

# Regulatory perspective on qualification of methodologies based on Digital Health Technologies and Artificial Intelligence/Machine Learning

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EMA workshop on qualification of novel methodologies



# Topics

1. Intention of presentation
2. EMA remit in qualifications for DHT/AI Validation Strategy
3. Clinical validation and technical validation
4. Digital Health Technology aspects
5. Artificial Intelligence/Machine Learning aspects
6. Lifecycle management

# 1. Intention



# Intention

## **Provide (selected) observations from recent qualification procedures**

- Highlighting topics
- Not intended to be comprehensive

## **Provide preliminary proposals**

- Not necessarily final
- Should enable discussion

## **Focus on**

- Digital Health Technology
- Artificial Intelligence/Machine Learning tools

## 2. Observations and preliminary proposals



# EMA remit in qualifications for DHT/AI

## Focus of qualification procedures

- Context of Use should be relevant for medicinal product lifecycle
  - Development in Phase 1, 2, 3
  - Evaluation at MAA
  - Monitoring after approval
- Digital endpoint examples
  - Digital biomarker
  - Electronic Clinical Outcome Assessment
  - Digital (objective) measures...

## Focus on components in EMA remit

- Separate technical validation from clinical validation
- Context of Use should focus on specific application

## EMA/SAWP intends to broaden expert range in assessment

- Clinical experts, patients, methodologists, Real World Data experts, GCP experts, Notified Bodies, HTA bodies...

# EMA remit in qualifications for DHT/AI

**Please see also**



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

1 June 2020  
EMA/219860/2020  
Human Medicines Division

Questions and answers: Qualification of digital  
technology-based methodologies to support approval of  
medicinal products

Status as of June 2020

# Clinical validation and technical validation

## Technical validation

- Not all parts may be in EMA remit
- Provide high level information on CE marked medical devices
  - Usually performance data are needed
- Check if CE mark and intended use covers application

## Clinical validation

- Separate clinical validation from technical validation
  - Separate questions to EMA
  - Structure discussion by technical/clinical aspects

## Context of Use should focus on specific application

- Usually performance data in target population are needed
  - Performance in patients could differ from healthy volunteers



# Digital Health Technology aspects

## Clinical performance evaluation

- Relate performance evaluation to (specific) Context of Use and application
  - Testing in clinical trial setting may be needed
  - Will depend on importance/risks (primary endpoint vs. exploratory endpoint)
- Tailor performance metrics and variables to Context of Use
- Consider if reference standard is available

## Considerations on devices

- Ideally application of DHT should be device agnostic
- Consider defining minimum requirements for technical performance
- Publication of minimum requirements not sufficiently addressed so far
- Use of layer model may be helpful (raw data → processing → derived device data → clinical endpoint data)

## Performance of devices or software that do not require a CE mark

- Define criteria to ensure performance
- Define limits for performance criteria

# Artificial Intelligence/Machine Learning aspects

## Clinical performance evaluation

- Consider secular trends for performance evaluation
- Interpretability and explainability may be paramount in regulatory use
- Envisage prospective validation for AI tools
  - Usually required
- Consider pre-qualification collaboration
  - Generalisability of single Sponsor developments may be questioned

## Model deployment

- Cover model deployment in plan
- Consider performance checks
  - Before and after application
- Cover model degradation
  - Technical aspects evolve quickly

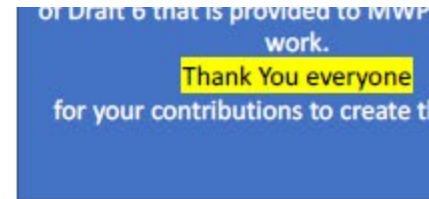
# Artificial Intelligence/Machine Learning aspects

Draft reflection paper is coming soon



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N.B. TITLE PAGE to be DETERMINED.  
This follows now the general structure of EMA Scientific Committees' reflection papers



- 1 [DATE]
- 2 EMA/83833/2023 – draft 6
- 3 <TBD/TBC (CHMP/CVMP)>

- 4 Reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle
- 5
- 6 Draft<sup>1</sup>

# Lifecycle management

## **Lifecycle management of the DHT / AI model**

- Consider quality control process
- Consider performance checks
- Consider how variations or updates of the technology could be addressed
- Consider online material
  - Static landing page
  - Repository

## **Lifecycle management of the Qualification Opinion**

- Qualification opinion can likely cover only a specific version/timepoint/stage
- Currently not sufficiently addressed

# Thank you very much for your attention!



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