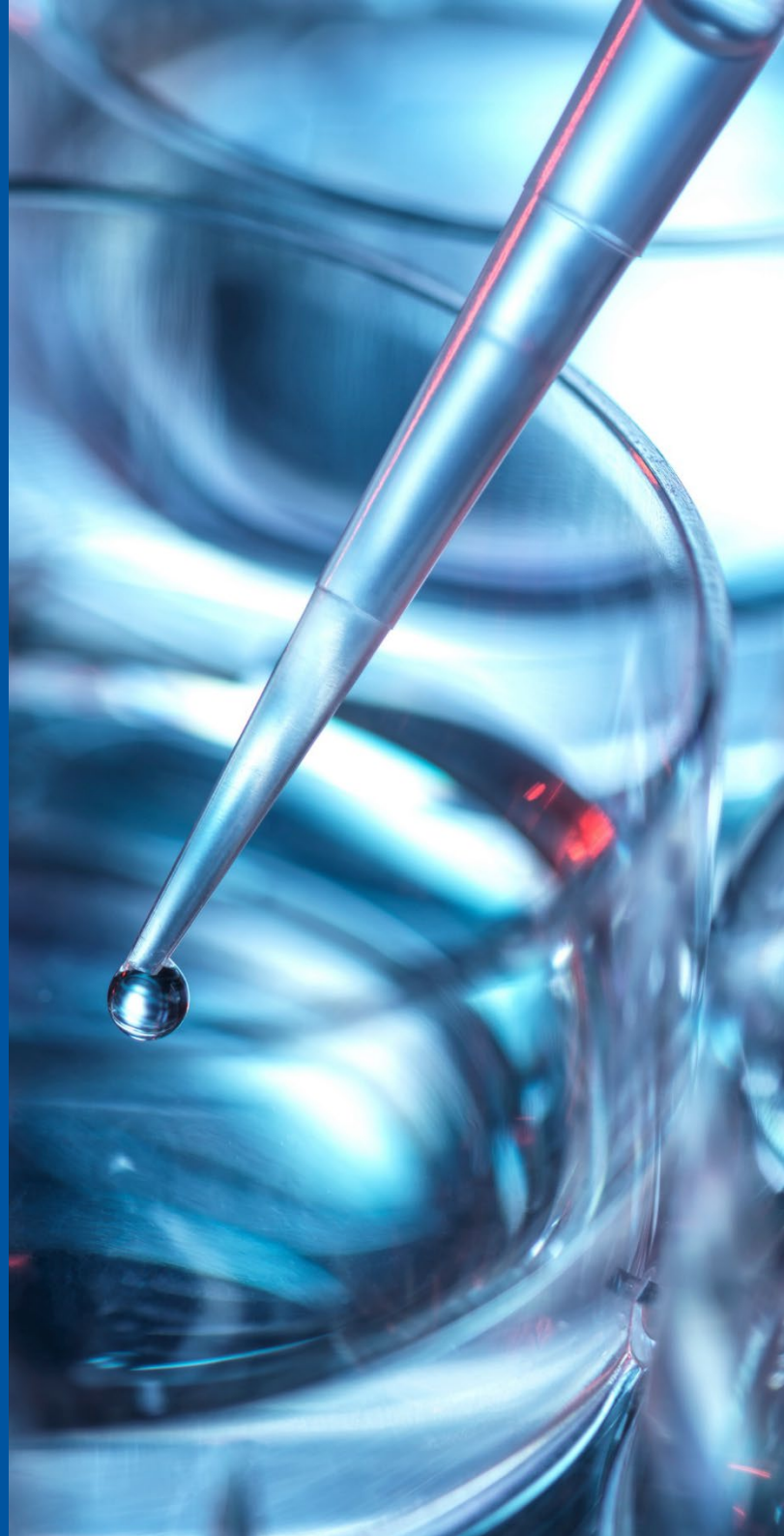
EMA
EUROPEAN MEDICINES AGENCY

Future-proofing Qualification of Novel Methodologies (QoNM)

Action plan

SEPTEMBER 2024



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Introduction

The qualification of novel methodologies process (QoNM) is a voluntary, scientific pathway allowing developers of innovative drug development methods to request from European medicines regulators the qualification of these instruments within a pre-defined Context of Use.

Since its introduction in 2008 it has provided a platform for iterative prospective discussion and agreement of evidence generation plans for future qualification (Qualification Advice), as well as for publication of CHMP Qualification Opinions once a novel methodology has been demonstrated to be valid for evidence generation to inform benefit/risk decision making.

It has also offered publication of 'Letters of Support' when a novel methodology cannot yet be qualified but is showing promise based on preliminary data to help fostering collaborative evidence generation and further development.

The European Medicines Agencies Network Strategy to 2025 (EMANS) and the EMA Regulatory Science Strategy (RSS) to 2025 have laid out strategic goals and core recommendations many of which are facilitated by the qualification of novel methodologies platform, e.g.:

- Catalyse the integration of science and technology in medicines development and ensure that the Network has sufficient competences to support innovators in various phases of medicines development. (EMANS)
- Enhance early engagement with novel biomarker developers to facilitate regulatory qualification: Critically review the EMA's biomarker validation process, including duration and opportunities to discuss validation strategies in advance, to encourage greater uptake and use. (RSS)

- Support the development of robust digital endpoints through qualification, scientific advice and the establishment of a multi-stakeholder platform to obtain feedback on their utilisation. (RSS)
- Establish an EU framework for data quality and representativeness. Develop guidelines, a strengthened process for data qualification through Scientific Advice, and promote across Member States the uptake of electronic health records, registries, genomics data, and secure data availability. (RSS)
- Reinforce patient relevance in evidence generation. (RSS)

In 2022, a focus group of industry representatives and EMA identified methodologies which will need qualification in the future and explored ways to futureproof the process.

In April 2023, the EMA organised a virtual multi-stakeholder workshop on the 'Qualification of Novel Methodologies' (QoNM) framework. The objectives of the workshop were to:

- Explore the scope of qualification of novel methodologies in the light of ever accelerating development of science and technologies to best help translate innovation into patient benefit.
- Look at use case examples of different groups of methodologies, share procedural experiences and solicit input from stakeholders to identify recommendations to future proof the qualification of novel methodologies process and its outcomes.

Discussions on how to foster development of robust novel methodologies and optimise regulatory qualification support have also been ongoing in other fora, e.g., the Sounding Board between EMA and Industry Trade Organisations, in the context of the EMA Multistakeholder workshop on 'Patient Experience data in medicines development' in September 2022, the ACT EU PA08 multi-stakeholder methodology workshop in November 2023, and the joint HMA/EMA multi-stakeholder workshop on Patient Registries in February 2024.

Key recommendations for future-proofing QoNM were identified and have been endorsed by the EMRN Scientific Coordination Board and are the basis for the action plan presented.

A **QoNM core group** of EMRN and EMA experts has been established to lead the process.

Members

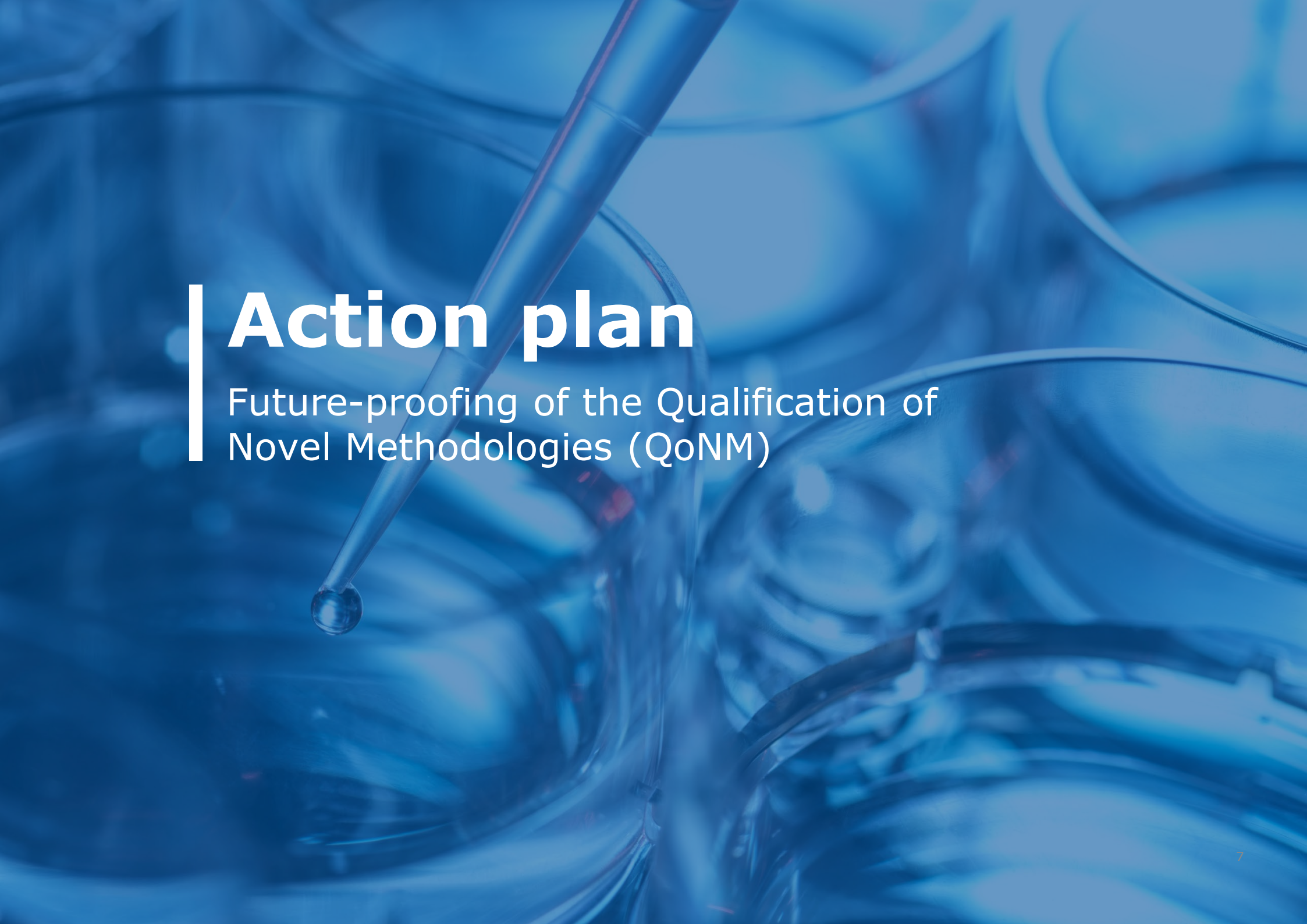
SAWP/CHMP/MWP:
Flora Musuamba-Tshinanu (FAMHP), Paolo Foggi (AIFA), Joerg Zinserling (BfArM), Andreas Kirisits (AGES), Peter Mol (CBG-MEB)

EMA:
Iordanis Gravanis (H-EG-SCA), Jane Moseley (H-EG-SCA), Efthymios Manolis (H-EG-SCA), Kelly Plueschke (TDA-RWE), Ina Rondak (TDA-MET), Maria Mavris (S-PH), Rosa Gonzalez-Quevedo (S-PH), Pierpaolo Moscariello (TRS-ACD), Riccardo Sacca (TRS-INO)

Coordination:
Thorsten Vetter (H-EG-SCA)

Tasks of the QoNM core group:

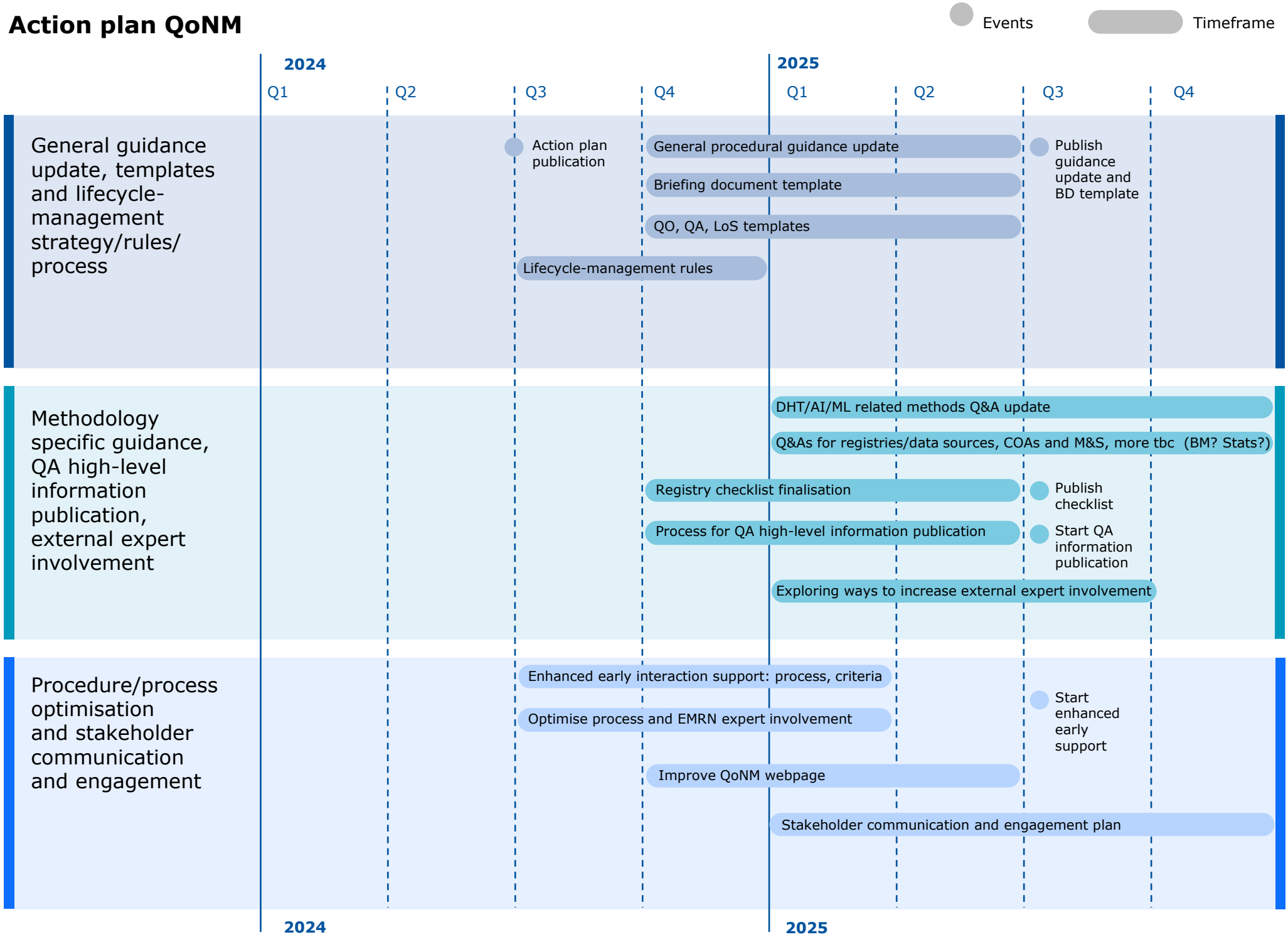
- Develop implementation action plan
- Enable and supervise the QoNM future-proofing process
- Discuss and agree process optimisation, guidance updates and life-cycle management measures
- Monitoring of successful implementation of the action plan
- Consultation with industry sounding board and other relevant stakeholder groups throughout the process

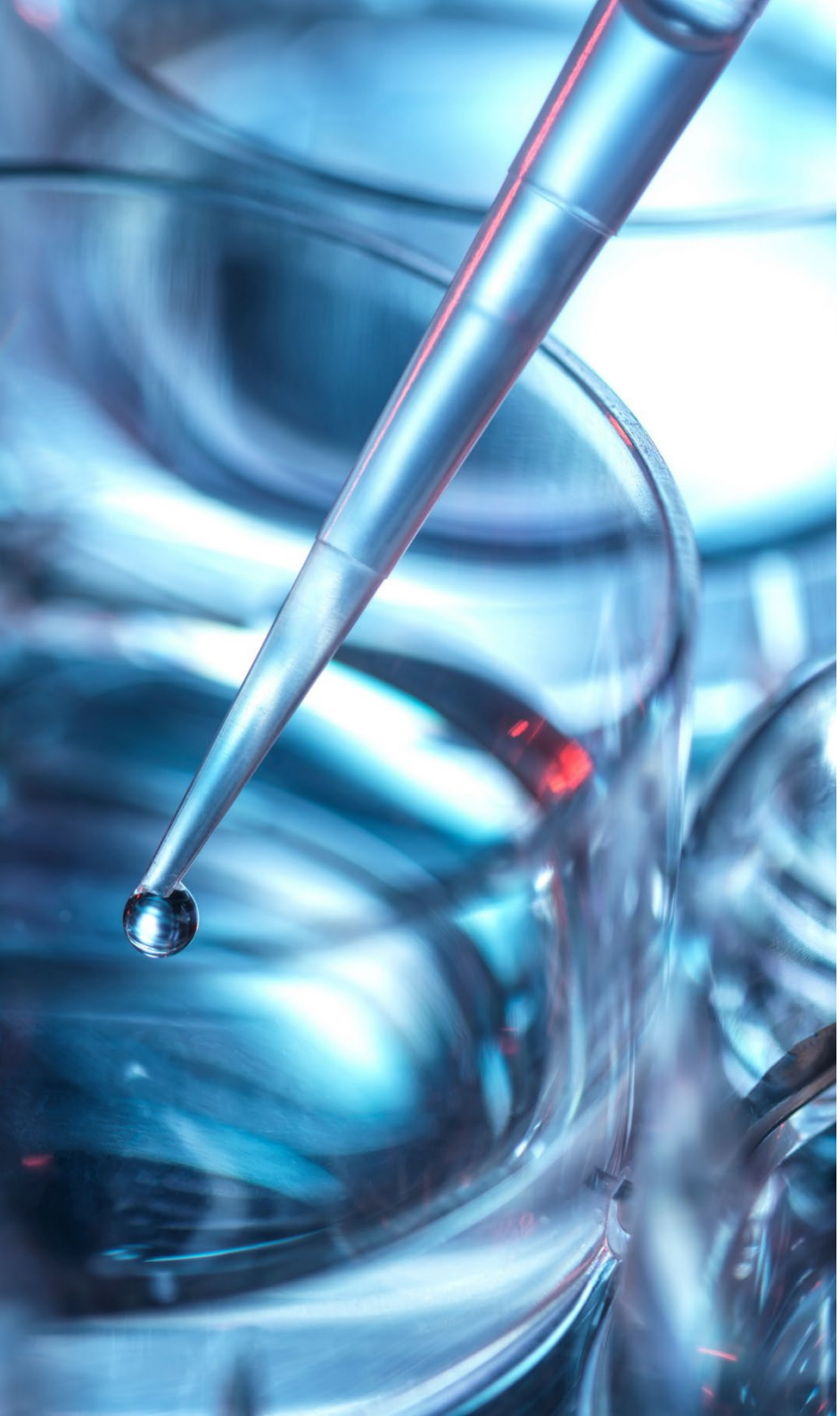


Action plan

Future-proofing of the Qualification of Novel Methodologies (QoNM)

Action plan QoNM





Potential actions for consideration in 2025

- Explore involvement of additional decision-makers during QoNM: e.g. HTA, MD/IVD regulators
- Training for methodology developers less experienced in regulatory interactions, e.g. academics, HCPs and patient representatives (e.g. in collaboration with PCWP, HCPWP and potentially public-private partnerships like IHI and C-Path)
- Publishing specific unmet needs for novel methodologies as identified by Committees or Working Parties and linking to Regulatory Science Research Needs (TRS-ACD)
- Establish active interaction with more professional societies and patient groups developing COAs (S-PH)
- Explore feasibility of (automated) monitoring and reporting of evidence generated by qualified methods that has informed regulatory decisions

Topic description

General guidance update, templates and lifecycle-management strategy/rules/process

The QoNM core group will discuss strategy, rules and process for the lifecycle-management of QOs, e.g. criteria defining the need for re-validation, whether there are options for abridged extensions of qualified CoUs, and how periodic trialogues for qualified registries (between registry holder, MAH and EMA) can be established. Considerations on lifecycle-management will be reflected in the updated general procedural guidance, targeting publication in Q3 2025.

A general briefing document template will be drafted to facilitate the preparation of high-quality briefing packages by applicants.

QO, QA and LoS templates will be introduced to facilitate report drafting by network experts and improve standardisation of information presentation in published documents.

Key dates:

- **Q3/Q4 2024** – Core group to discuss and agree on lifecycle management and key process updates
- **By end Q1 2025** – General procedural guidance draft
- **Q2 2025** – General procedural guidance consultation with stakeholders
- **Q3 2025** – Publish updated general procedural guidance and BD template; QO, QA and LoS templates to be made available to network experts

Methodology specific guidance, QA high-level information publication, external expert involvement

A registry checklist will be published by Q3 2025.

Methodology specific Q&A documents will be drafted/updated in 2025. The Q&A for Qualification of DHT/AI/ML-based methodologies will reflect strategy for lifecycle-management of qualifications with short technological iteration cycles. Additional Q&A's will be drafted for qualification of registries/data sources, clinical outcome assessments and modelling & simulation related methods. The need for further Q&A's will be considered by the QoNM core group in consultation with stakeholders in 2025 (e.g. for qualification of biomarkers, statistical methods or other) .

Content and process for (mandatory) publication of high-level QA information will be discussed with relevant stakeholders. Start of publication of high-level QA information in Q3 2025.

Options for increased involvement of external experts (HCPs/ Academia) will be explored in line with CoI considerations.

Key dates:

- **Q3 2025** – Publish registry checklist
- **End 2025** – Publish Q&A documents for qualification of DHT/AI/ML based methods (update), registries/data sources, COAs and M&S; consider need for additional Q&A's (e.g. BM and statistical methods)
- **Q3 2025** – Start publication of high-level QA information

Procedure/process optimisation, stakeholder communication and engagement

A process for early Qualification support will be introduced, including a mailbox for informal inquiries by methodology developers and establishing a cross-functional EMA team to provide written clarification on the QoNM process. Early scoping meetings will be introduced to support applicants, in particular developers with limited regulatory experience (e.g. patient organisations, HCP groups, academics, PPPs, SMEs). This will allow guiding optimised timing and improving quality of QoNM requests.

Together with the EMA Webteam, the QoNM webpage will be updated: improving the presentation of QOs and LoS, introducing the publication of high-level QA information, options to introduce versioning of documents to reflect lifecycle management and establishing a catalogue to improve access to QoNM information for developers and stakeholders.

A stakeholder communication and engagement plan will be prepared to inform on general procedural guidance update and process improvements in the course of 2025.

Key dates:

- **By end Q1 2025** – Agree on process for early Qualification support for reflection in procedural guidance
- **By end Q2 2025** – Update of QoNM webpage
- **2025** – Develop stakeholder communication and engagement plan to inform on general procedural guidance update and process improvements

List of abbreviations

BM	Biomarker
COA	Clinical Outcome Assessments (e.g. Patient Reported Outcomes, Observer Reported Outcomes)
CoI	Conflict of interest
CoU	Context of Use
DHT	Digital Health Technologies
LoS	Letter of Support
M&S	Modelling and Simulation
PPP	Public-private-partnership (e.g. IHI, C-Path institute)
Q&A	Questions & answers document
QoNM	Qualification of Novel Methodologies
QO	Qualification Opinion
QA	Qualification Advice
RWE	Real World Evidence (Registries and data sources)
Stats	Statistical methods

List of affiliations

AGES	Austrian Agency for Health and Food Safety
AIFA	Italian Medicines Agency
BfArM	German Federal Institute for Drugs and Medical Devices
CBG-MEG	Dutch Medicines Evaluation Board
CTCG	Clinical Trials Coordination Group
FAMHP	Belgian Federal Agency for Medicines and Health Products
H-EG-SCA	EMA Scientific Advice Office
IWG	Inspectors Working Group
S-PH	EMA Public and Stakeholder Engagement Department
TDA-RWE	EMA Task Force Data Analytics – Real World Evidence
TDA-MET	EMA Task Force Data Analytics – Methodologies
TRS-ACD	EMA Task Force Regulatory Science – Academia
TRS-INO	EMA Task Force Regulatory Science – Innovation

European Medicines Agency

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Telephone +31 (0)88 781 6000
Send us a question Go to www.ema.europa.eu