EU perspective:
European procedure for “Qualification of novel methodologies for medicine development”

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The views expressed in this presentation are primarily those of the author and do not necessarily express those of the BfArM, nor of the EMA.
Nothing to disclose

See:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/experts.jsp&mid=WC0b01ac058043244a
Qualification of Novel Methodologies in Europe

Overview:

- Current framework of European Qualification Procedures
- Conduct of procedures
- Results/Evaluation of previous procedures
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• EMA website: “The European Medicines Agency offers Scientific Advice to support the qualification of innovative development methods for a specific intended use in the context of research and development into pharmaceuticals”

• There is currently no separate legal framework for the qualification of novel methodologies (unless the character of the product makes it a medical device or a medicinal product)

• The applicant’s guidance document refers to Regulation No 726/2004 (which itself refers to Scientific Advice only, but not to „Qualification“).

• Given by the CHMP on the basis of recommendations by the SAWP.

• Leads to a “Qualification opinion” a “Letter of Support” or a “Qualification advice”
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• Qualification Opinion:
  – The CHMP can issue an opinion on the acceptability of a specific use of a method, such as the use of a novel methodology or an imaging method in the context of research and development. The method can apply to non-clinical or to clinical studies, such as the use of a novel biomarker.
  – Before final adoption of qualification opinion, the CHMP makes its evaluation open for public consultation by the scientific community. This ensures that the CHMP shares information, as agreed with the applicant, and is open to scientific scrutiny and discussion.

• Letter of Support:
  – Based on qualification advice, the Agency may propose a letter of support as an option, when the novel methodology under evaluation cannot yet be qualified but is shown to be promising based on preliminary data.
  – Letters of support aim to encourage data-sharing and to facilitate studies aimed at eventual qualification for the novel methodology under evaluation.
  – These letters include a high-level summary of the novel methodology, context of use, available data, and on-going and future investigations. The Agency publishes letters of support on this page, if the sponsors agree.

• Qualification advice:
  – The CHMP can issue advice on protocols and methods that are intended to develop a novel method with the aim of moving towards qualification.
  – The advice is based on the evaluation of the scientific rationale and on the preliminary data submitted to the Agency.
Reminder: How does the European System work?

The EU regulatory network:

European Medicines Agency (EMA)
- "Networking agency" with about 900 staff members and 4,500 Experts from National Authorities

Committee for Human Medicinal Products – CHMP
- Responsible for preparing the Agency’s opinions concerning all human medicines (including qualification advice and qualification opinions/LoS)
- Mandating Working Parties
- Composed of expert delegates from the Member States

Scientific Advice Working Party – SAWP
- Appointed by CHMP (experts of the European experts database, members of Committees)
- Facilitate access of medicinal products to patients by optimising research and development
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• **Scope:**
  – Addressed at: Consortia, networks, public/private partnerships, learned societies and pharmaceutical industry
  – Not focussed on specific products or indications but on “innovative drug development methods and tools”

• **Applicant input:**
  – Protocols, full study reports and supportive data for Qualification
  – Draft protocols and development plans for future studies along with preliminary data available

• **Operations**
  – Pre-submission meeting(s)/Briefing meeting(s) - CHMP appoints a “qualification team” led by two co-ordinators (Members of the SAWP, further experts appointed according to expertise)
  – Public consultation phase prior to final qualification opinion, potentially confidential information removed, input from scientific community.
  – Timing agreed with applicant in advance (but “flexible”)
  – Potential follow-up procedure
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• **Documents available:**

• **Guidance to applicants**
  – Referring to the legal basis and scope of the procedure
  – Characterises the necessary applicant’s input
  – Describes the procedures on EMA side
  – Potential outcome - Time-lines

• **Letter of intent - template**
  – Generally divides between biomarker and COA (clinical outcomes assessment)

• **Draft formats for qualification opinion/advice for:**
  – Non-clinical/clinical
Joint EMA-FDA Biomarker Qualification Procedure.

- In operation since December 2014
- Intention: Exchange views between the agencies
- Harmonisation between agencies
- Simplification for applicants
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- Encouraged by both Agencies
- Voluntary, at request of sponsor
- Discussion between FDA-EMA and tripartite meeting with sponsor
- Alignment of procedural flow between agencies is important and challenging: preparatory interactions with all agencies should start early
- Each Agency will issue separate responses to sponsor’s questions in line with their usual procedures

→ Increased dialogue between Agencies and sponsor from early stages of development
→ Exchange views, share expertise
→ Optimise and facilitate global development, meeting both agencies requirements
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- **Time course:**
  - 3-months for qualification advice, variable duration for qualification opinion

Figure 1: Procedure for the qualification of novel methodologies and/or scientific advice on future protocols and methods for further method development towards qualification.
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Quantitative aspects: Number of finalised procedures per year
(including advices, Letters of Support, and Qualification Opinion)
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• **Qualification Opinion:** 13 published reports
  – Therapeutic fields:
    » 5 Alzheimer’s disease
    » 3 renal biomarkers (one pre-clinical)
    » 1 statistical modelling for dose finding
    » HFS for tuberculosis drug development
    » 1 Outcome measure in COPD (exacerbations)
    » Tool to measure patient adherence

• **Letter of support:** 13 procedures finalised
  – Therapeutic fields:
    » biomarkers for skeletal muscle injury,
    » drug-induced kidney injury (2)
    » Drug-induced liver injury
    » Imaging biomarker in Parkinson’s
    » microaneurysm rate (enrichment biomarker ophthalmology)
    » Reading speed as outcome measure in geographic atrophy
    » Outcome measures in autism spectrum disorder (4)
    » 2 PROs (Dravet Syndrome and Functional Dyspepsia)

• **Qualification advice:** 79 procedures since 2007
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Quantitative aspects: Number and clinical context of methods in qualification procedures (including advice only).
• **Most frequent categories:**

• “Longitudinal categories” according to context of use:
  – 58 methods for endpoint evaluation
  – 36 for enrichment of patient populations
  – 11 clinical safety biomarkers
  – 6 pre-clinical biomarkers

• “Vertical categories” according to method:
  – 42 Protein biomarkers
  – 19 clinical scores
  – 19 dedicated patient-reported outcomes (PROs)
  – 10 Modeling and simulation methods
  – 10 Imaging methods
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• **Further Reading:**
  

  • Manolis E et al: The European Medicines Agency Experience with Biomarker Qualification.
    
Thank you for your attention!