Digital Health Tools in Clinical Investigations

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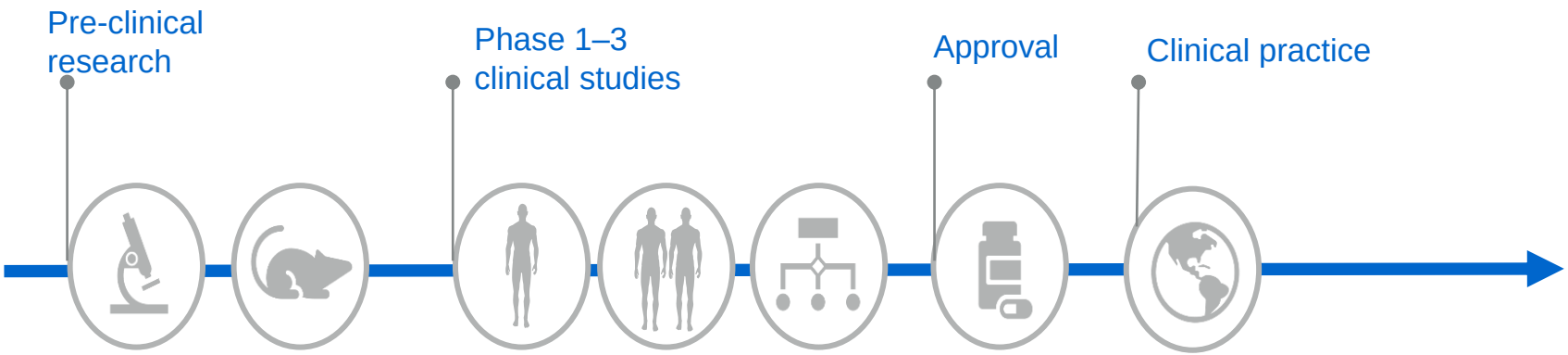
Digital Health Technology and Regulation Conference
Food and Drug Law Institute
Nov 10, 2021

Digital health technologies employed throughout product lifecycle



DHTs in R&D

Digital technologies in pre-clinical research

Digital health technology (DHT) in drug trials

Digital Data Capture (incl Remote)

DHT for patient management

Digital measures/endpoints

DHTs in Clinical Practice

Software as a Medical Device (SaMD)

Digital Data Capture[1] (incl Remote)

Clinical decision support systems (CDSS)

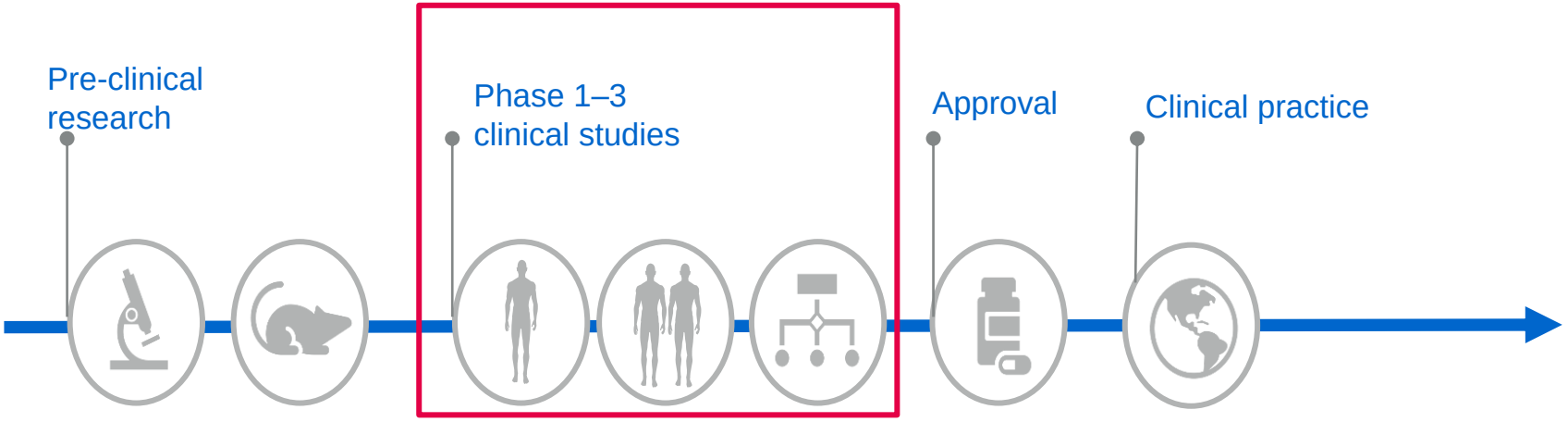
Digital therapeutics (DTx)

Artificial Intelligence/Machine-Learning

Generation and Use of Data/ RWD

[1] Assuming a medical purpose

Use of Digital Health Technologies (DHTs) in Drug Development



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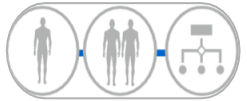
Examples



DHT used in Drug Development (i.e. DHT will NOT be marketed)

DHT **MAY NOT** qualify as SaMD

- DHT capturing important measures such as (but not limited to): Baseline characterization, safety monitoring, etc.
- Monitoring treatment administration via smart packaging/ connected devices
- Measure treatment response via Virtual Reality based tasks
- Measure treatment response by algorithm-based reading of imaging

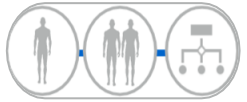
DHT **MAY** qualify as SaMD

- Safety monitoring via measuring of vital signs
- Detecting/monitoring disease via a digital tool that measures passive signs
- Monitoring disease progression via app-based active tests
- Prognosis of treatment effect using digital pathology

DHT: digital health technology; CT: Clinical Trial; SaMD: Software as a Medical Device

Use of Digital Health Technologies (DHTs) in Drug Development

Which center(s) do we work with?



DHT used in Drug Development (i.e. DHT will NOT be marketed)

DHT **MAY NOT** qualify as SaMD

2 levels of regulatory oversight:

- CDER/CBER review the appropriateness of what is being measured
- CDER/CBER review whether the DHT is adequately validated to capture the measure

DHT **DOES** qualify as SaMD

3 levels of regulatory oversight:

- CDER/CBER review the appropriateness of what is being measured
- CDER/CBER review whether the DHT is adequately validated to capture the measure
- CDRH reviews the DHT according to device regulation requirements

➢ The DHT is reviewed by both centers in parallel

DHT: digital health technology; CT: Clinical Trial; SaMD: Software as a Medical Device

Challenges

- Lack of “common regulatory denominator” between CDER/CBER and CDRH on appropriate methods for technical and analytical validation of the DHT
- Unclear level of communication between and across centers to support development and review of the DHT used in drug development
- Unclear on how to engage with CDER/CBER and CDRH regarding appropriate pathway for the review of a DHT
- Currently DHT development cannot be discussed without an accompanying IND which disincentivizes utilization in CTs

PDUFA VII - Enhancing Use of Digital Health Technologies (DHT) To Support Drug Development and Review

DHT framework to guide the use of DHT-derived data in regulatory decision-making for drugs and biological products.

The framework will:

a. Define objectives for workshops and demonstration projects;

b. Develop methodologies for evaluating DHTs proposed as measuring key (primary or important secondary) endpoints or other important measures (e.g., for safety monitoring, or baseline characterization) in clinical trials;

c. Manage submissions with extensive and continuous data, e.g., in order to develop acceptable approaches to capture adverse events; and

d. Develop a standardized process for data management and analysis of large datasets from DHTs.

PDUFA VII - Enhancing Use of Digital Health Technologies (DHT) To Support Drug Development and Review

5 public meetings with key stakeholders to gather input into issues related to the use of DHTs in regulatory decision-making.

The meetings and workshops will help:

a. Understand priorities for development of DHTs to support clinical trials, including the potential for DHTs to increase diverse patient populations in clinical trials;

b. Identify approaches to DHT validation;

c. Gain understanding of DHT data processing and analysis and inform need for novel analytical techniques; and

d. Address the regulatory acceptance of safety monitoring tools that utilize artificial intelligence/machine learning-based algorithms for pharmacovigilance purposes, e.g., continuous data streams from DHT.

Doing now what patients need next

DIGITAL HEALTH TECHNOLOGY:

CAPTURING PATIENT INSIGHTS AT THEIR LOCATION

ANINDITA SAHA

11.10.2021

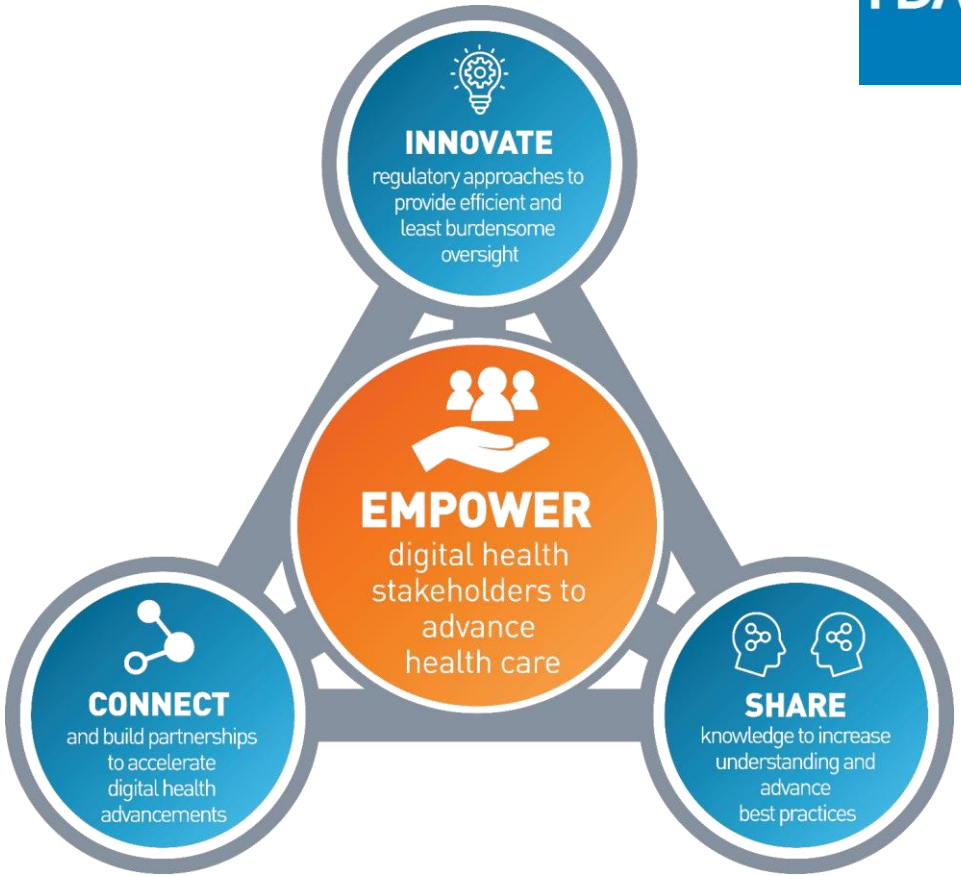
FDA's Digital Health Center of Excellence

Empowering All to Advance Healthcare

Our goal: Empower stakeholders to advance health care by fostering responsible and high-quality digital health innovation.

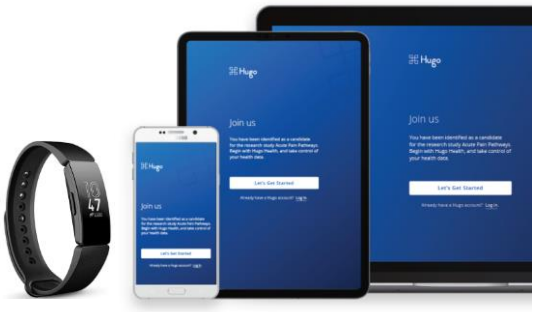
The Digital Health Center of Excellence aims to:

- **Connect and build partnerships** to accelerate digital health advancements.
- **Share knowledge** to increase awareness and understanding, drive synergy, and advance best practices.
- **Innovate regulatory approaches** to provide efficient and least burdensome oversight .



Collaboration Example

- CERSI collaboration between FDA and clinical investigators at Yale University and Mayo Clinic (Rochester, MN) to investigate physical function as evaluated by 4 modalities: ClinRO, PRO, PerfO, and wearable data
- Plan to assess in two populations of cancer patients undergoing frontline cytotoxic chemotherapy
  - Solid tumor: breast cancer patients
  - Hematologic malignancy: lymphoma patients
- Patients will receive a wearable device (Fitbit) and a mobile device application (Hugo™) that will aggregate wearable, PRO, and electronic health record data in one platform



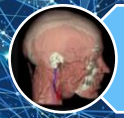
*Slide courtesy of Dr. Gita Thanarajasingam, Mayo Clinic

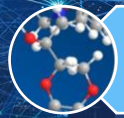
Digital Health Technology (DHT)

"A system that uses computing platforms, connectivity, software, and sensors for healthcare and related uses"*


Used as a medical product


Incorporated into a medical 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

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

DHTs can be used in a variety of ways when evaluating medical products

Remote data collection

Clinical investigation enrichment strategies

Electronic informed consent

DHTs can offer many unique benefits when used in a clinical investigation

- Decentralized clinical investigations
- Improved participant recruitment and retention of participants
- Continuous or more frequent data collection compared to traditional methods
- Longitudinal monitoring of a patient's health status without requiring visits to study sites
- Improved study accessibility for participants
- Capture of real-world data (RWD) and patient-generated health data (PGHD)
- Transmit data directly from participant to study staff
- Potential to inform novel endpoints

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

- Population of interest
- Clinical event or characteristic of interest
- Ability of DHT to measure clinical event or characteristic of interest
- DHT physical properties (e.g., design, operation)

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

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

Participant Safety

Participant and Staff Training

Technical Support

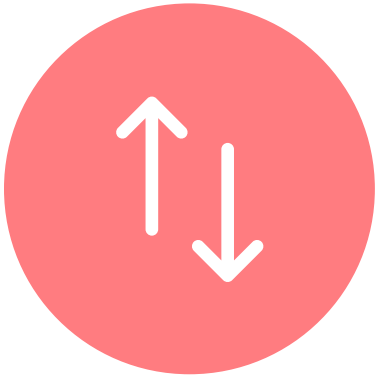
Data Retention and Protection

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.)

Further Questions or Feedback

www.fda.gov/digitalhealth

DigitalHealth@fda.hhs.gov

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