EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA multistakeholder workshop on Qualification of Novel Methodologies (QoNM) – Outcome report and Recommendations

R&D industry platform meeting, 4 December 2023

Iordanis Gravanis and Thorsten Vetter, Scientific Advice Office, EMA

Reminder: Sessions at the Workshop on 17-18 April 2023

Session 1: From innovation to qualified tools – the scope of qualification of novel methodologies

Chairs: Marjon Pasmooij (CBG-MEB) and Falk Ehmann (EMA)

Session 2: Patient-, Observer- and Clinician-reported outcomes (PROs, ObsROs, ClinROs) – key elements of patient centred medicines development

Chairs: Elmer Schabel (BfArM) and Andreas Kirisits (AGES)

Session 3: Methods based on Modelling and Simulation, Digital Health Technologies and Artificial Intelligence/Machine Learning (AI/ML)

Chair: Joerg Zinserling (BfArM) and Thorsten Vetter (EMA)

Session 4: Real World Evidence – Qualification of data sources

Chairs: Peter Mol (CBG-MEB) and Juan Jose Abellan Andres (EMA)

Session 5: Using "Qualification" going forward – ways to optimise the platform

Chairs: Paolo Foggi (AIFA), Pierre Demolis (AFSSaPS/ANSM) and Iordanis Gravanis (EMA)

Outcome report headlines

Session 1: From innovation to qualified tools – the scope of qualification of novel methodologies

- Regulatory interactions should be planned up-front and start early
  - Introduction of early interaction possibility and of scoping meetings
- Guidance revision should clarify scope on QoNM, importance of CoU and corresponding evidentiary requirements
- Importance of pre-competitive collaboration
  - Mandatory publication of high-level qualification advice information
  - Regulatory direction towards areas of unmet methodology needs
  - Monitoring of uptake and impact can inform whether needs are being met

Outcome report headlines

Session 2: PRO, ObsRO, ClinRO – key elements of patient centred medicines development

- Need to improve awareness of and familiarity with regulatory qualification for stakeholders and particularly patient organisations and professional/learned societies
- Involvement of patients in PRO development from its inception is pivotal
- Parallel qualification interactions with HTA bodies would be valuable given the importance of patient experience data in HTA assessments
- Public repositories of PRO/COA tools (qualified and not) and development by consortia could improve pre-competitive collaboration

Outcome report headlines

Session 3: Methods based on Modelling and Simulation, Digital Health Technologies and AI/ML

- Qualification is highly recommended for M&S methods including iterative interactions and submission of code and raw data
- DHT can offer more objective and patient-relevant measures of treatment benefit but sit at the intersection of different regulatory frameworks and require multi-decision-maker involvement; qualified methods should remain device-agnostic
- Collaboration during development and assessment as well as lifecycle management becomes critical
  - To allow extensions of context of use
  - (esp. for AI/ML-based methods) to define changes to be handled by Qual. mgmt. system

Outcome report headlines

Session 4: RWE – Qualification of data sources

- Clear definition of CoU (towards definition of essential data elements) and consideration of data quality frameworks are important reference points for qualification of registries and data sources
- Evolution of registries over time creates the need for lifecycle management to maintain or reconfirm registry validity
  - Would be facilitated by trialogues between registry holder, medicine developers performing studies based on registry data and regulators

Recommendations from workshop

- Recommendations to be presented in the following categories:
  - For direct implementation (information only)
  - For implementation after further development
  - For future consideration in collaboration with others (non-EMA/network stakeholders)

For implementation

EUROPEAN MEDICINES AGENCY

Guidance update

- One overarching guidance (procedural and general evidence considerations) to **clarify value, purpose** (for the common good) **and scope of QoNM** (e.g., QoNM is no substitute for MD/IVD conformity assessment as QoNM should be device/software agnostic and method publicly available and reproducible) and the role of **Context of Use**
- Additional modules/Q&As to be added later for specific methods (e.g. COAs; DHT/AI; RWE; data sources/registries; M&S, Statistical?)
- **Update and standardise templates** for Briefing Document, Qualification Advice Letter and Qualification Opinion

Define needs/criteria for life-cycle management of QO (for data sources, registries, DHT, AI/ML related methods, i.e., methods for which conditions and/or technologies change over time or if not used for evidence generation over a period)

- **re-validation or QO update**, if changes impact significantly on risks, functionality or performance specifications
- if impact is minor, changes may be managed by a **Quality Management System (QMS)**

For implementation

EUROPEAN MEDICINES AGENCY

Enhance early interactions - Create an early qualification support mini-team

- Cross-functional group reachable via dedicated mailbox
- Tasks
  - Identifying developments out of scope or immature for formal regulatory procedures
  - Helping improve briefing documents (e.g., develop checklists facilitating description of data quality in line with relevant data quality frameworks)
  - Offering early scoping meetings
  - Identifying necessary additional expertise
  - Clarifications/prep for updates following initial QO

Improve webpage presentation of procedural guidance, Qualification Opinions and Letters of Support to improve visibility, accessibility and uptake

For implementation after further development

EUROPEAN MEDICINES AGENCY

- **In relation to RWE data source qualification**
  - What is the optimal forum/process for data source qualification beyond registries?
  - Offer post-qualification triangular interactions involving all stakeholders (registry holder, MAH, EMA) as part of life cycle management
- **(Mandatory) Publication of high-level Qualification Advice information**: value for scientific community, foster collaboration and avoid duplication of efforts
- **Dynamic presentation of information on webpage (e.g., versioning)** to reflect how tools evolve transparently and record life cycle management
- **Procedural aspects**
  - Maintain formal assessment procedure timelines as well as flexibilities (e.g., clock-stops, additional time for initial assessment or QO prep and publication) around it
  - Should qualifications be free-of-charge for applicants (coordinators to continue getting paid) coupled with a strict initial triaging process?

For consideration in collaboration with others

EUROPEAN MEDICINES AGENCY

- **Training with public-private partnerships** (e.g., IHI, C-Path), **for patient representatives** (e.g., with EURORDIS patient training / PCWP / PED initiative)
- **Publishing specific unmet needs** for novel methodologies as identified by Committees or Working Parties by linking to **Regulatory Research Science Needs**
- **Workshops on emerging or complex technologies in the regulatory context** (e.g., AI-workshop, RNA workshop, etc.)
- **Workshops and/or Q&As on high-impact Qualification Opinions** to facilitate understanding by stakeholders, build trust and clarify the Qualification process
- Establish **active interaction with professional societies developing COAs**
- **Scientific publications on Qualification Opinions and Advice** – also in collaboration with consortia
- **Monitoring and reporting of evidence from qualified tools considered in regulatory decision making** (AI/LLM-based EPAR or scientific literature screening tool, updates from QO holders as part of post-Opinion commitment)

Draft recommendations for futureproofing the QoNM platform

- Next steps:
  - Industry sounding board TC end-November
  - SAWP presentation in November
  - Update R&D platform 4 Dec 2023
  - Implementation of comments and finalisation
  - Publication WS report in December
  - Involvement in RWE/Registries workshop in Feb 24 to discuss draft checklists for preparation of Qualification requests for data sources and registries
- Establishment of EMA+SAWP group (industry informed via sounding board) to start implementing recommendations