Federal Institute
for Drugs
and Medical Devices

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

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

4 Reflection paper on the use of Artificial Intelligence (AI) in
5 the medicinal product lifecycle
6 Draft[1]

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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!

Contact

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