

Recommendations for
**subject privacy
assurance, data
collection, & study
monitoring**

in clinical studies
utilizing digital
measurement of
nocturnal scratch

NOCTURNAL SCRATCH



Digital Measures Development

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A project by the





Subject privacy protection considerations for studies utilizing digitally measured nocturnal scratch

Always collect the minimum data necessary for the purpose of the study

Monitor for breach

- Ensure data is secure at rest and transit
- Make sure monitoring practices for breach are in place during data acquisition, transfer, and storage (monitoring practices shall be implemented at the technology vendor side)

Learn about regional regulations

- Different jurisdictions may have local requirements - work on the strictest requirement first
- For example, DCTs regulation differ in respective EU countries, but GDPR regulation is unified across all of them (refer to this [IMI resource](#) for a comprehensive overview)

For more information, refer to the **additional resources:**



- FDA Guidance: [Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects](#)
- CIOMS: [Ethical framework for biomedical research](#)
- [21 CFR Part 11](#)
- EMA: [Guideline on computerised systems and electronic data in clinical trials](#)
- [GCP Guideline E6\(R2\)](#)
- IMI: [Mapping and analysis of the EU legislation on Remote Decentralised Clinical Trials including legal, regulatory, ethical and stakeholder recommendations for the conduct of the pan-EU pilot](#)



Tips for **interactions with IRB** for studies utilizing digitally measured nocturnal scratch

Describe value of the digital measurement

For additional information about the value of digital measurement of nocturnal scratch, refer to toolkit document: Case study: Defining value and identifying benefits of integrating digital measurement of nocturnal scratch to clinical studies

Disclose everything that happens with patient data in informed consent form (ICF):

- **What** are the collected data & data types
- **Why** are these data collected - what happens with each of data type (at the point of acquisition, storage, processing, analysis)
- **Who** and what entities have access to the data and for what purpose
- **How** will each of these data types be used

Some tips & tricks for your ICF:

- Don't use contract language in ICF - ICF is not EULA, it is a disclosure document. Use informative and simple language.
- When you say the data will be de-identified or anonymized - describe how.
- Disclose if patients' participation will give them access to information, what that information would be, and what they can do with this information.
- Disclose who to contact with specific types of issues: Is there one point of contact, or multiple for multiple purposes?
- Disclose potential medical risks connected to the DHT which are of relevance in atopic dermatitis, such as skin irritation, use with moisturizers, etc. - and who the patients should contact if they encounter these issues.



Tips for **interactions with IRB** for studies utilizing digitally measured nocturnal scratch

Describe how and where digital measurement of nocturnal scratching has been previously used in research studies.

Find some examples in the following publication:

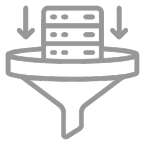
[Use of technology for the objective evaluation of scratching behavior: A systematic review](#)

- **20 examples** of studies exploring wrist actigraphy and smartwatch applications measuring scratching behavior (both adult and children patients)
- **12 examples** of studies exploring acoustic, vibratory, pressure, and strain gauge devices measuring scratching behavior (both adult and children patients)

To address information risks and IRB strategies for technologies used in research, refer to this guidance for in depth information:



- *Harvard Clinical and Translational Science Center: [Information Risks & IRB Strategies for Technologies Used in Research: A Guide for Researchers, IT, and IRBs](#)*



Data collection considerations for studies utilizing digitally measured nocturnal scratch

Ensure 21 CFR Part 11 compliance of your technology vendor

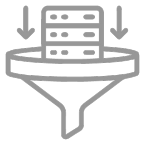
All collected data should be valid, traceable and auditable

- Describe entire data flow from sensor all the way through to the analysis dataset
- Example of nocturnal scratch: Describe how the data is transferred from acceleration -> scratch -> scratch event -> clinical endpoint supporting efficacy of the drug
- Include this description in CSR as well
- How is source data defined? Source data can be:
 - Raw data (e.g. accelerometer readouts) or aggregates (already pre-processed data). **Both may be acceptable;** however, the technology manufacturer should define and describe what constitutes the source data & how it was generated and verified

Know where your data are flowing

- Always perform regional data mapping - sometimes data may fly between multiple regions
- Make sure to know which regions your technology vendors are transferring the data through, and in which regions they are storing it (this information is usually provided by cloud services' vendors, or directly from technology vendors if they are using their own data centers)





Data collection considerations for studies utilizing digitally measured nocturnal scratch

If possible, perform pre-processing, processing, or even analysis to extract events on a device or as close to the patient as possible to minimize breach or issue risk if transferring large data files

- For example, calculating scratch events in the device before transfer is less risky than transferring raw accelerometer data to the cloud for processing & analysis. Raw data can be extracted from the devices after the end of the study.

If using consumer technology, devices, or applications for data collection in the trial setting, additionally consider.

- What extra information is collected
- If sharing or social sharing is allowed and under what conditions
- Whether and which third parties have access to the data, thus creating risk of breach

For more information, refer to the **additional resources**:



- The Playbook: [Optimizing data management](#)
- CTTI: [Managing data](#) in digital health trials
- CTTI: [Selecting Mobile Technologies for Data Capture in Clinical Trials](#) (Page 7: Data Collection, Analysis, and Interpretation)
- CTTI: [Selecting Mobile Technologies for Data Capture in Clinical Trials](#) (Page 13: Data Management)



Study monitoring considerations for studies utilizing digitally measured nocturnal scratch

It is important to establish responsibilities for study data monitoring

- What aspects are required to be monitored by the technology vendor?
- What aspects are required to be monitored by a site or investigator?
- What aspects are required to be communicated back to the sponsor?

Pro Tip! According to FDA Guidance: [Digital Health Technologies for Remote Data Acquisition in Clinical Investigations](#), statistical analysis plans should prespecify **intercurrent events** that may be related to the DHTs, and how these events will be accounted for in the analyses to address the scientific questions of interest. In a clinical investigation using DHTs, **missing or erroneous data** may occur as a result of intercurrent events, such as:

- Software updates that change how the data are collected or that change the algorithms used to process data
- Software incompatibility caused by operating system upgrades
- Trial participant error or non-compliance with study procedures using the DHT or general-purpose computing platform
- DHT or general-purpose computing platform failure
- Data transmission failure



Study monitoring considerations for studies utilizing digitally measured nocturnal scratch

Monitor for:

Technology aspects

Human aspects

Medical aspects

Describe technological aspects (**functionality, stability, fidelity, quality, connectivity, data, security, etc.**) that need to be monitored and evaluated

- Additional metadata monitoring sensor and device performance are useful & provide context (e.g. monitoring connection stability, devices' battery, user's interactions with the device)

Great resource for more in depth knowledge: WHO: [Monitoring and Evaluating Digital Health Interventions](#), Chapter 3.



Example aspects to monitor for:

- Full platform monitoring for outages & breaches - each step of data acquisition, storage, processing, and transfer
- Device hardware malfunction or outage
- Software or operating system updates
- Measured data not saved correctly (corrupt files, full hard drive, etc.)
- Loss of connection (Wi-Fi, cellular, connection to server, etc.)
- Monitoring for missing data and data quality
- Etc.



Study monitoring considerations for studies utilizing digitally measured nocturnal scratch

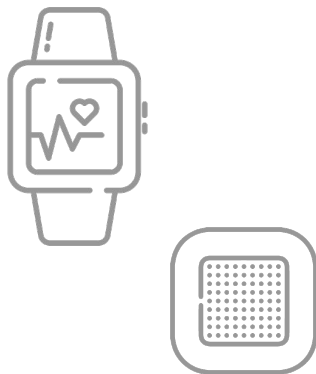
Monitor for:

Technology aspects

Human aspects

Medical aspects

Describe user-specific aspects (**wear time, compliance, proper use, etc.**) of nocturnal scratch measure that need to be monitored and evaluated



Example aspects to monitor for:

- Participant not using the device at all
- Participant using the device incorrectly
- Participant tampering with the device's setup
- User other than participant using the device
- Etc.



Study monitoring considerations for studies utilizing digitally measured nocturnal scratch

Monitor for:

Technology aspects

Human aspects

Medical aspects

Have a policy or process for handling incidental events that require medical attention.

- According to ICH E6 & FDA guidance, investigator institution should inform the patient if medical care is needed for intercurrent illnesses



Specifically in the AD population, monitor for:

- Skin irritation
- Erroneous use due to used materials on the technology
- Erroneous use due to use of creams and lotions by the participants
- Erroneous use due to using over/under clothing or wraps

Is it better to monitor data in **real-time** or **during study visits**?

Real-time monitoring



Pros

- + Detecting issues much sooner and resolving them to continue intended study progress & data acquisition, lowering risk of study failure
- + Standardized approach to monitoring selected aspects of technology performance and use

Cons

- Additional overhead on sites, investigators, or sponsors
- Increased costs associated with development of monitoring and dashboard overview solutions from technology vendors

Study visit monitoring



Pros

- + Less overhead on sites, investigators, or sponsors
- + Human approach to resolving issues patients may have with the technology

Cons

- Detecting issues with technology or use too late, or not at all
- Non-standardized approach to monitoring for issues (depending on the personnel providing the monitoring at the site)



Additional Relevant Resources

- The Playbook: [Post-go live study operations](#)
- The Playbook: [Optimizing data management](#)
- WHO: [Monitoring and Evaluating Digital Health Interventions](#), Chapter 3.
- FDA [Guidance: Oversight of Clinical Investigations - A Risk-Based Approach to Monitoring](#)
- FDA Guidance: [Digital Health Technologies for Remote Data Acquisition in Clinical Investigations](#)
- FDA Guidance: [Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects](#)
- Harvard Clinical and Translational Science Center: [Information Risks & IRB Strategies for Technologies Used in Research: A Guide for Researchers, IT, and IRBs](#)
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- [GCP Guideline E6\(R2\)](#)
- [GDPR Regulation](#)
- [EU-U.S. and Swiss-U.S. Privacy Shield Frameworks: 14. Pharmaceutical and Medical Products](#)

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