Reviewer's Perspective on Data Collected by Wearable Digital Health Technology in Clinical Trials

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Learning Objectives

- Describe a DHT and the data it collects
- Learn who to contact at FDA with DHT questions
- List the types of datasets
- Understand the importance of DHT data

Digital Health Technology

"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 (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.

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

Uses of Digital Health Technologies (DHT)

- Generate rich and comprehensive information on how patients are functioning and feeling
- Help minimize barriers to obtaining patient experience data during clinical trials
- Allow patients access to data about their health
- Assess study endpoint concepts that are meaningful to patients

Novel types of data obtained from continuous recording by biosensors

Opportunities	Examples
Richer data instead of snapshots	• Average steps per day vs 6MWD • CGM - blood glucose versus HbA1c
Ability to detect rare events	• Arrythmias, seizures
Data from patient who cannot report	• Scratching in infants with atopic dermatitis
New types of measurements	• Accelerometer measurements of gait stability that may predict falls • Measurements of coughing, sneezing, tremor

INTERACTING WITH FDA ON DHT

Framework for Use of DHT in Drug and Biological Product Development

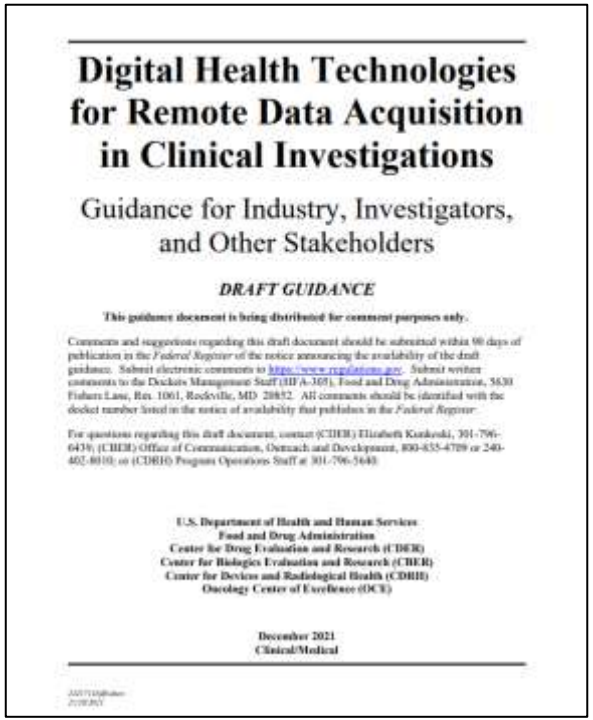
- Promote regulatory consistency and coordination
- Convene public workshops
- Identify demonstration projects
- Issue DHT-related guidances
- Enhance IT capabilities

DHT for Drug Development Website

https://www.fda.gov/science-research/science-and-research-special-topics/digital-health-technologies-dhts-drug-development

Tracking Submissions Containing DHT Data
Form 1571 and Form 356H

Draft Guidance on Digital Health Technologies for Remote Data Acquisition in Clinical Investigations



Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Guidance for Industry, Investigators, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Elizabeth Kunkoski, 301-796-6439; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; or (CDRH) Program Operations Staff at 301-796-5640.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Oncology Center of Excellence (OCE)

December 2021
Clinical/Medical

- This draft guidance provides recommendations to facilitate the use of DHTs in clinical investigations
- Helps accelerate efficient medical product development
  - Helps bring new innovations and advances to patients
- It builds on the launch of the Digital Health Center of Excellence

Engage early with the appropriate Center to discuss the use of DHTs in a specific clinical investigation

Follow each FDA Center's procedures for engaging with the Agency in the context of a development program

If the medical product under investigation is:

Drugs and biological products

See these Draft Guidance for industry:

- Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products (December 2017);
- Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products (June 2018).

Devices

See this Guidance for industry:

- FDA Staff Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program (January 2021).

DHT AND ENDPOINT CONSIDERATIONS

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

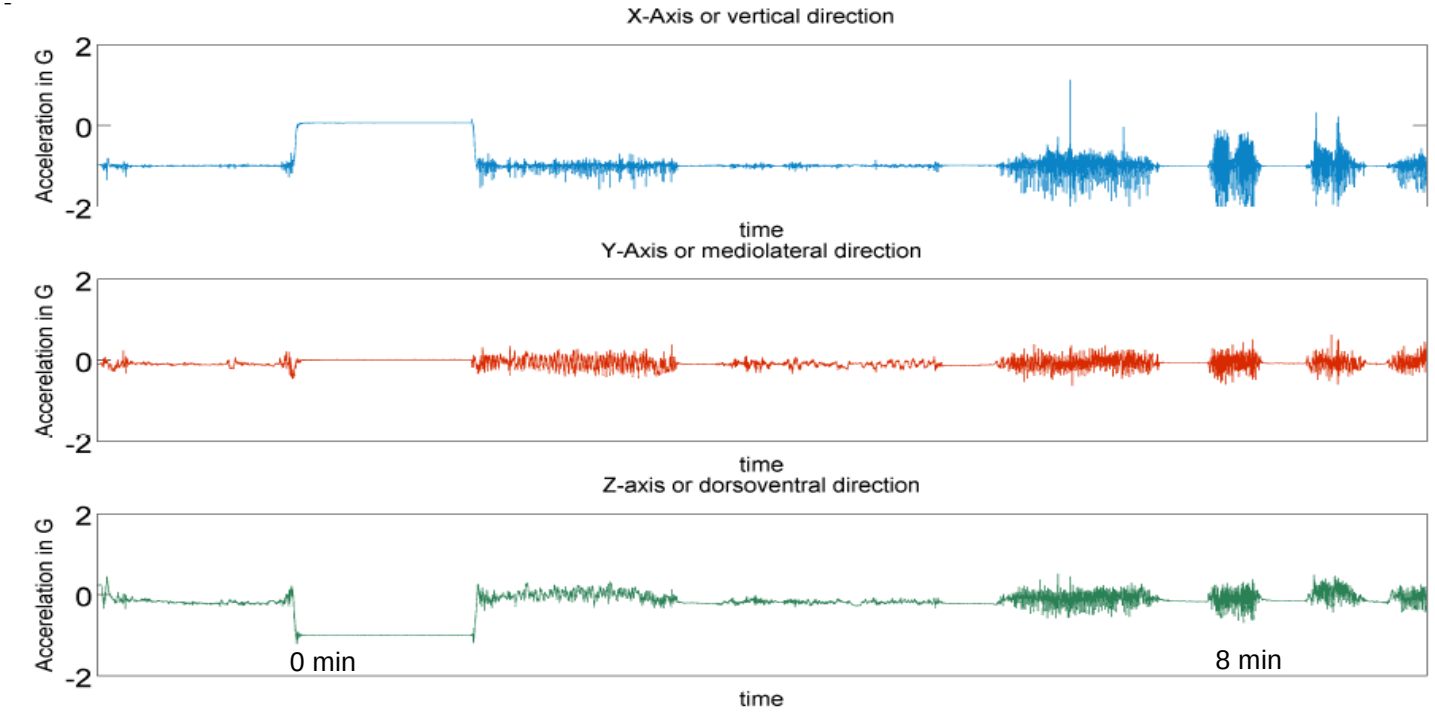
Verification and validation are important steps to help ensure a DHT is fit-for-purpose

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*

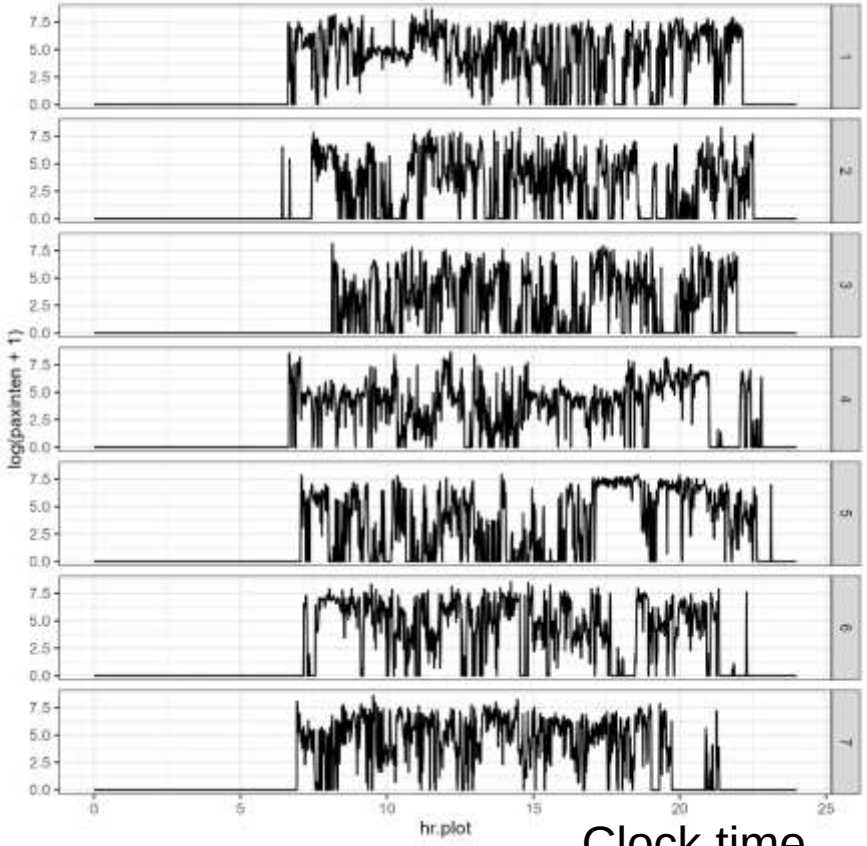
DATA CONSIDERATIONS

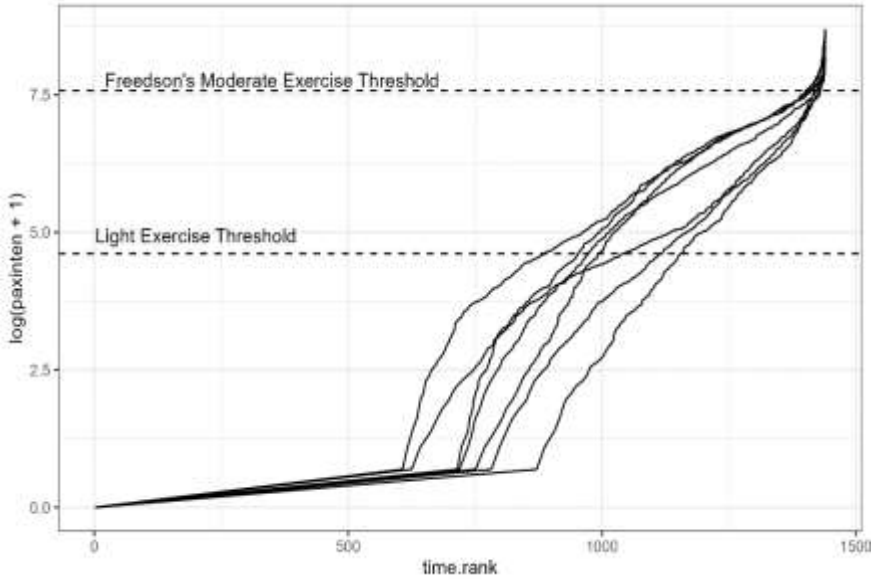
Movement Data from Acceleration Sensors



Gyllensten, IC, Physical Activity Recognition in Daily Life using a Triaxial Accelerometer, Master's Thesis, 2010.

Daily Activity Counts

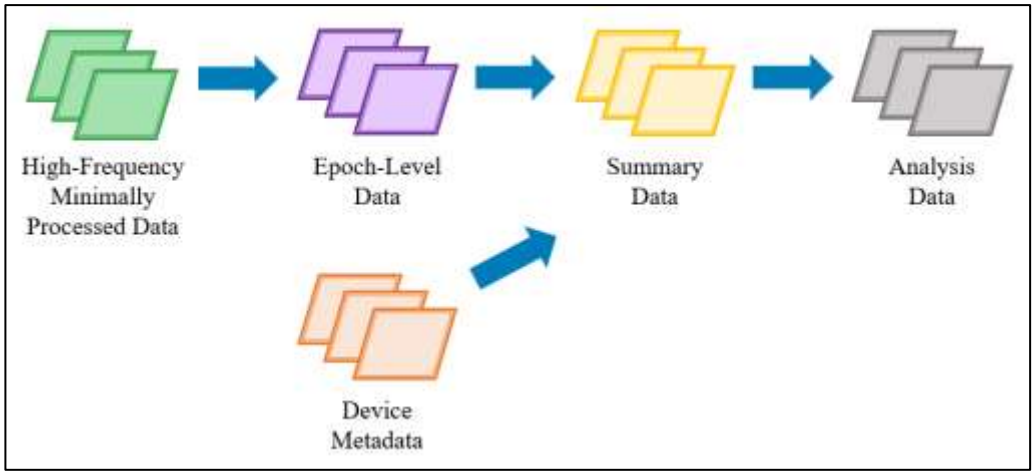




- Example subject from NHANES 2003-2004 dataset
- Each curve – activity count at a minute

Datasets: An Overview

- Data Flow



- What to Submit?
  - Required: Summary Data, Analysis Data, Device Metadata
  - As needed: Epoch-level Data, High-Frequency Minimally Processed Data

Dataset Size

- Epoch-level data (if submitted) represents aggregated or captured DHT data and is tabulated in SDTM format.
- An actigraphy watch using a one-minute epoch length results in 1,440 epochs captured for each day of patient wear
- A CGM device using a five-minute epoch length results in 288 epochs captured for each day of patient wear

Dataset Considerations

- Summary data represents the data summarized from the epoch-level data
  - Bridge the epoch-level data and the analysis data to address the clinical trial objectives
- Analysis data contains analysis-ready DHT data
  - Standardized using ADaM business rules and assumptions

Data Traceability

- Sponsor should provide a well-documented data flow
  - Each step can be traced back to its previous step
  - Aids in FDA's review and support data provenance and traceability within the data flow
- Sponsor should get agreement on which data needs to be submitted with NDA

Data Standards

- Currently, no standard formats for analysis and summarization of continuous data from DHTs
- Summaries (activity counts, steps, calories) with the same name have different meaning
- Difficult to translate or generalize results
- More to come

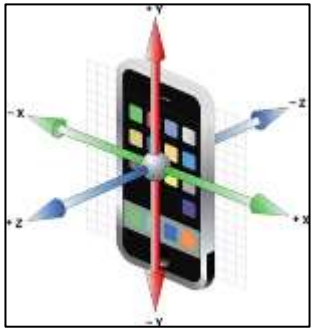
WHERE THE DATA GOES

Clinical Uses of Digital Health Technologies (DHT)

- Capture new information on how patients feel or function
  - Novel study endpoints
  - Supplementary data capturing patient experience
- Capture continuous measurement of biomarkers

Statistics Uses

- What are the important features to capture the concept of interest?
  - How to capture these features?
  - Clinical knowledge
  - Machine learning



- Analysis of more frequent outcome observations
- How to address missing data and related concerns
- Development of approaches to DHT validation

Challenge Question #1

Summary and analysis datasets must be:

A. Small
B. Excel files
C. Human readable
D. Traceable to DHT measurements

Challenge Question #2

Which datasets should be submitted to FDA?

A. High-frequency minimally processed, analysis
B. Device metadata, summary
C. Device metadata, summary, analysis, others as needed
D. Epoch level, analysis

Summary

- DHTs may capture novel and important endpoints
- Organize large volumes of data into several related datasets
- Make data and endpoints traceable

Questions?

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Closing Thought

DHTs have the potential to gather important data on a patient's disease but need plan to handle the volume of data.


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