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Digital Health Technologies (DHTs)

Focus on remote data collection in Clinical Trials

Fit-for-purpose: Intended Use

- Verification – evidence that the parameters the DHT measures are accurate. (i.e temperature, blood pressure, etc)
- Validation – confirming evidence that the device is assessing the clinical events/instances accurately (i.e step counts or heart rate)

Consider Clinical (i.e: Data output Accuracy) and Non-clinical risks (Cybersecurity and Patient Privacy)

3

Digital regulation requires a balanced approach between innovation flexibility and patient safety

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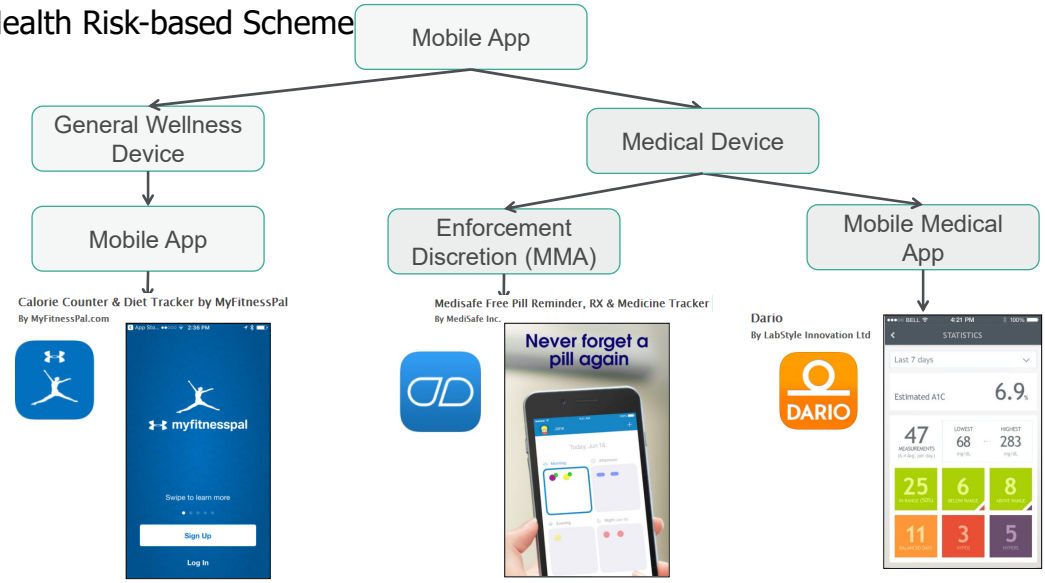
FDA Categorization of Mobile Medical Apps

Health Risk-based Scheme



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DHT Examples in the Pharma Industry

Immunlogy | Neurology | Rare Disease

Patient Support mobile application

- Self-configured medication reminders
- Access disease awareness content from SmartPatient
- Signup to access brand-indication material from Sponsor via QR code or package number

Lennox–Gastaut Syndrome(LGS) clinician questionnaire

- Developed using latest publication from the International League Against Epilepsy (ILAE).
- Medical education to support the identification of patients with LGS. [4 EU countries]

Digital Dose Calculator

- Calculate recommended doses for 3 stages of treatment titration
- Input patient body weight
- Input exposure to treatment, or not, with concomitant medications

Patient Support | **Clinical Decision Support (CDS)** | **Software as a Medical Device (SaMD)**

Increasing level of stringency to meet Regulatory compliance →

Software Development Lifecycle + **clinical report / referencing current best practice** + **Clinical Evaluation** + **Benefit/Risk activities**

ISO 13485 Medical Devices - Quality Management Systems
ISO 14971 Medical Devices – Application of Risk Management
IEC 62304 Medical device software – Software life cycle processes

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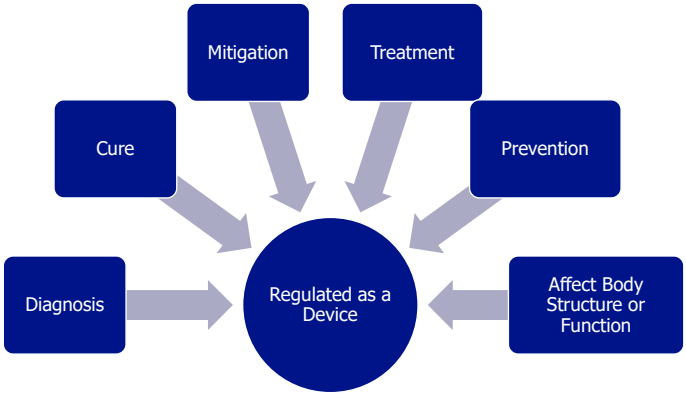
Intended Use determines if Software is a Medical Device

Classification is independent of Platform – website, tablet, mobile phone

- ***Intended Use*** *is shown through labeling claims, advertising materials, or oral and written statements made by manufacturers or their representatives*



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Understanding Intended Use and Context Use is critical.

Intended Use
The purpose for which the device was designed or intended by the manufacturer (

Context of Use
The actual conditions and environment that the device is being used in.

- **Both are crucial to ensuring the safe and effective use of the medical devices and technologies.**

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BA1

Risks of SaMD and ALL Digital Health Technologies (DHTs)

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Clinical Risks

Errors in patient clinical management due to use of unvalidated application

Risk of injury/death (e.g., incorrect dose)

Cybersecurity Risks

Impact on data privacy storage and transmission

Impact on SaMD functionality

Data Privacy

Loss of Patient Anonymity

Data Breaches

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Instant Blood Pressure App: AuraLife

The IBP App estimates blood pressure when the top edge of the smartphone is placed on the left side of the chest with the right index finger over the smart phone's camera

A Johns Hopkins University School of Medicine Study concluded that:

"the low sensitivity for hypertensive measurements means that approximately four-fifths (77.5%) of individuals with hypertensive BP levels will be falsely reassured that their BP is in the nonhypertensive range."

Plante TB et. al, JAMA Internal Medicine 2016 176(5) p 701

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Slide 9

BA0 Update image from myUCB
Boutrin Anmarie, 2024-02-12T21:37:57.763

BA1 Update graphic.
Boutrin Anmarie, 2024-02-13T19:34:35.402

Instant Blood Pressure App: AuraLife

FTC Action: Barred from Making Claims

AuraLife has "represented, directly or indirectly, expressly or by implication, that the Instant Blood Pressure App:

A. Serves as a replacement for a traditional blood pressure cuff; and

B. Measures blood pressure as accurately as a traditional blood pressure cuff."

Case No. 8:16-cv-2147, US District Court for the Central District of California

"For someone with high blood pressure who relies on accurate readings, this deception can actually be hazardous," said Jessica Rich, director of the FTC's Bureau of Consumer Protection. "While the Commission encourages the development of new technologies, health-related claims should not go beyond the scientific evidence available to support them."

https://www.ftc.gov/news-events/press-releases/2016/12/marketers-blood-pressure-app-settle-ftc-charges-regarding

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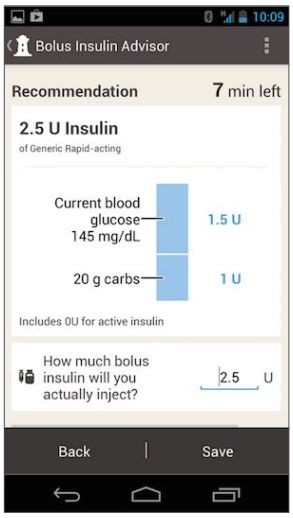
FDA Recall: Roche's Accu-Chek Diabetes Management App

- **FDA Medical Device Recall:** Class II on Feb 15, 2018
- **Mobile Medical App:** Affects iOS and Android Operating Systems (OS)
- **Issue:** Changing OS region may cause unit of measure to change unexpectedly
- **Increases Risk:** MMA might not transfer the blood glucose result or the user might not correctly input numerical values for carbohydrate used for bolus advice

http://www.mobihealthnews.com/content/roche%E2%80%99s-accu-chek-diabetes-management-app-receives-its-fifth-fda-recall



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MyFitnessPal App: Under Armour

Data Breach

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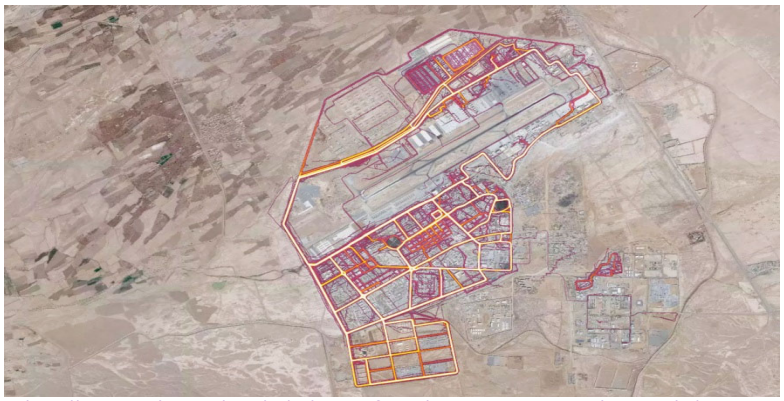
Patient Privacy Considerations: GPS Location

GPS Mobile App functionality could cause a privacy breach.

Strava Fitness App Metadata reveals information about military installations.



https://www.engadget.com/2018/02/02/strava-s-fitness-heatmaps-are-a-potential-catastrophe/

Strava heatmap of an area in Kandahar, Afghanistan

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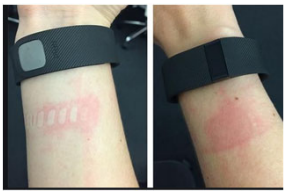
Wearable Sensor Risks

Wearable Sensors are used in UCB clinical trials often to monitor patient symptomology.

Sensors pose additional risks to patient safety.



- **Product Hardware Risks**
- Material Discomfort and Biocompatibility
- Material Allergies (Nickel)
- Injury resulting from breakage of device

- Electrical Safety
- Battery Safety-i.e., risk of overheating
- Electromagnetic interference-i.e., pacemakers

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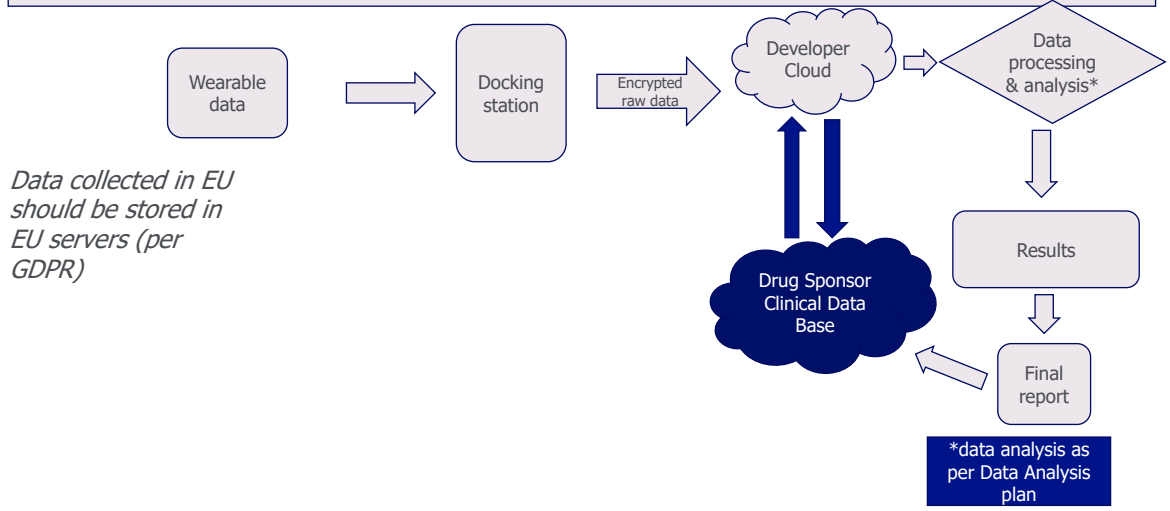
Sensor Data Flow



Data collected in EU should be stored in EU servers (per GDPR)

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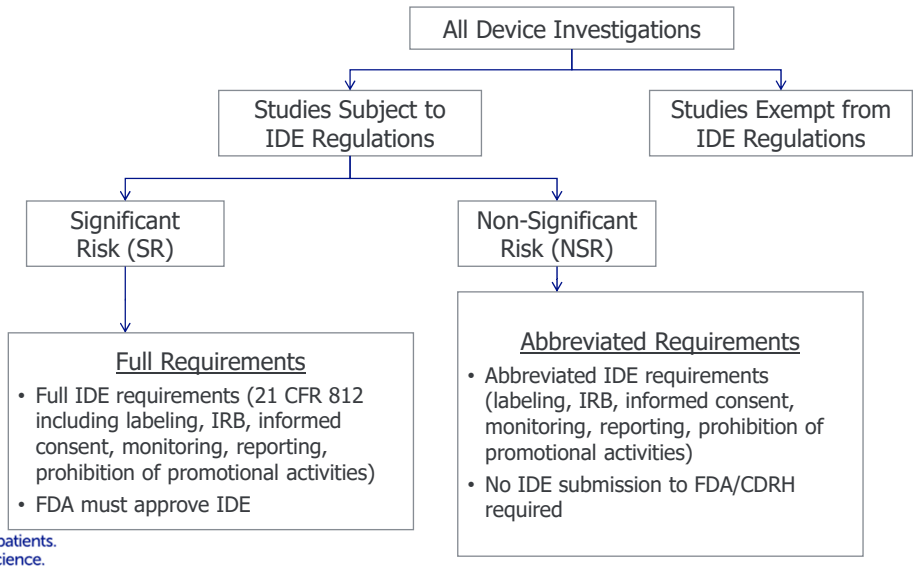
Investigational Mobile Medical Apps/Sensors

Investigational Device Exemption (IDE) Submission Requirements



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Risk Mitigation of DHTs in Clinical Trials

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- **DHTs for clinical trial use that fall outside of medical device regulations are subject to a risk-based approach in which the study sponsor considers and mitigates risks to the patient**
  - Performed on a Case by Case Basis
- **This risk mitigation information is often submitted to IRBs/ethics committees in support of clinical trial applications using DHTs.**
- **If the use of the DHT could present a significant health risk to study subjects, an investigational device exemption (IDE) submission to the FDA may also be required**

RE: 2023-Patient-Technology-Regulatory-Landscape-Tool_4.21.23.pdf (transceleratebiopharmainc.com)

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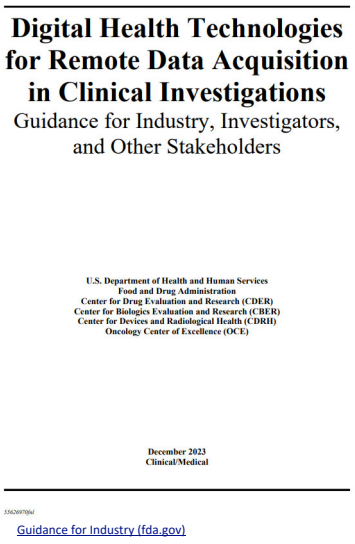
Purpose of FDA DHT Guidance:

- Aims to foster innovation, improve regulatory compliance, and enhance the conduct of clinical research through the responsible use of digital health technologies.



Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Guidance for Industry, Investigators, and Other Stakeholders

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 2023
Clinical/Medical

Guidance for Industry (fda.gov)

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Key Regulatory Considerations

Navigating and Executing on the Guidance

- ❑**Informed consent** (*Describe risks, data protection*)
- ❑**Training** *(Trial Personnel and Patients)*
- ❑**Technical assistance** *(Access to assistance)*
- ❑**Device error, loss or damage** *(Corrective action plan)*
- ❑**Safety monitoring** *(plan,abbnormal measurements)*
- ❑**Data management** *(Data repository)*
- ❑**DHT updates** *(system lock for trial duration)*
- ❑**Adherence monitoring and alerts** *(long term)*

RE:AG_WhitePapers_DHTGuidance.pdf (hubspotusercontent-na1.net)

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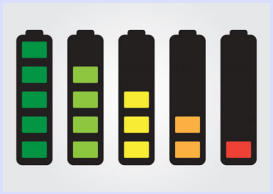
Design and ease of use

Are trial participants able and willing to use the DHT for the duration specified by the protocol???

Data Storage & Transfer

Is the DHT capable of transferring the amount of data collected for later use and retention, with minimal burden on the participants???

DHT Alerts



Does the DHT have the right user interface to alert the users about low battery or technical issues to prevent data loss???

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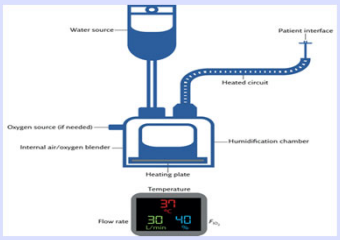
Data Privacy & Security

Can the DHT prevent unauthorized access and ensure the privacy and security of the data it collected???

Clinical Risk



Can the DHT manufacturer provide evidence from safety testing that the DHT is safe for use by trial participants

Software Updates

Is there a risk that software updates might impact data collection???

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Key Considerations - Clinical Meaningfulness

Early evaluation is key…

- Real world importance for patients
- Understanding patient view of symptoms
- Understanding the impact on quality of life

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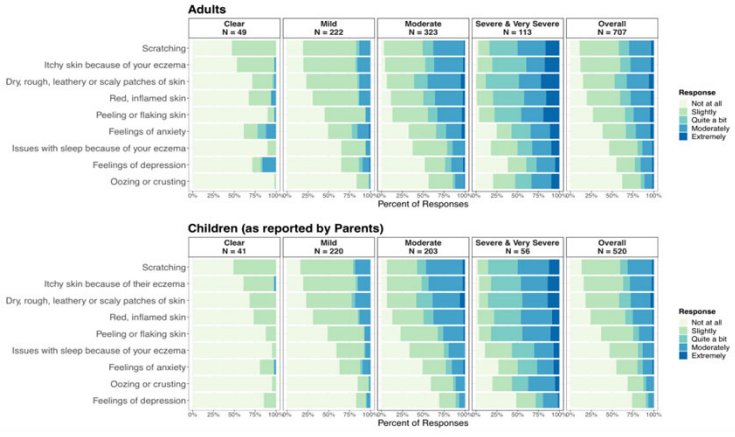
NCA0

3.3. Applicant Response:

- **Nocturnal Scratch is a key symptom in AD that not only impacts the disease, but the persons and caregivers QoL.**

"During the past two weeks, how burdensome did you/your child find the following?"

- Response to the Phase 2 Survey Question asking, "During the past two weeks, how burdensome did you find (Adults)/ what is your impression of how burdensome your child found (Parents on behalf of children) the following?" The results are shown per severity of AD (based on POEM score) and overall. Responses are ordered separately for Adults and Children by percentage of participants overall. Data re displayed for 707 (Adults)/ 520 (Parents on behalf of Children) participants who correctly identified itch as a sensation in the test question).



Digital Measures: Nocturnal Scratch – Digital Medicine Society (DiMe) (dimesociety.org)

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Slide 24

NCA0 Data is in the stack

Northcott, Carrie Annalice, 2024-01-09T20:54:58.252

Digital Technology Use Scenarios

Exploratory Endpoint for Clinical Trial	Primary/Secondary Endpoint for Clinical Trial	Commercial use Medical or Consumer Device
CE mark as telecommunications device (Radio Equipment Directive/FCC) demonstrates electrical safety	Same as exploratory use criteria AND	Same as Primary/2ndary Endpoint for Clinical Trial use AND
Cybersecurity certification	Comparison to Gold standard of measurement and clinical meaningfulness (patient input)	For Medical Device: CE Mark or 510K clearance/DeNovo authorization
Data Privacy	AND	AND
Fit for purpose clinical testing of software and sensor in a **healthy volunteer** population	Fit for purpose clinical testing of software and sensor in a **clinical intent to treat** population	For Medical Device: Clinical Evaluation Plan and Reporting And Post Market Surveillance Plan and Reporting
Review Complaints and Safety events in prior Clinical Trials		

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Key Considerations-Stakeholders

Responsibilities:

- The sponsor is ultimately responsible for the patient safety of DHT use in a clinical trial
- Contracts with QA and Safety Agreements should be customized based on the context of use
- Fit for purpose validation and DHT risk migration is a **collaborative effort**
- For example, evidence from safety testing conducted by the DHT manufacturer (i.e. biocompability of wearable materials) may be helpful to show that risks associated with use of a DHT by trial participants are mitigated

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Key Takeaways

- The aim of the FDA DHT Guidance is to ensure patient safety during remote data collection
- Understanding the Intended and Context Use case is a critical prerequisite for the DHT regulatory assessment
- DHTs should be fit for purpose -The required level of prior testing is greater for a primary/secondary endpoint compared to an exploratory endpoint

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Key Takeaways…..cont

- Risk mitigation of clinical, cybersecurity and privacy risks are required to ensure patient safety within the individual clinical trial the DHT is deployed in……

Trust But Verify – to avoid undesired outcomes!!!

- Effective collaboration between the DHT Developer and Drug Trial Sponsor is critical to ensure project success

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Thank you. Any Questions?
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