Generating evidence for clinically meaningful SaMD

Software as a Medical Device (SaMD) Software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.
IMDRF SaMD Risk Categorization

<table>
<thead>
<tr>
<th>State of Healthcare Situation or Condition</th>
<th>Significance of Information Provided by SaMD to Healthcare Decision</th>
<th>Treat or Diagnose</th>
<th>Drive Clinical Mngmnt</th>
<th>Inform Clinical Mngmnt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical</td>
<td></td>
<td>IV</td>
<td>III</td>
<td>II</td>
</tr>
<tr>
<td>Serious</td>
<td></td>
<td>III</td>
<td>II</td>
<td>I</td>
</tr>
<tr>
<td>Non-Serious</td>
<td></td>
<td>II</td>
<td>I</td>
<td>I</td>
</tr>
</tbody>
</table>

**Category I Example:**
SaMD that analyzes images, movement of the eye or other information to guide next diagnostic action of astigmatism.
IMDRF SaMD Risk Categorization

Arrows illustrate possible change to SaMD definition statement.

Category I
Retrieves Information
- None

Category II
- Optimizes Processes
- Informs Non-Serious

Category III
- Informs Critical
- Drives Non-Serious

Category IV
- Treats/Diagnoses Non-Serious
- Drives Critical

Not SaMD
- Treats/Diagnoses Critical
- Closed Loop Interventions
- No Clinical Intermediary

Increasing Impact/Risk
Clinical Evaluation & Evidence Gathering

Clinical Evaluation

① Valid Clinical Association

Generate evidence to demonstrate a valid clinical association between a SaMD output and a SaMD’s targeted clinical condition

• Use existing evidence (e.g., literature searches, original clinical research, professional society guidelines), or
• Generate new evidence (e.g., secondary data analysis, perform clinical trials)

② Analytical Validation

Generate evidence to demonstrate that the SaMD correctly processes input data to generate accurate, reliable, and precise output data

• Generate evidence as part of quality management system or good software engineering practices

③ Clinical Validation

Generate evidence to demonstrate that the SaMD’s accurate, reliable, and precise output data achieves its intended purpose in its target population in the context of clinical care

• Generate evidence that shows:
  • The SaMD has been tested for its target population and for its intended use;
  • Users can achieve clinically meaningful outcomes through predictable and reliable use.
SaMD manufacturers are encouraged to leverage SaMD’s technology capability to capture real world performance data to understand user interactions with the SaMD, and conduct ongoing monitoring of analytical and technical performance to support future intended uses.

1. Additional clinical data is gathered.
2. The data may create and support new intended use(s).
3. The SaMD manufacturer will update the clinical evaluation and generate a new definition statement.
4. Then the cycle repeats.
Opportunities and Challenges

- Dealing with measures that are new
- Accessing trial participants data outside of the clinical setting
- Patient-generated vs. patient-reported outcomes
- Not so gold standards in light of evolving data availability
Our Digital Health Center of Excellence will develop more efficient ways to ensure the safety and effectiveness of technologies like smart watches with medical apps.

Timeline for launch is TBD.
Get More Information

www.fda.gov/digitalhealth

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