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SCIENCE MEDICINES HEALTH

Qualification of Novel Methodologies (QoNM) – Current procedure and experiences

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EMA multi-stakeholder workshop on Qualification of Novel Methodologies

Qualification of Novel Methodologies (QoNM) - scope as introduced in 2008

The EMA qualification process is a new, voluntary, scientific pathway leading to either a CHMP Qualification opinion or a qualification advice on innovative methods or drug development tools:

- **CHMP qualification opinion** on the acceptability of a specific use of the proposed method (e.g. use of a novel methodology or an imaging method) in a research and development (R&D) context (non-clinical or clinical studies), based on the assessment of submitted data;
- **CHMP qualification advice on future protocols and methods for further method development towards qualification**, based on the evaluation of the scientific rationale and on preliminary data submitted.

Scope

The qualification process addresses innovative drug development methods and tools. It will focus on the use of novel methodologies developed by consortia, networks, public/private partnerships, learned societies and pharmaceutical industry for a specific intended use in pharmaceuticals R&D.

The Qualifications platform is key to achieving objectives of EMA Regulatory Science Strategy to 2025 (‘*RSS to 2025*’)

‘To underpin its mission of protecting human health, EMA must catalyse and enable regulatory science and innovation to be translated into patient access to medicines in evolving healthcare systems’

‘RSS to 2025’ strategic goals related to QoNM

- Enhance **early engagement with novel biomarker developers to facilitate regulatory qualification**: Critically review the EMA’s biomarker validation process
- **Support the development of robust digital endpoints through qualification** and scientific advice
- **Establish an EU framework for data quality and representativeness**. Develop guidelines and **a strengthened process for data qualification through Scientific Advice**

Qualification Advice (QA)

- On strategy and protocols for further development of a methodology towards qualification
- Based on the review of the scientific rationale and on preliminary data
- Intended for early and iterative interactions to allow for efficient and adequate evidence generation planning to support future qualification
- Confidential
- a ‘Letter of Support’ can be proposed

Letter of support

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Based on qualification advice, when the novel methodology cannot yet be qualified but is shown to be promising based on preliminary data.

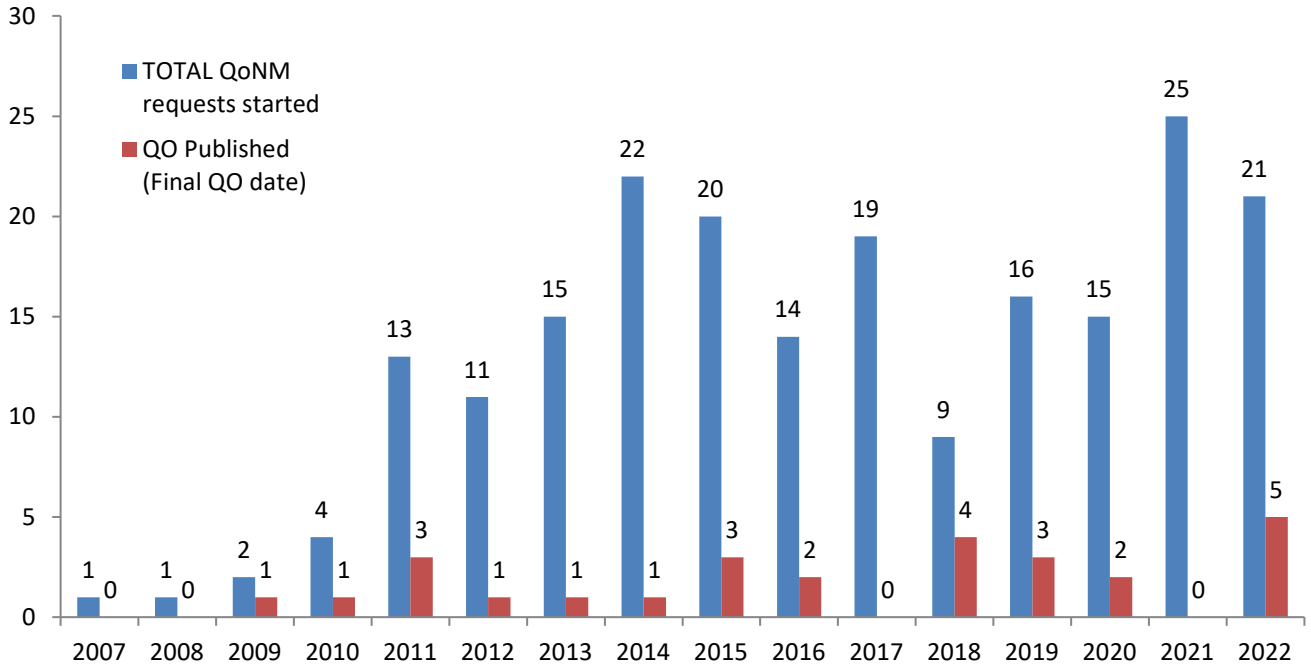
Aim is to encourage data-sharing and to facilitate studies aimed at eventual qualification.

A high-level summary of the novel methodology, its context of use, available data, and on-going and planned investigations is published if the sponsor agrees.

Qualification Opinion (QO)

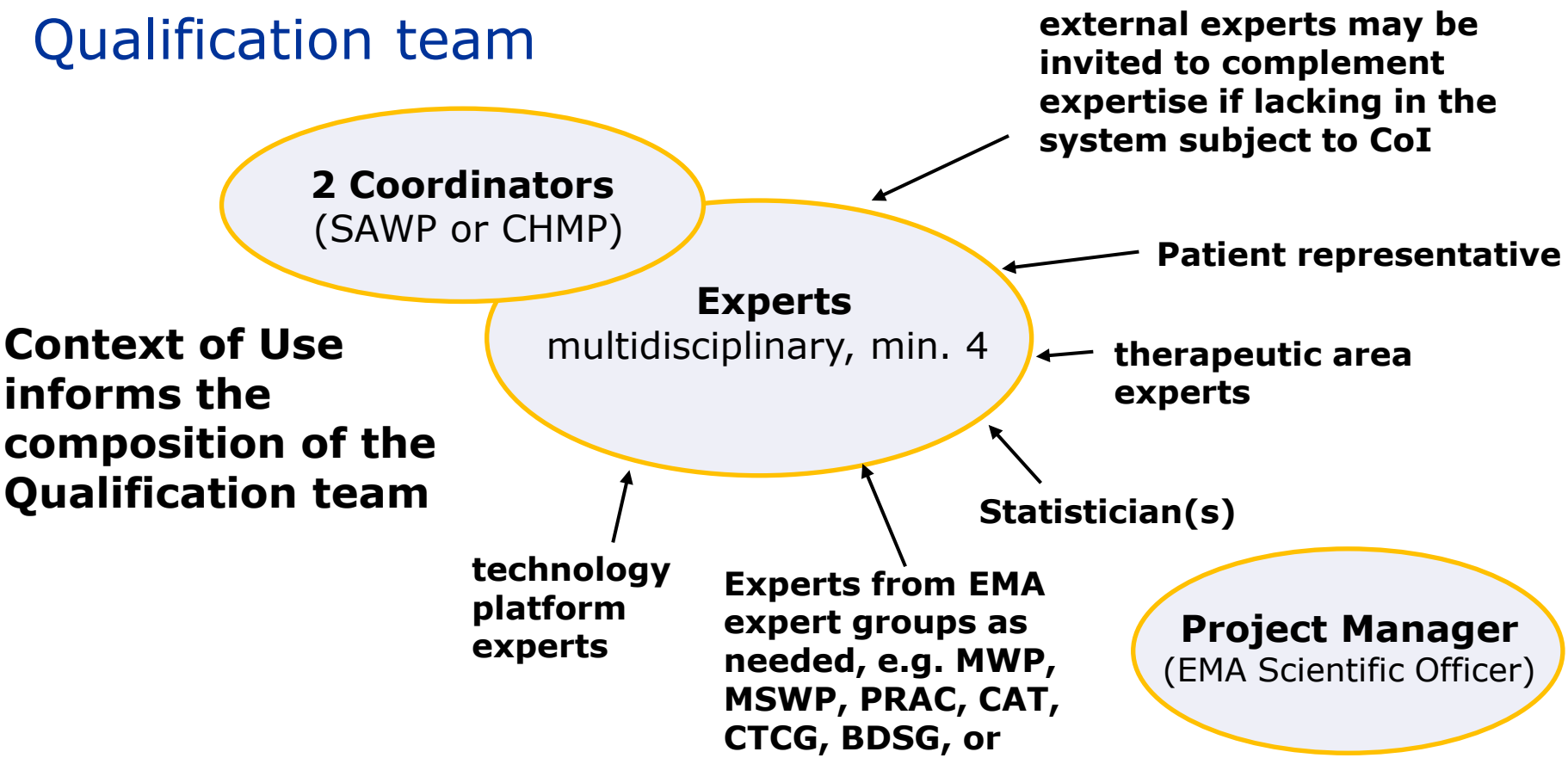
- Based on the assessment of submitted data, a QO confirms acceptability of a specific use ('Context of Use') of the proposed method (e.g. use of a biomarker) in a research and development (R&D) context to generate data for regulatory assessment
- The procedural route (QA/QO) is not fixed but will follow the assessment of the data
- Public consultation ensures scrutiny and input from the scientific community and interested stakeholders before final Qualification Opinion is published

Qualification of novel methodologies – procedure numbers



- Published: 27 Qualification Opinions, 38 Letters of Support

Qualification team



Procedure

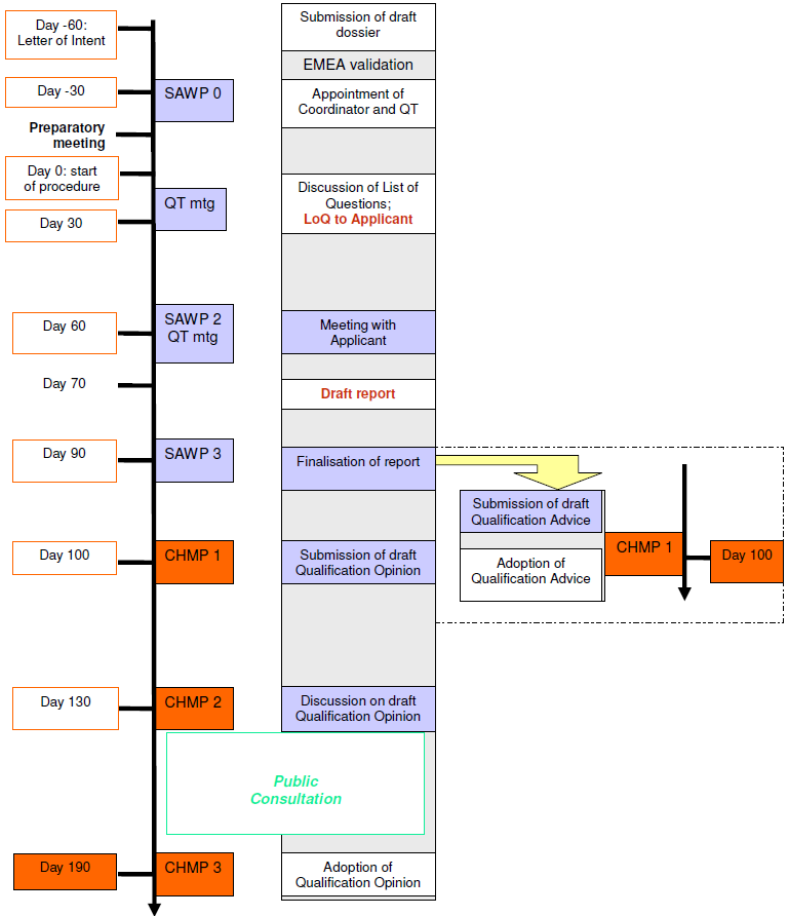
Qualification advice:

100 days

Qualification opinion:

130 days + 60 days public consultation

Meetings with applicant and overall process are adjusted flexibly depending on the procedural needs on a **case by case basis.**



QoNM procedure duration analysis 2019 - 2022

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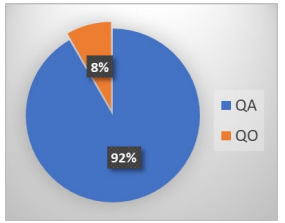
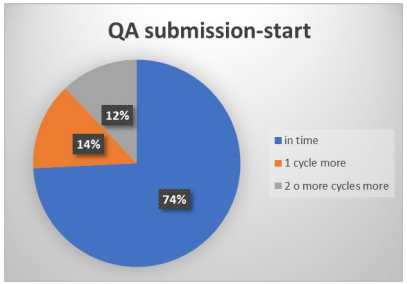
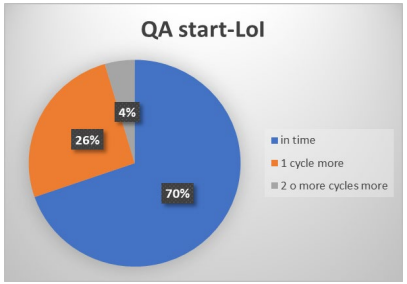
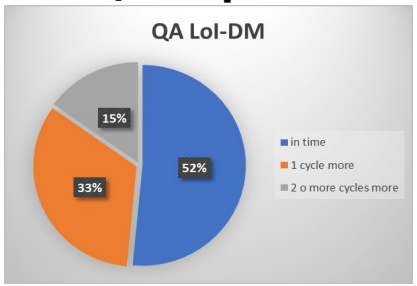
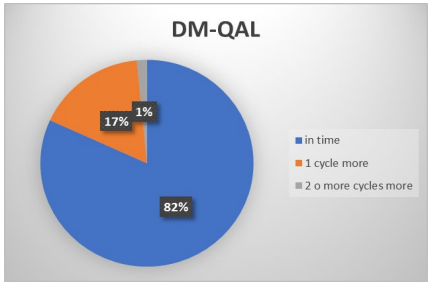
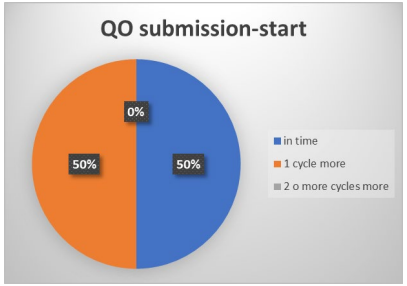
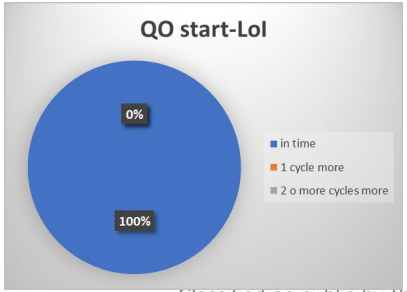
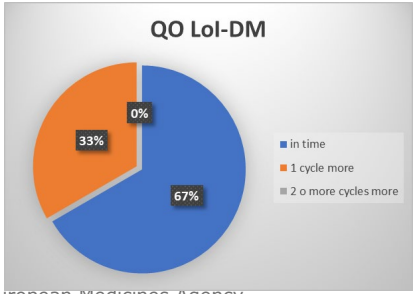
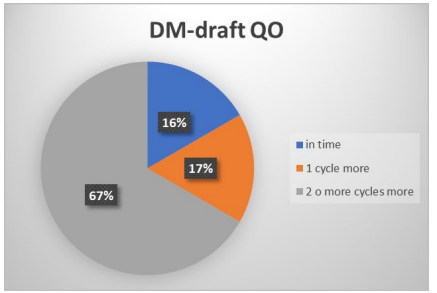
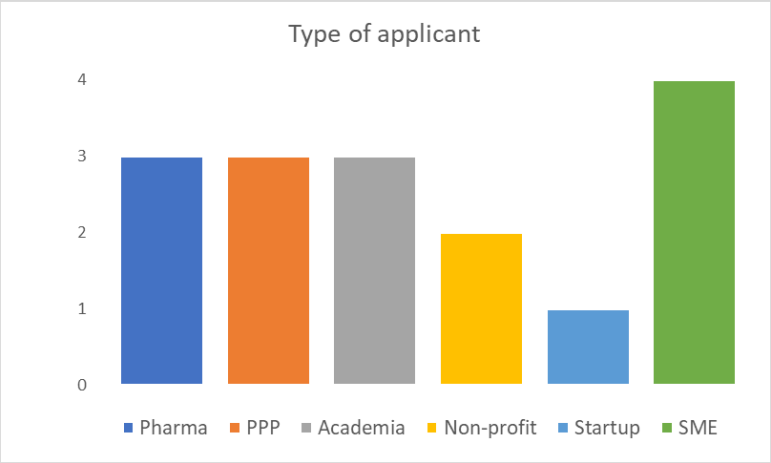
- 66 Qualification Advices, 6 Qualification Opinions (draft QO date)
- Analysis per SAWP meeting cycles in relation to optimal timing
- **Average procedure duration** in days from start of procedure to QA letter or draft QO:
  - Qualification Advice: 170 days (optimal: 100 days)
  - Qualification Opinion: 196 days (optimal: 130 days)



	Validation	Initial Review	DM/LoI phase	Outcome
QA				
QO				

Survey to Qualification Opinion and Letter of Support holders

- 28 Qualification Opinion holders and 39 Letter of Support holders have been invited
- 12 respondents, providing relevant representation of stakeholder groups for QoNM



- Procedural experience per applicant varied from 1 request (eight respondents) to 3 requests (1 respondent) to 6 request (3 respondents)

Survey to Qualification Opinion and Letter of Support holders Key findings

- **3/12 respondents had ITF meeting before engaging in QoNM**
  - 2 of those with intention to prepare QoNM request and found ITF helpful to prepare

- **6/12 respondents also engaged in FDA Qualification**
  - Preferences mixed: EMA process flexibility, shorter timelines and confidentiality of QA mentioned as positive by some, while other respondents mentioned that there should be full transparency from the QA stage including CHMP responses; EMA fees perceived as barrier and fee incentives/waivers should be promoted
  - **11/12 respondents would have been interested in a parallel FDA/EMA Qualification process**: to foster global alignment, efficiency

Survey to Qualification Opinion and Letter of Support holders Key findings

- **Validation phase experience**
  - 4 positive, 1 mixed, 3 negative, e.g. lack of preparation of Qualification Team (QT) for preparatory meeting, delays due to expert assignment to QT

- **Review and discussion meeting phase experience**
  - 4 positive (scientific rigour), 5 mixed, 1 negative
  - Points of criticism: broader expertise needs, List of Issues too extensive, insufficient time to prepare the discussion meeting and meeting too short

- **Qualification phase experience**
  - **5/7 of the respondents considered that timelines for QO drafting are not sufficiently transparent and not well communicated**

Survey to Qualification Opinion and Letter of Support holders Key findings

- **Proposals for efficiency gains:** only 4/12 respondents made proposals, 2/12 considered the process works fine, 6/12 did not respond
  - Clarify scope/value/timelines in guidance to applicants
  - Update and consolidate procedural guidance
  - Refine procedural steps, in particular for drafting of QO and public consultation
  - Introduce standardisation of output formats/templates, in particular for Qualification Opinion
  - Include lay language Q&A for Qualification Opinion, potentially request already as part of the briefing document drafted by the applicant to facilitate understanding for patient representatives involved
  - Increase patient and HCP participation in the Qualification Team
  - Global alignment and work sharing with other regulators
  - Involve HTA and Notified Bodies
  - Monitor uptake of Qualification Opinions to show impact on decision making

Survey to Qualification Opinion and Letter of Support holders Key findings

- Should there be a **mandatory publication of Qualification Advice information**?
  - **8/12 yes**
  - 1/12 no
  - 1/12 unsure
  - 2/12 no reply

Survey to Qualification Opinion and Letter of Support holders Key findings

- Has the **Letter of Support (LoS) been helpful to facilitate further evidence generation for QO**?
  - 7/12 yes, 2/12 no, 3/12 no reply
  - How?: facilitated data sharing and collaboration, finding investors, enhanced credibility with key stakeholders

- Has the **method acknowledged by the LoS been qualified or otherwise recognised**?
  - 2x QO granted
  - 1x validity confirmed as part of MAA review
  - 7x planning QO request in the future
  - 1x statement that LoS has clearly increased research and publications related to the method
  - 4 respondents mention that LoS has helped progressing IMP development

Workshop objectives

- Confirm the future scope of qualification of novel methodologies in light of ever accelerating development of science and technologies, to best support translation of innovation into patient benefit;
- Look at use case examples of different methodologies (Clinical Outcome Assessments, Modelling & Simulation, Digital Health Technology and Artificial Intelligence/Machine Learning related methods, Modelling and Simulation and Real World Evidence related methods), share procedural experiences and solicit input from stakeholders to identify recommendations to futureproof the qualification of novel methodologies process and its outcomes.