Challenges for the Implementation of Digital Monitoring Technologies in Drug Development

Jen Goldsack
Executive Director, DiMe

February 18, 2020 | Remote Monitoring for Medical Product Development Workshop
Digital health industry categorization

<table>
<thead>
<tr>
<th>DEFINITION</th>
<th>DIGITAL MEDICINE</th>
<th>DIGITAL THERAPEUTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital health includes technologies, platforms, and systems that engage consumers for lifestyle, wellness, and health-related purposes; capture, store or transmit health data; and/or support life science and clinical operations.</td>
<td>Digital medicine includes evidence-based software and/or hardware products that measure and/or intervene in the service of human health. ¹</td>
<td>Digital therapeutic (DTx) products deliver evidence-based therapeutic interventions to prevent, manage, or treat a medical disorder or disease. ²</td>
</tr>
<tr>
<td>CLINICAL EVIDENCE</td>
<td>Clinical evidence is required for all digital medicine products.</td>
<td>Clinical evidence and real world outcomes are required for all DTx products.</td>
</tr>
<tr>
<td>Typically do not require clinical evidence.</td>
<td></td>
<td></td>
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<tr>
<td>REGULATORY OVERSIGHT</td>
<td>Requirements for regulatory oversight vary. Digital medicine products that are classified as medical devices require clearance or approval. Digital medicine products used as a tool to develop other drugs, devices, or medical products require regulatory acceptance by the appropriate review division.</td>
<td>DTx products must be reviewed and cleared or certified by regulatory bodies as required to support product claims of risk, efficacy, and intended use.</td>
</tr>
</tbody>
</table>

² [https://www.dbxalliance.org/dtxproducts/](https://www.dbxalliance.org/dtxproducts/)
³ It is important to check with local regulatory requirements in each jurisdiction the product is manufactured, registered, or used in.

<table>
<thead>
<tr>
<th>PRODUCT EXAMPLES</th>
<th>Data &amp; information capture, storage, and display</th>
<th>Measurement products</th>
<th>Software that delivers a therapeutic intervention</th>
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<tbody>
<tr>
<td></td>
<td>User-facing technologies</td>
<td>Digital diagnostics</td>
<td>Medical claims include:</td>
</tr>
<tr>
<td></td>
<td>Health Information Technology (HIT)*</td>
<td>Digital biomarkers</td>
<td>• Treat a disease</td>
</tr>
<tr>
<td></td>
<td>Consumer health information</td>
<td>Electronic clinical outcome assessments</td>
<td>Digital therapeutics that deliver a medical intervention to treat a disease.</td>
</tr>
<tr>
<td>Data &amp; information transmission</td>
<td>Telehealth</td>
<td>Remote patient monitoring</td>
<td>• Manage a disease</td>
</tr>
<tr>
<td></td>
<td>Decision support software*</td>
<td>Decision support software*</td>
<td>Digital therapeutics that deliver a medical intervention to manage a disease.</td>
</tr>
<tr>
<td></td>
<td>Enterprise support</td>
<td>Measurement &amp; intervention products</td>
<td>• Improve a health function</td>
</tr>
<tr>
<td></td>
<td>Clinical care administration &amp; management tools</td>
<td>Digital companion²</td>
<td>Digital therapeutics that deliver a medical intervention to improve a health function and/or prevent a disease.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Digital products that both 1) measure and intervene, and 2) do not require human intervention to serve primary purpose</td>
<td></td>
</tr>
</tbody>
</table>

*See full categorization chart for details

1 In the United States, ONC-certified EHR functions are not devices according to the FD&C Act, as amended by 21st Century Cures Act
2 Note: 1) Integration of the digital tool with an existing drug or biologic requires a label change for the drug or biologic, and 2) regulatory requirements may recognize digital tools coupled with a drug or biologic as a combination product

Digital Health, Digital Medicine, Digital Therapeutics (DTx): What’s the difference?

Clarity matters. Here’s what you need to know.

Jennifer Goldsack
Nov 10 · 6 min read

Authors: Jennifer Goldsack, Megan Coder, Chandana Fitzgerald, Natalie Navar-Mattingly, Andy Coravos, and Ashish Atreja

Why digital medicine?

Worldwide Digital Health Market to Hit $504.4 Billion by 2025: Global Market Insights, Inc.

The U.S. digital health market accounted for largest share in 2018 supported by increasing prevalence of chronic diseases along with growing geriatric population in the country.

Healthcare is in crisis

US household spending on health care tops $1 trillion in 2018 for first time

More Alzheimer's drug trial failures: are researchers on the wrong track?

One-quarter of people with diabetes in the U.S. are rationing their insulin

This is the real reason most Americans file for bankruptcy

Suicide rates for doctors and young physicians among highest in the US population
Digital capabilities


Mount Sinai to build new precision medicine supercomputer

The health system's second "big omics data engine," or BODE 2, funded in part by HHS, will have 15 terabytes of memory, 14 petabytes of raw storage and a peak speed of 220 teraflops per second – nearly double that of its predecessor.

By Mike Miliard | November 18, 2019 | 03:49 PM

Present and future generations have expectations that are markedly different than those of the past. Raised as digital natives, they not only adopt new technologies faster, but can also imagine for themselves how these technologies can be used to improve their lives, making them much harder to surprise.

Digital consumption

Products and services to experiences

Hyper-personalization

Ownership to access

Government initiatives

Notice of Proposed Rulemaking to Improve the Interoperability of Health Information

Government initiatives

FDA’s Technology Modernization Action Plan (TMAP)

September 18, 2019

Available at: https://www.fda.gov/media/130883/download

Modernizing FDA’s Data Strategy

MARCH 27, 2020

Government initiatives

2020-2025
Federal Health IT Strategic Plan

When you’re a hammer, everything looks like a nail.

Photo credit: Charlie Hankin @The New Yorker
The evidence base for the safety and effectiveness of these new products has not kept pace with their development. Given the great divide between the promised benefits of digital medicine and its potential risks, we need to know —not just believe —that the tools we use are trustworthy.

Jennifer Goldsack, Beau Woods, & Eric Perakslis
Source: https://www.statnews.com/2019/06/05/new-digital-medicine-society/
The ‘Internet of Bodies’ Is Here. Are Courts and Regulators Ready?

A network of smart devices attached to or implanted in bodies raises a host of legal and policy questions

By Andrea M. Matwyshyn

Nov. 12, 2018 11:19 am ET

Disparities in accuracy of digital sensor technologies

Fitbits and other wearables may not accurately track heart rates in people of color

By RUTH HAILU / JULY 24, 2019

Racial Bias Found in a Major Health Care Risk Algorithm

Black patients lose out on critical care when systems equate health needs with costs

By Starre Vartan on October 24, 2019

Urgent Cyber Warning For Hospitals Over Threat Of 'WannaCry Repeat': Report

The report's findings are bleak to read, made worse because so much of the defense is relatively straightforward—outdated equipment, unpatched software, a lack of skills, training and awareness.

Our phones can now detect health problems from Parkinson’s to depression. Is that a good thing?

Digital phenotyping, which can detect patterns from text messages, movements, and even our speech, could transform health care. But is our personal information at stake?

By Lois Parshley | Updated Feb 12, 2020, 8:30am EST

SicGRL vulnerability is still not fixed

By ftrotter  |  September 12, 2019  |  No Comments

Source: https://lightcollective.org/2019/09/12/sicgrl-update/
If you are not paying for it, you're not the customer; you're the product being sold.
Digital medicine: A weapon or a tool?
HIPPOCRATIC OATH

I SWEAR by Apollo the physician and Asclepius and Hygeia and Panaceae, invoking all the gods and goddesses to be my witnesses, that I will fulfill this Oath and this written covenant to the best of my powers and of my judgment. I will look upon him who shall have taught me this art even as on mine own parents: I will share with him my substance, and supply his necessities if he be in need: I will regard his offspring even as my own brethren, and will teach them this art, if they desire to learn it, without fee or covenant.

I WILL IMPART it by precept, by lecture and by all other manner of teaching, not only to my own sons but also to the sons of him who has taught me, and to disciples bound by covenant and oath according to the law of the physicians but to none other.

THE REGIMEN I adopt shall be for the benefit of the patients to the best of my power and judgment, not for their injury or for any wrongful purpose. I will not give a deadly drug to any one, though it be asked of me, nor will I lead the way in such counsel; and likewise I will not give a woman a pessary to procure abortion. But I will keep my life and my art in purity and holiness. I will not use the knife, not even, venally, on sufferers from stone, but I will give place to such as are craftsmen therein.

WHATSOEVER HOUSE I enter, I will enter for the benefit of the sick, refraining from all voluntary wrongdoing and corruption, especially seduction of male or female, bond or free.
Where is the professional society for people like us building the field of digital medicine?
The Digital Medicine Society (DiMe) launched eight months ago.

Source: https://www.statnews.com/2019/06/05/new-digital-medicine-society/

The Intersection of Two Communities
Who is involved in DiMe?

You. Individuals, not companies.

We are a professional society!
Where do our members come from?

REGULATORY & GOVERNMENT
- FDA
- U.S. Department of Veterans Affairs
- European Medicines Agency
- NIH

INDUSTRY
- Dexcom
- Pfizer
- Philips
- Advarra
- Roche
- Novartis
- AstraZeneca

INNOVATION
- Sage Bionetworks
- biovotion
- PEAR Therapeutics
- AKILI
- Actigraphy
- koneksa
- Hu-manity.co
- BehaVR

ASSOCIATIONS
- Clinical Transformation Initiative
- Digital Therapeutics Alliance
- Biohacking Village

HEALTHCARE DELIVERY
- Moffitt Cancer Center
- HealthCore

INVESTORS
- Digitalis
- Tamarisc

ACADEMIA & ACADEMIC MEDICINE
- Northumbria University
- UNC Lineberger Comprehensive Cancer Center
- UC San Diego School of Medicine
- Scripps Research Translational Institute
- Duke Clinical Research Institute

PATIENTS & PATIENT GROUPS

Over 900 members have joined DiMe in the past 10 months
900+ Members

39 Countries
DiMe is advancing digital medicine to optimize human health

- Research
- Communication & Education
- Community Building
Become a founding member

Is digital measurement in clinical trials just hype?

Has any pharmaceutical company actually used a digital measure to inform a primary or secondary endpoint?
Digital endpoint collection in industry-sponsored trials is here

<table>
<thead>
<tr>
<th>PRIMARY, SECONDARY OR LABEL CLAIM</th>
<th>Sponsors start digital endpoint development early</th>
<th>Pharma trusts digital tools with primary &amp; secondary endpoints</th>
</tr>
</thead>
</table>
| [List of logos]                   | [Diagram showing distribution by phase: Phase 0: 5%, Phase 1: 24%, Phase 2: 29%, Phase 3: 17%, Phase 4: 24%] | ENDPOINT POSITIONING
|                                   | [8 Primary endpoints, 15 Secondary endpoints, 1 Label claim, 17 Exploratory] | UNIQUE ENDPOINTS
Digital endpoints library can aid clinical trials for new medicines

By JEN GOLDSACK, RACHEL A. CHASSE, and WILLIAM A. WOOD / NOVEMBER 6, 2019

Modular evaluation of digital measures

- **VERIFICATION**: Evaluates and demonstrates the performance of a sensor technology within a BioMeT, and the sample-level data it generates, against a pre-specified set of criteria.

- **ANALYTICAL VALIDATION**: Evaluates the performance of the algorithm, and the ability of this component of the BioMeT to measure, detect, or predict physiological or behavioral metrics.

- **CLINICAL VALIDATION**: Evaluates whether a BioMeT acceptably identifies, measures, or predicts a meaningful clinical, biological, physical, functional state, or experience, in the stated context of use (which includes a specified population).

Modular evaluation of digital measures

V3 processes are typically conducted by experts across disciplines and domains

V3 is the first step of the process

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<tr>
<th>Evaluation Dimension</th>
<th>Elements to Consider</th>
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<tbody>
<tr>
<td>Verification, Analytical Validation and Clinical Validation (V3)</td>
<td>Does the tool measure what it claims to measure? Is the measurement appropriate for the target population?</td>
</tr>
<tr>
<td>Security</td>
<td>Does the manufacturer build with safety by design? Is there a Disclosure Policy? Software Bill of Materials?</td>
</tr>
<tr>
<td>Data Rights and Governance</td>
<td>Who has access to the data and when? Is the privacy policy publicly accessible?</td>
</tr>
<tr>
<td>Utility and Usability</td>
<td>How is the tool worn? Battery life? Available technical support?</td>
</tr>
<tr>
<td>Economic Feasibility</td>
<td>What’s the net benefit versus price? Is cost a one-time or subscription model?</td>
</tr>
</tbody>
</table>

WE HAVE TO BE AS BRAVE AS THE PEOPLE WHO NEED US.

Source: Gaping Void at https://www.gapingvoid.com/blog/2016/01/22/be-as-brave/
Thank you!

jennifer@dimesociety.org

www.dimesociety.org