European procedure for
“Qualification of novel methodologies for medicine development”

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No Conflict of Interest

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

Biomarker Qualification Procedure

("Qualification of novel methodologies for medicine development")

- **Given by the CHMP on the basis of recommendations by the SAWP.**
- **Leads to a "Qualification opinion" or a "Qualification advice"**
  - **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.

  - **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.

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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**
  - Presubmission meeting(s)/Briefing meeting(s)
  - CHMP appoints a "qualification team" led by one co-ordinator
  - Public consultation phase prior to final qualification opinion, potentially confidential information removed, input from scientific community.
    - Timing agreed with applicant in advance
  - Potential follow-up procedure

Biomarker Qualification 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**
  - Joint format for parallel FDA/EMA submission available
  - Generally divides between biomarker and COA (clincal outcomes assessment)

- **Draft formats for qualification opinion/advice for:**
    - Non-clinical/clinical

Biomarker Qualification Procedure

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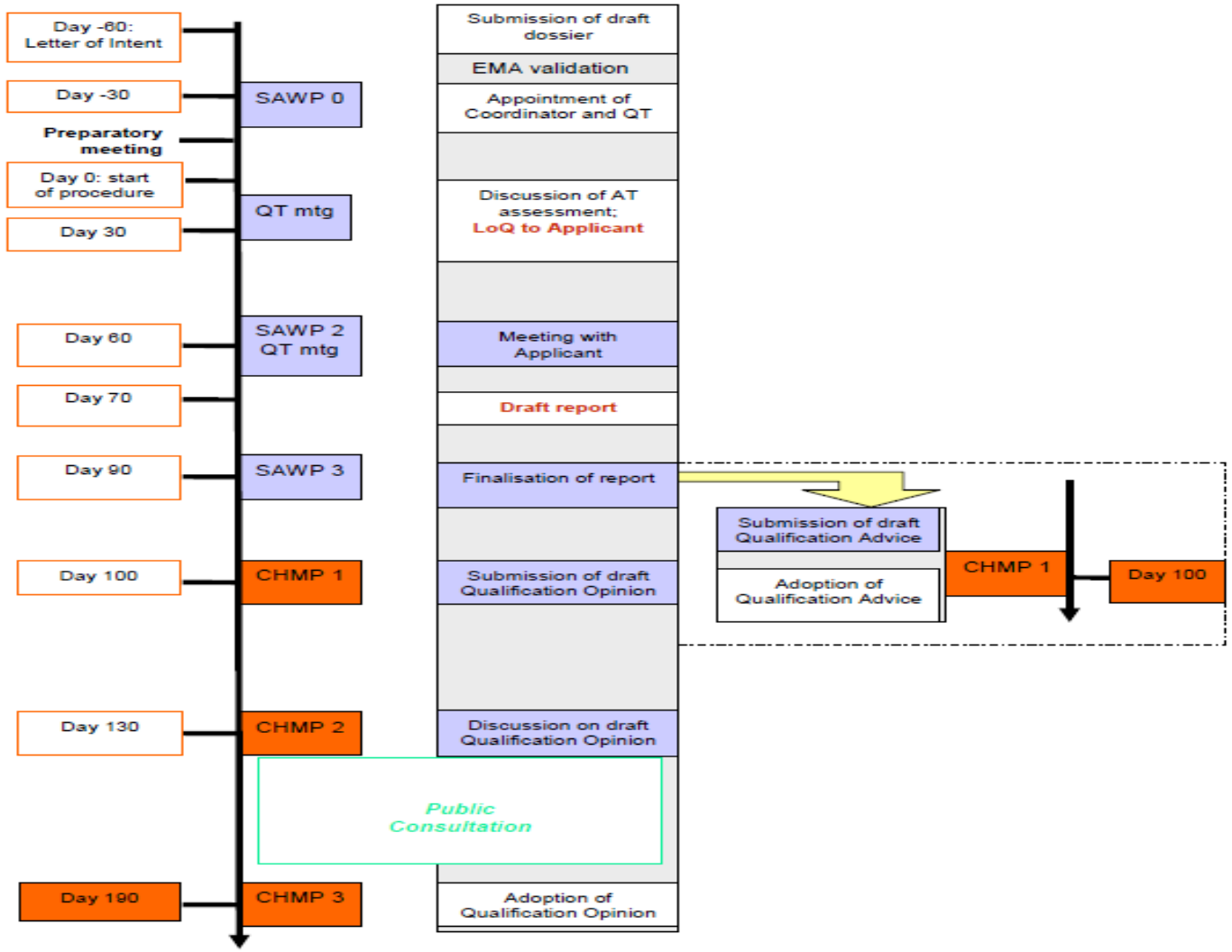
- **Time course:** 3-months for qualification advice,
  variable duration for qualification opinion



Biomarker Qualification Procedure

Evaluation of experience/Statistics:

- **Qualification Opinion: 7 published reports**

  Therapeutic field: **4 Alzheimer's disease**
  1 pre-clinical renal tox biomarker
  1 statistical modelling for dose finding
  HFS for tuberculosis drug development
  Outcome measure in COPD (exacerbations)

- **Letter of support:** (based on Qualification advice)

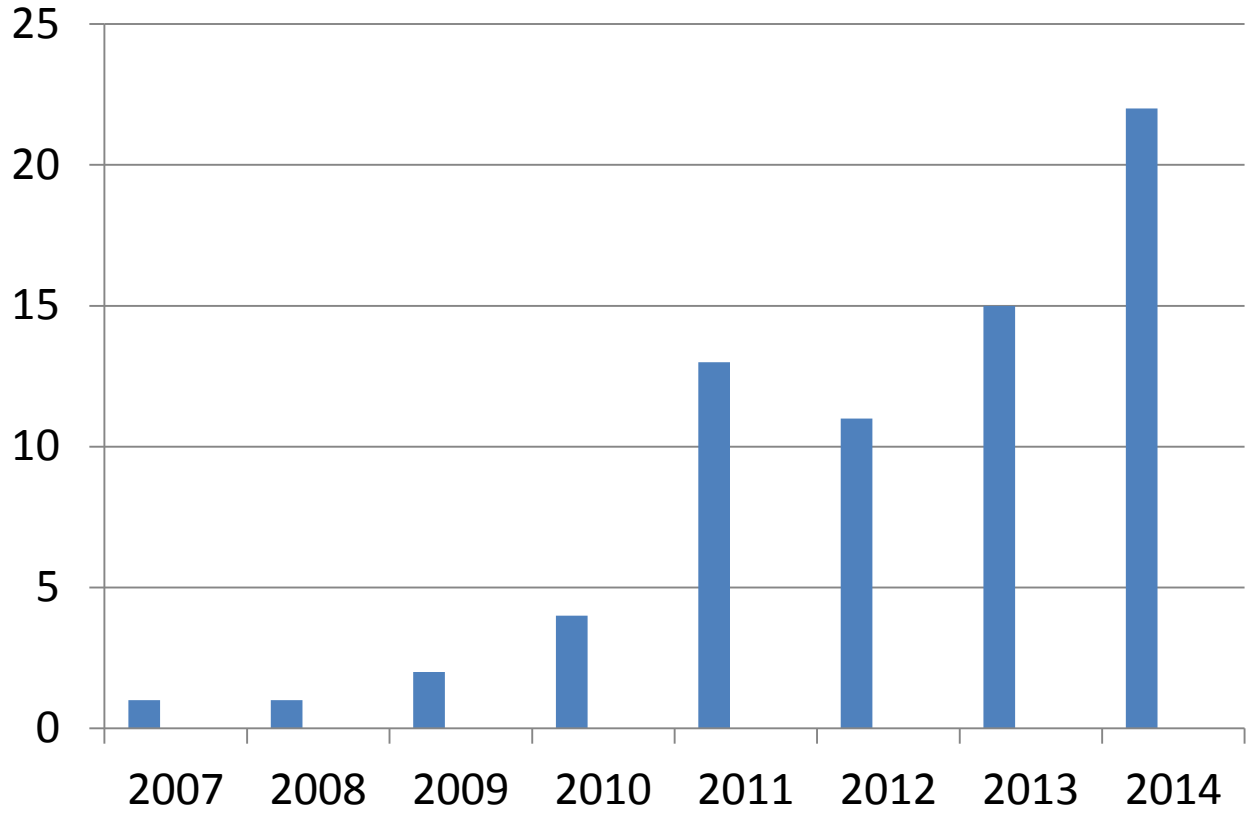
  3 procedures finalised
  Therapeutic fields: **biomarkers for skeletal mucle injury,**
  drug-induced kidney injury,
  microaneurysm rate

- **Qualification advice:**

  59 procedures since 2007

Biomarker Qualification Procedure

Qualification of novel methodologies for medicine development, Statistics: total No. of procedures: 69 since 2007 (Source: EMA)



Biomarker Qualification Procedure

(Qualification of novel methodologies for medicine development, Cavaleri and Manolis, in press))

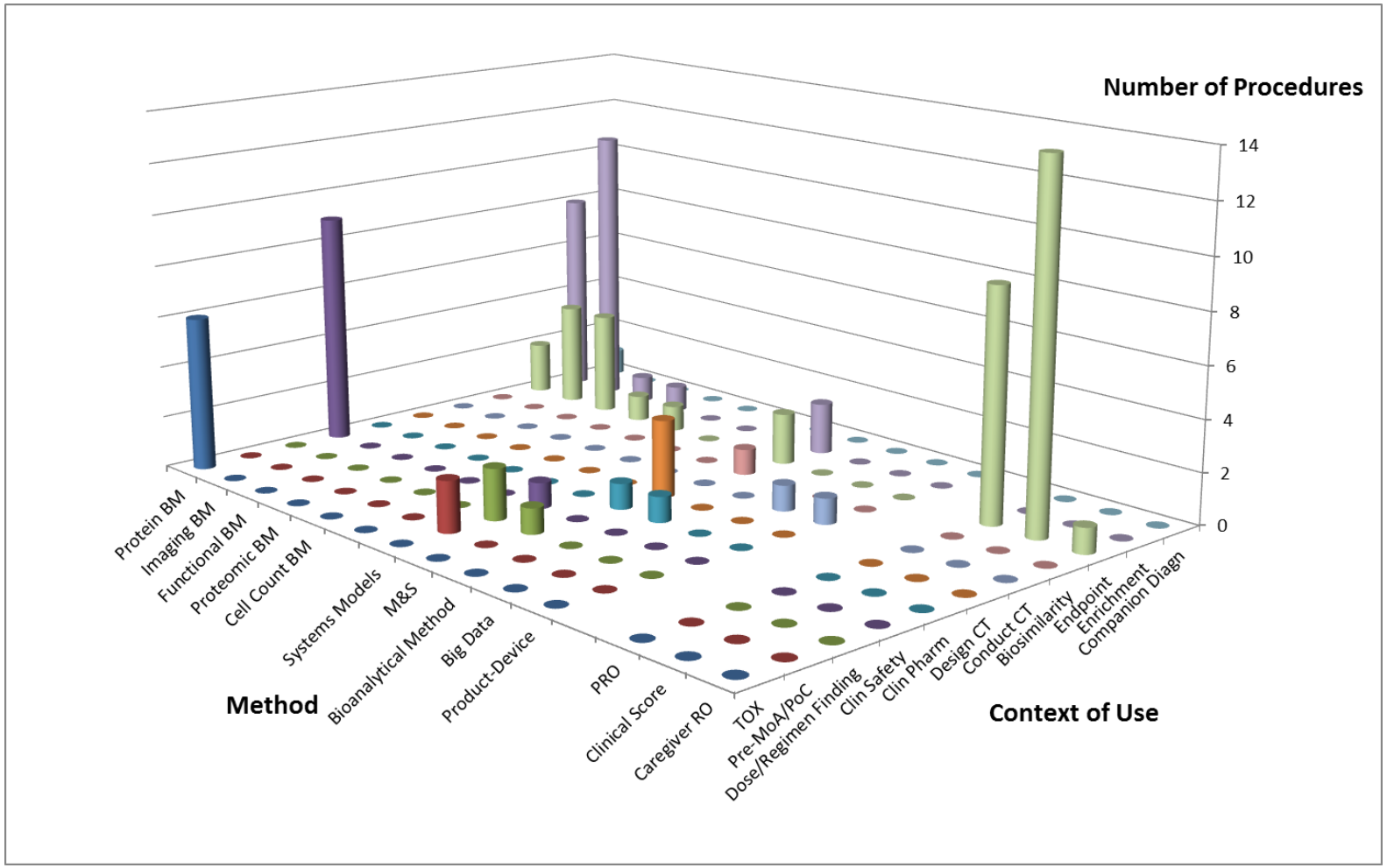


Figure 1 acronyms: BM: Biomarker, M&S: Modelling and Simulation, PRO: Patient reported outcome, RO: Reported outcome, TOX: toxicology, Pre-MoA/PoC: Preclinical Mechanism of Action/Proof of Concept, Clin: Clinical, CT: Clinical Trial, Diagn: Dignostic

Biomarker Qualification Procedure

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- **Most frequent categories:**
  - 42 procedures on biomarkers of which are:
    - 18 biomarkers for „enrichment" and of these
      - 8 „conventional" protein BMs
      - 10 imaging biomarkers
    - 9 clinical safety biomarkers
    - 6 pre-clinical toxicity biomarkers
  - 11 procedures relating to clinical scores as endpoint
  - 7 procedures relating to PROs as endpoint

Biomarker Qualification Procedure

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- Further Reading:
  - EMA Homepage:

    http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000319.jsp&mid=WC0b01ac0580022bb0

  - Manolis E et al: The European Medicines Agency Experience with Biomarker Qualification.

    In: Antonia Vlahou and Manousos Madrikakis (eds.): Clinical Proteomics: Methods and Protocols. Methods in Molecular Biology Vol 1243; New York 2015; p 255-272

Thank you for your attention!