Digital measures of nocturnal scratch

Janssen Case Study

Cathelijne de Gram, PharmD
EMEA Regulatory Policy Lead
Global Regulatory Policy & Intelligence
Janssen – pharmaceutical companies of Johnson&Johnson

17 April 2023

DISCLAIMER

The opinions expressed are my own and not necessarily the opinions of Janssen, the Pharmaceutical Companies of Johnson and Johnson, or any other organization or individual.

Nocturnal Scratch As a Novel Digital Measure in Atopic Dermatitis

Janssen case study

Aim: Development of a novel clinical endpoint using a DHT (wearable/sensor) to be used in drug clinical development programs with the ultimate aim to include this **clinical endpoint in the labeling of a drug** to communicate the impact on the quality of life of patients with AD

Background

- High prevalence in atopic dermatitis (AD)
- Meaningful to patients
- Exacerbated at night => skin damage and sleep disruption
- Objectively measure scratch frequency and intensity
- No validated instruments to measure scratch

janssen | Pharmaceutical Companies of Johnson & Johnson

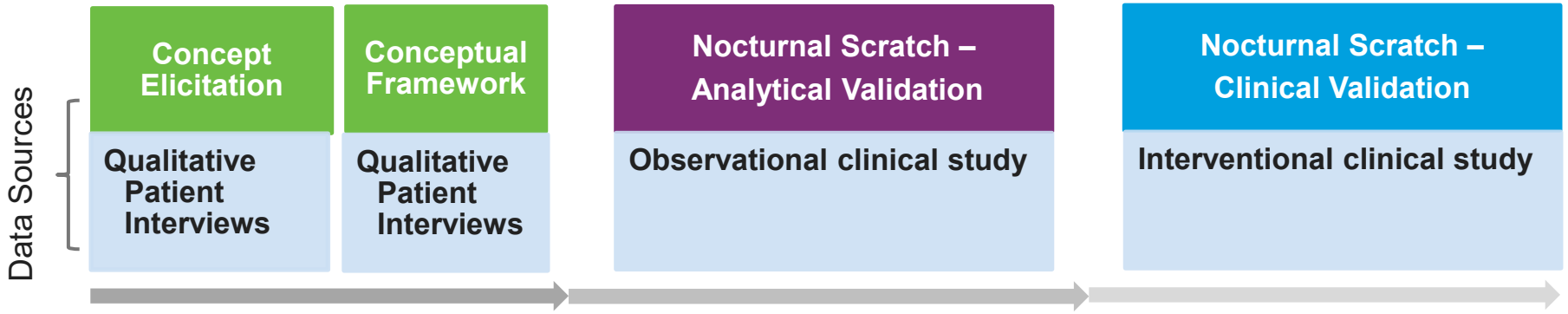
DHT = digital health technology; AD = atopic dermatitis

Development and Validation Framework

Janssen - Nocturnal Scratch as Digital Measure in Atopic Dermatitis

Comprehensive development and validation plan was created consisting of:

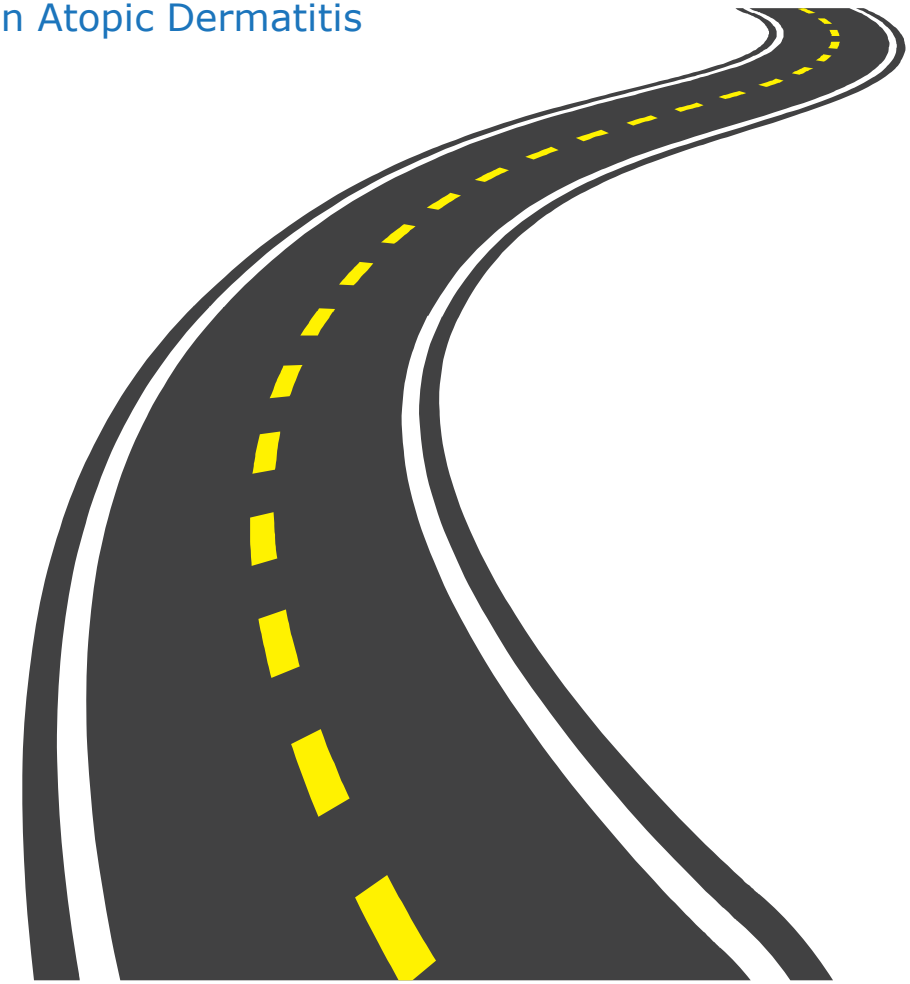
- completed work,
- ongoing study, and
- planned studies



Digital Measure Development Challenge

Janssen - Nocturnal Scratch as Digital Measure in Atopic Dermatitis

- Limited precedence
- No roadmaps available for regulatory acceptance
- Limited health authority guidance for validation



Solution

Engage global Health Authorities (FDA/EMA) to define development strategy to increase success of robust digital measure acceptable for regulatory decision making

Success = nocturnal scratch in product labeling & improve patients' lives

Preparation EU Health Authority Engagement

Janssen - Nocturnal Scratch as Digital Measure in Atopic Dermatitis

Selection of Regulatory Pathway

- Janssen considered both Scientific advice and QoNM as possible **regulatory engagement options** in the EU
  - Decided on QoNM option as this pathway is specific for novel methodologies
- Advantage of **dedicated regulatory pathway** – focused discussion on novel digital measure
  - Complex regulatory framework as it contains both COA and digital component

Timing of Regulatory Interactions

- **Early engagement** is relevant for timely input in digital measure development plans
  - Janssen engaged prior to start of Analytical Validation
  - Planning for multiple rounds of engagement
- Digital Measure development program needs to be in line with drug development program to ensure inclusion in MAA

Recommendations to enhance regulatory pathway

- Emphasize **purpose** (value) of qualifying a method
- Clarify the optimal regulatory **pathway**
- Clarify **scope** of EMA QoNM advice
- Clarify optimal **timing**
- Support integration of novel method in drug development and MAA

QoNM = qualification of novel methodologies; COA = Clinical Outcome Assessment; MAA = marketing authorization application

Guidances and Frameworks Related to Development of Digital Measures

Janssen - Nocturnal Scratch as Digital Measure in Atopic Dermatitis

EMA Guidance

FDA Guidance

Other frameworks

Recommendations to enhance regulatory pathway

- Provide more detailed QoNM briefing book template
- Share lessons learned
- Optimize visibility of LoS and QO
- Provide further clarification on expectations

EU guidance could provide more details on agency expectations, e.g.:

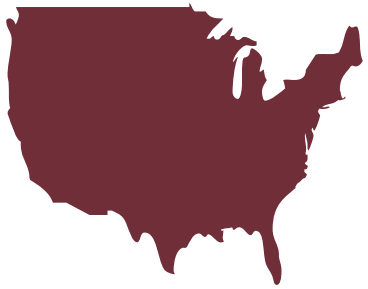
- Considerations for different types of tools (wearables, AI/ML, etc)
- Patient acceptance / usage and device clinical utility
- Requirements for analytical and clinical validation, e.g. need for interventional study for clinical validation

QoNM = qualification of novel methodologies; LoS = Letter of support; QO = Qualification Opinion; AI/ML = artificial intelligence/machine learning

Reference: https://pubmed.ncbi.nlm.nih.gov/32087341/

Health Authority Engagements

Janssen - Nocturnal Scratch as Digital Measure in Atopic Dermatitis



FDA - 2021

EMA - 2022

Health authority feedback was overall positive and resulted in important changes strengthening our validation strategy.

Key Discussion Questions	
1	**Nocturnal Scratch -** *Clinically relevant and meaningful in AD?*
2	**DHT Suitability -** *Suitable for measuring nocturnal scratch in AD?*
3	**Validation Framework** - *Proposed studies/analyses adequate for validating DHTs and a scratch endpoint?*
4	DHT **–** investigational **medical device** / CE marking yes/no
5	**Lifecycle management**

DHT = digital health technology; AD = atopic dermatitis

Qualification Advice – Overall Experience

Janssen - Nocturnal Scratch as Digital Measure in Atopic Dermatitis

Experience

Comprehensive plan was key to success

Thoughtful agency feedback on operational and developmental aspects of digital measure

Meeting was useful considering the novelty of development of digital measures

Additional time granted to respond to questions was considered helpful

Feedback

Agreement on Concept of Interest

Alignment on proposed analysis to support analytical and clinical validation

Substantive statistical feedback

Definition of investigational medical device outside remit of EMA

Next Steps

Follow-up Qualification Procedure when additional data becomes available

Need for separate health authority interactions to clarify application of device regulations to DHT

Recommendations to enhance regulatory pathway

Clarify what falls under EMA remit

Increase efficiency by setting up coordinated multistakeholder advice

Develop guidance on lifecycle management

Flexible Follow Up procedure

DHT = digital health technology

Conclusion

Janssen - Nocturnal Scratch as Digital Measure in Atopic Dermatitis

- ✓ Very positive experience
- ✓ Comprehensive submission package contributed to relevant agency input
- ✓ EMA feedback was of high quality and very useful
- ✓ Flexibility during procedure

Key recommendations

- Clarify and emphasize early engagement
- Clarify EMA remit
- Emphasize purpose/value of QoNM
- Issue more guidance relevant to novel methods
- Coordinated multistakeholder engagement
- Lifecycle management
- Increase visibility of qualification outcomes

QoNM = qualification of novel methodologies


janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson