USE OF DIGITAL HEALTH TECHNOLOGIES IN CLINICAL PROGRAMS

Anindita Saha

Assistant Director, Digital Health Center of Excellence

Center for Devices & Radiological Health (CDRH), US FDA

CDRH's Digital Health Center of Excellence provides world-class digital health expertise and policy direction

Our team brings extensive experience:

105+ YEARS	90+ YEARS	50+ YEARS	45+ YEARS	40+ YEARS	40+ YEARS	15+ YEARS
FDA	DIGITAL HEALTH INDUSTRY	ACADEMIA	OTHER INDUSTRY (NON-DIGITAL HEALTH)	MEDICAL	NONPROFIT	OTHER GOVERNMENT (NON-FDA)

Current as of June 2022

We are setting the stage for the advancement of digital health to help protect and promote public health

Select Accomplishments

29	14	80+	3400+	5000+
Public Documents	Guidance Documents since FY18	Experts in the Network of DH Experts	Inquiries addressed since FY18	Medical device submissions with DH considerations since FY18

Notable Authorizations

- Substance use disorder
- Opioid use disorder
- Colon Cancer
- Chronic Pain Reduction
- Capture Cardiac Ultrasounds
- Diabetes Management

New Regulatory Frameworks

- Released AI/ML Action Plan
- Piloted a software pre-certification program
- Published list of currently marketed AI/ML-enabled medical devices
- Jointly published list of 10 Good Machine Learning Practice (GMLP) Principles with the UK and Canada
- Workshop on Transparency of AI/ML-enabled medical devices

CDRH's Digital Health Center of Excellence (DHCoE) launched in September 2020.

There is a large spectrum of DHTs available for potential use

DHTs may take the form of hardware and/or software

Consumer general wellness product (e.g., sleep monitor, basic pedometer)

Electronic patient-reported outcome (ePRO) instrument

Continuous blood glucose monitor

Digital therapy virtual reality device

Electrocardiograph (ECG) software for over-the-counter use

Portable electroencephalogram (EEG)

Digital health technologies can transform how we study medical products

Enable Remote Data Collection in Decentralized Clinical Investigation

- More frequent or continuous monitoring compared to traditional methods
- Longitudinal view of participant's health status
- Improved recruitment and retention of participants leading to less missing data

Improve Access to Clinical Investigations

- Meet a participant where they are at for a clinical investigation
- Fewer visits to a study site places less burden on participants
- Reach a more diverse population, advancing health equity

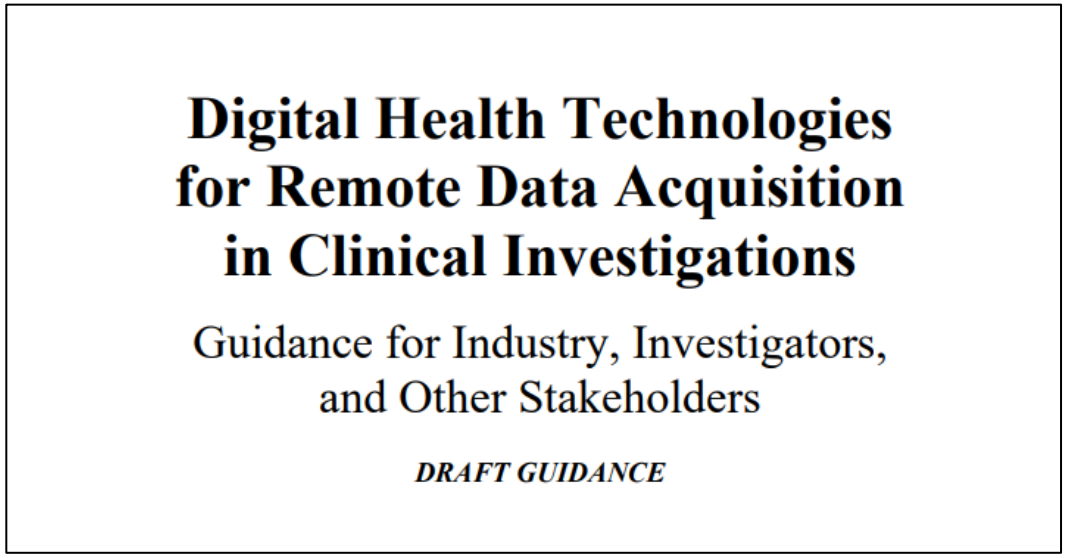
Facilitate Innovative Clinical Investigation Endpoints

- New types of data to inform novel endpoints
- Complementary to other forms of data used to support a regulatory submission

Capture Real-World Data (RWD) and Patient-Generated Health Data (PGHD)

- Data reflects a participant's daily life
- Remote and longitudinal follow-up with participants beyond the clinical investigation
- More detailed picture of the impact of a medical product on a participant

Draft Guidance on Digital Health Technologies for Remote Data Acquisition in Clinical Investigations



- This draft guidance provides recommendations to facilitate the use of DHTs in clinical investigations
- It is designed to help accelerate efficient medical product development to help bring new innovations and advances to patients
- It builds on the launch of the Digital Health Center of Excellence to empower digital health stakeholders and provide regulatory clarity and collaboration across FDA

Some DHTs meet the definition of a medical device* while others do not

*A device is defined by the Federal Food, Drug, & Cosmetic Act, Section 201(h) as:

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

- 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
- 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…

Is marketing authorization (premarket clearance or approval) required to use a DHT in a clinical investigation?

Devices intended only for use in clinical investigations are typically exempt from many requirements applicable to Devices – including premarket clearance or approval – as long as the investigation complies with applicable requirements under 21 CFR part 812

The CDRH Digital Health Center of Excellence (DigitalHealth@fda.hhs.gov) is a resource for questions on DHTs

If a DHT has marketing authorization (premarket clearance or approval), does that mean it is appropriate for use in a clinical investigation?

DHTs used in clinical investigations should be ***fit-for-purpose****

Fit-for-purpose: A conclusion that *the level of validation associated with a biomarker or COA is sufficient to support its proposed use.*

Clinical investigation ***endpoints**** should reflect an outcome of interest

Endpoint: *A precisely defined variable intended to reflect an outcome of interest* that is statistically analyzed to address a particular research question…

*Definitions from FDA-NIH BEST Glossary. Available at https://www.ncbi.nlm.nih.gov/books/NBK338448/

DHTs should be *fit-for-purpose* when used in a clinical investigation

***Fit-for-purpose**: a conclusion that the level of validation associated with a DHT is sufficient to support its proposed use in the clinical investigation*

- Clinical event or characteristic of interest
- Ability of DHT to measure clinical event or characteristic of interest
- Population of interest, including age, technical aptitude, and education level, as appropriate
- DHT design and operation (for example, physical properties, power needs, alerts)

Applies regardless of if the participant is bringing their own DHT or general-purpose computing platform

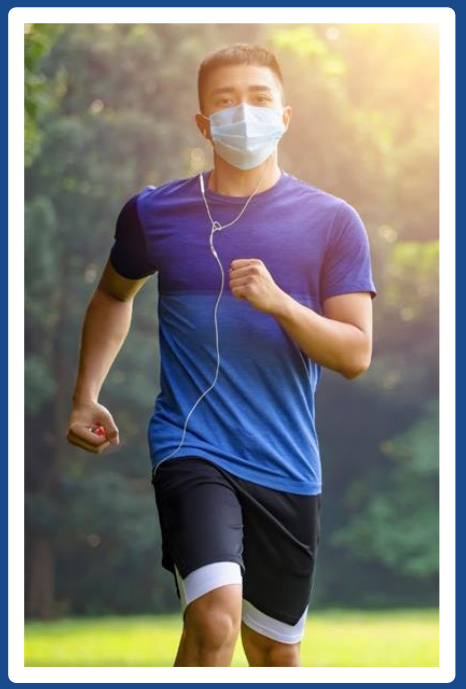
Verification and validation are important steps to help ensure a DHT is fit-for-purpose

Verification: confirmation by examination and provision of objective evidence that the physical parameter that the DHT measures (e.g., acceleration, temperature, pressure) *is measured accurately and precisely over time.* Verification is often viewed as part of the validation process

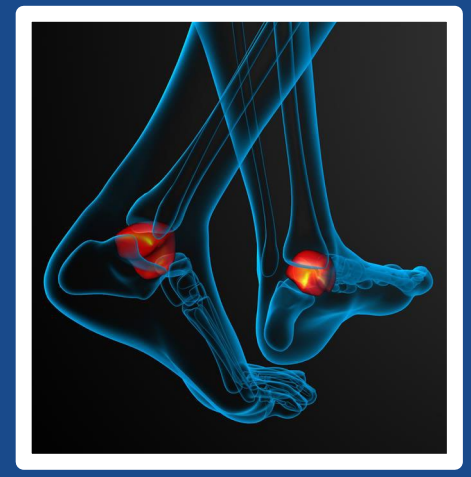
Validation: confirmation by examination and provision of objective evidence that the DHT appropriately assesses the clinical event or characteristic *in the proposed participant population*

Third party verification and validation data may be leveraged, when appropriate

Benchtop studies



Studies with healthy volunteers



Studies with individuals representing the clinical population of interest

Further considerations when using a DHT for remote data acquisition in a clinical investigation

Participant Safety

Participant and Staff Training

Technical Support

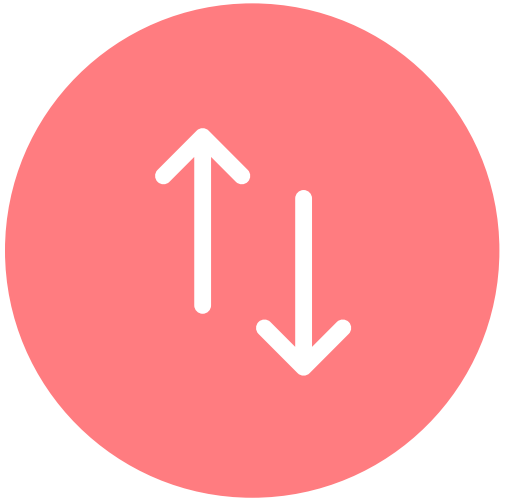
Data Retention and Protection

When using data from a DHT to inform an endpoint, treat the endpoint like you would any other endpoint

Definition

Justification

Type
(Safety, Effectiveness)



Positioning
(Primary, Secondary, etc.)

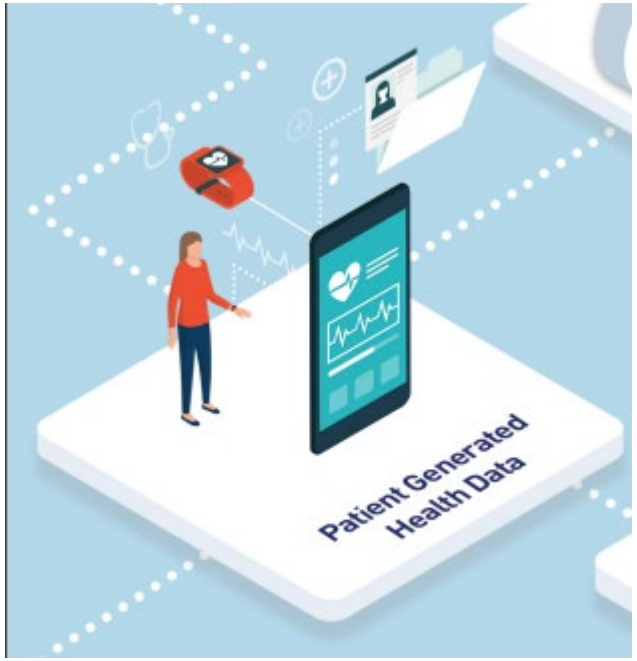
DHT Guidance Update

- Docket closed March 2022
- Received over 600 comments from 47 commentors
  - Patient and consumer advocacy groups
  - Regulated industry
  - Pharmacists and third-party payers
  - Science and academic experts
  - Legal/regulatory consulting
  - Private citizens

DHT Guidance Update

- Key themes from comments
  - Terminology
  - Medical device regulation
  - Verification and validation
  - Endpoint development
    - Difference between the technology and the clinical measure
  - Examples

Regulatory Science Challenges



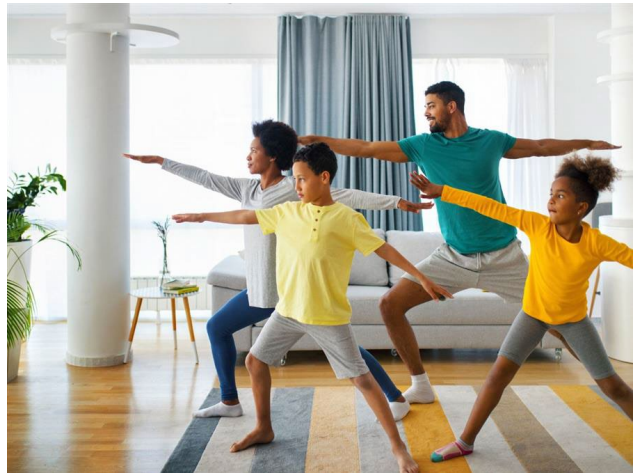
Near-Term	Longer-Term
• Consumer-grade DHTs verification and validation in specific clinical and regulatory applications • Novel digital biomarkers validation in relevant contexts of use • Platform usability requirements for patients • Data characteristics/requirements to be used in clinical, regulatory, and other decision making • Privacy and security, along with other cybersecurity considerations • Data sharing and governance • Maintenance and management of large volumes of PGHD • Integration into existing health care systems' workflows	• Standardization of PGHD from different sources • Data synchronization and interoperability of multiple sources of PGHD • Performance specifications for use when considering interchangeability of wearables (for example, "bring-your-own wearable" approaches to clinical investigations) • Clinically meaningful and patient-relevant composite endpoints derived from multiple data sources • Integrated analytical tools • Visualization tools to advance transparency • Reliable metrics to compare standard disease outcomes (for example, sleep quality, performance status) as measured by DHTs to traditional collection methods

Spotlight: Digital Health Regulatory Science Research Opportunities:
https://www.fda.gov/media/162644/download

In summary, DHTs can revolutionize the ability to remotely obtain clinically relevant information from diverse individuals

Potential for continuous or more frequent data collection

Opportunities to record data directly from trial participants wherever the participants may be



Can facilitate the direct collection of information from participants who are unable to report their experiences

Further Questions or Feedback

www.fda.gov/digitalhealth

DigitalHealth@fda.hhs.gov

Anindita Saha

Assistant Director, Digital Health Center of Excellence

Center for Devices and Radiological Health, U.S. Food and Drug Administration

anindita.saha@fda.hhs.gov