

NEW TECHNOLOGIES ENABLING INNOVATIVE CLINICAL RESEARCH: Regulatory Perspective

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Disclaimer

- This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.

Overview

- Introduction
- Regulatory Considerations of Digital Health Technologies (DHTs)
- Verification and Validation of DHTs
- Endpoints using DHTs
- Clinical Trial Considerations
- Conclusions

Chronic Disease Challenges

- Chronic diseases are a leading cause of disability and death
- Patient perspective is crucial to the development of treatments for chronic diseases
- Need methods to track symptom progression over time
- Need to encourage patient involvement and retention in studies regarding chronic diseases

Digital Health Technologies

- Technologies that use computing platforms, connectivity, software, and/or sensors, for health care and related uses
- May collect passive measurements
 - Accelerometers, glucometers, electrocardiograms
- May require interaction from study participants to gather data
 - Mobile phone apps, smart watches



Digital Health Technologies

Overview



- Opportunities for remote data acquisition are remarkable
- Time is of the essence to use these technologies to capture data
- Possibilities of data collection are endless
 - Is it possible to find the optimal drug at the right dose at the right time for a patient?
 - New therapeutic monitoring and management strategies

Benefits of Digital Health Technologies in a Clinical Trial



- Dose ranging studies
- Characterizing the response over dosing cycle (e.g., Parkinson's disease)
- Obtaining continuous or frequent measurements over time rather than “snapshot” assessments at periodic study visits
- Capturing responses of participants in their real-world settings (e.g., home, work) rather than in the artificial research environment
- Potentially fewer in-person visits for subjects enrolled in clinical trials

Regulatory Considerations

- Regulations do not directly address the use of DHTs in clinical trials
- DHTs used in clinical trials do not need to be approved/cleared by FDA for marketing
- 1962 FD&C act- the evidence standard: “For drug approval, substantial evidence of effectiveness is required, consisting of adequate and well-controlled investigations from which experts could conclude that the drug would have the effect described in labeling”
 - Is the quality of the evidence from DHTs adequate to draw conclusions?

Verification and Validation

- **Verification** in the laboratory
 - How accurate and precise is the accelerometer in measuring acceleration?
 - Is it reliable in different environments (e.g., temperature, humidity)?
 - Does the algorithm used to interpret the raw signal reliably represent the clinical characteristic or event we are trying to capture (e.g. steps, breaths)?
- **Validation** in the field
 - Is the data recorded by the DHT the same as the data we would report if we were watching the patient (e.g., steps in a patient with Duchenne's or Parkinson's Disease)?
 - Is the result affected by how the patient wears or uses the DHT?
 - Are there things that a patient might do that would be misinterpreted by the DHT (e.g., riding a bike)?

Example: Duchenne's Muscular Dystrophy



- Standard Evaluation
– 6 minute walk test

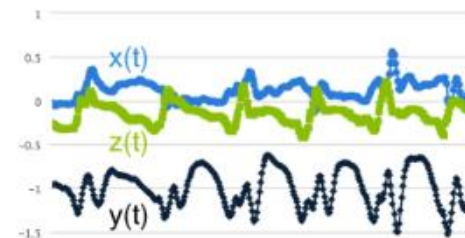


- Novel Evaluation
– Accelerometer



total acceleration
measured by the phone

$(x(t), y(t), z(t))$



Formulating the Endpoint

- The clinical characteristic(s) or event(s) being measured for each subject
- How the measurements are incorporated into the endpoint
- Whether the endpoint is a single clinical measurement (e.g., blood pressure or FEV1)
- Repeated clinical measurements (e.g., 24-hour ambulatory blood pressure monitoring)
- A combination of different clinical measurements at prespecified timepoints, (e.g., PRO plus actigraphy)

Formulating the Endpoint



- Time frame
- How the response outcome variable is reported for each subject (e.g., change from baseline, mean value, peak value, area under the curve, number of events, time to event)

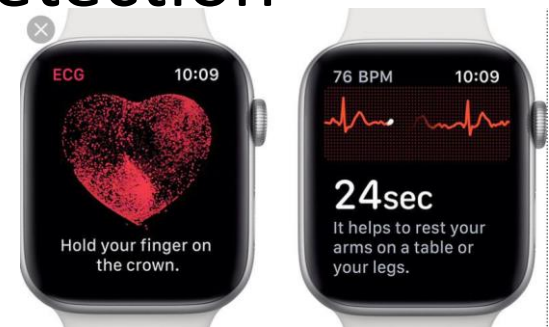
Examples of Endpoints using DHTs



- Clinical laboratory measurements
 - Continuous glucose monitoring, pulse oximetry
- Physiological measurements
 - Heart rate and rhythm, breathing and lung function, seizures, syncope, temperature, weight
- Performance assays
 - Stamina, strength, coordination, gait assessment, abnormal movements, sleep, cognition

Case Example 1

- Smart watch atrial fibrillation detection
 - Potential to detect AF in larger/healthier patient populations
 - Early detection has the potential to improve pharmacologic outcomes
 - Potential to determine if patients maintain sinus rhythm



Case Example 2



- Osteoarthritis and wearable sensors with an accelerometer, gyroscope and GPS
 - Track position, movement, acceleration, vital signs
 - Remote postoperative monitoring
 - Measure patient reported outcome measures
 - Facilitate gait and motion analysis
 - Real time feedback, improves patient engagement

Bini SA, Schilling PL, Patel SP, et al. Digital Orthopaedics: A Glimpse Into the Future in the Midst of a Pandemic. *J Arthroplasty*. 2020;35(7S):S68-S73.

Considerations for Conducting Clinical Trials using DHTs



- Disease area
- Study population
- Usability of the technology
- Study design
- Safety monitoring
- Support for technology and trial
- Training

DHT Conclusions

- COVID-19 has changed the way we will conduct all clinical trials
- DHTs allow us to collect many types of data remotely
- DHTs allow for broader participation and retention in clinical trials
- DHTs allow for more data collection
- Now is the time for innovating thinking, we cannot afford to miss this opportunity

Thank You!

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