



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Qualification of Novel Methodologies – Streamline DDT development for regulatory Qualification

C-Path DDT-KD Consortium September 2015



Presented by Thorsten Vetter on 25 September 2015
'Science Advice Office

An agency of the European Union



- ...on the regulatory validity and acceptability of a specific use of a proposed method in R&D context
- Voluntary, scientific pathway for innovative methods or drug development tools not yet integrated in the drug development and clinical management paradigm
- **One procedure** with **two outcomes**:
- Qualification Advice, OR
- Qualification Opinion



10 November 2014
EMA/CHMP/SAWP/72894/2008
Revision 1: January 2012¹
Revision 2: January 2014²
Revision 3: November 2014³
Scientific Advice Working Party of CHMP

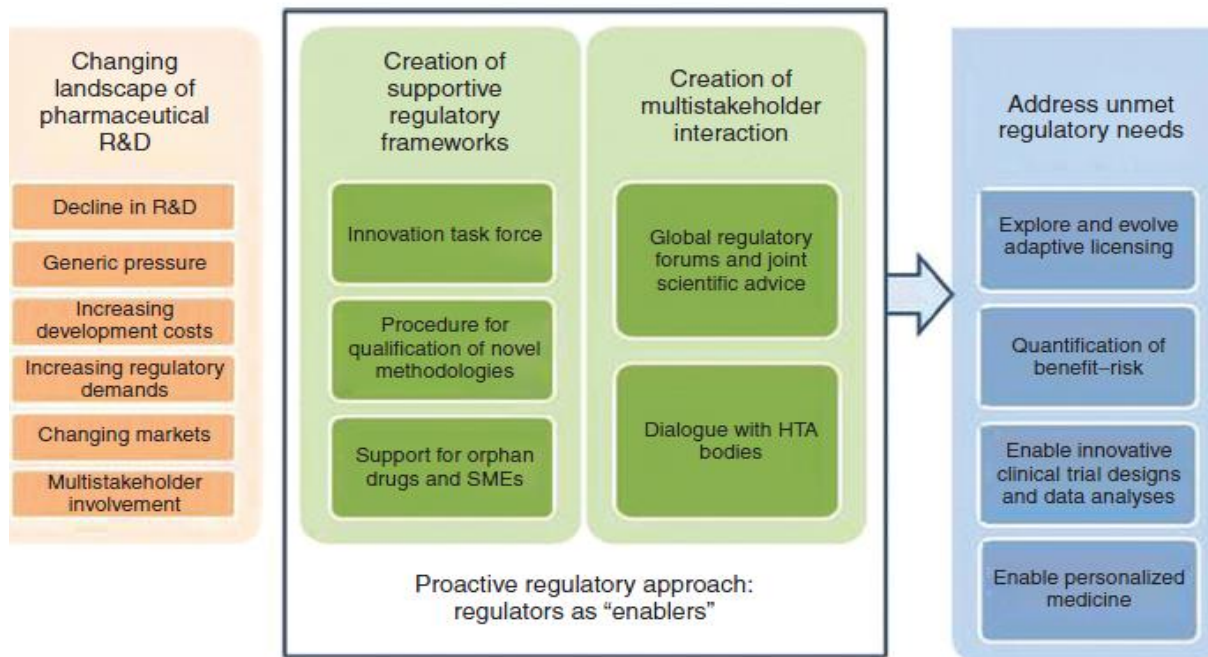
Qualification of novel methodologies for drug development: guidance to applicants

Agreed by SAWP	27 February 2008
Adoption by CHMP for release for consultation	24 April 2008
End of consultation (deadline for comments)	30 June 2008
Final Agreed by CHMP	22 January 2009

Long-term benefits from EMA perspective: Speed-up the time to regulatory acceptance of novel approaches and time to new marketing authorisations, improve public health



The proactive regulatory approach: “Be part of it and shape it together.”



Qualification advice on future protocols and methods for further development towards qualification, based on the evaluation of the ***scientific rationale and on preliminary data*** submitted, **confidential**

Qualification opinion on the acceptability of a specific use of the proposed method (e.g. use of a BM) in a R&D context, based on the assessment of data, not product-specific. CHMP discussion and adoption, public consultation, publication

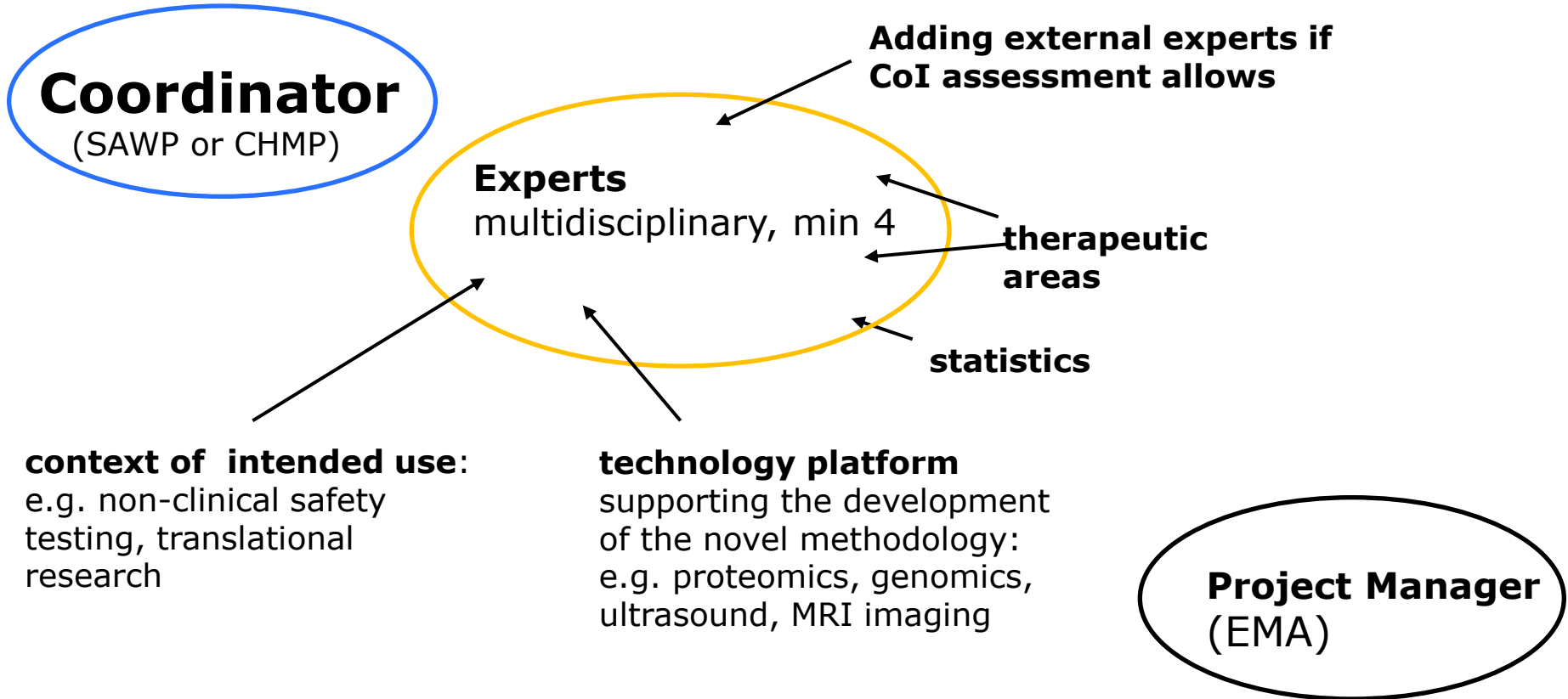
The procedural route is not fixed but will follow the assessment of the data

Aims: early and preferably iterative involvement to support the design the development strategy and during the project at key milestones, with commitment to evaluate data from agreed studies and to provide opinion

Clear proposal for a Qualification claim (Context of Use, CoU)

- **Technical aspects:** e.g. Analytical platform, biological matrixes, timing for evaluation
- The relation of the **marker response** with normal biological processes, or pathogenic processes, or pharmacologic responses to a therapeutic intervention and the expected **quantitative response-threshold**
- The **intended use of the DDT in drug development and clinic** (e.g. **exploratory vs. confirmatory, prognostic vs. predictive:** preclinical, translational, toxicity biomarker, inclusion criterion, stratification factor, enrichment tool, therapeutic drug monitoring, primary endpoint, secondary endpoint, initiation of treatment in clinic or change of intervention)

Final CoU will be informed by assessment of submitted data



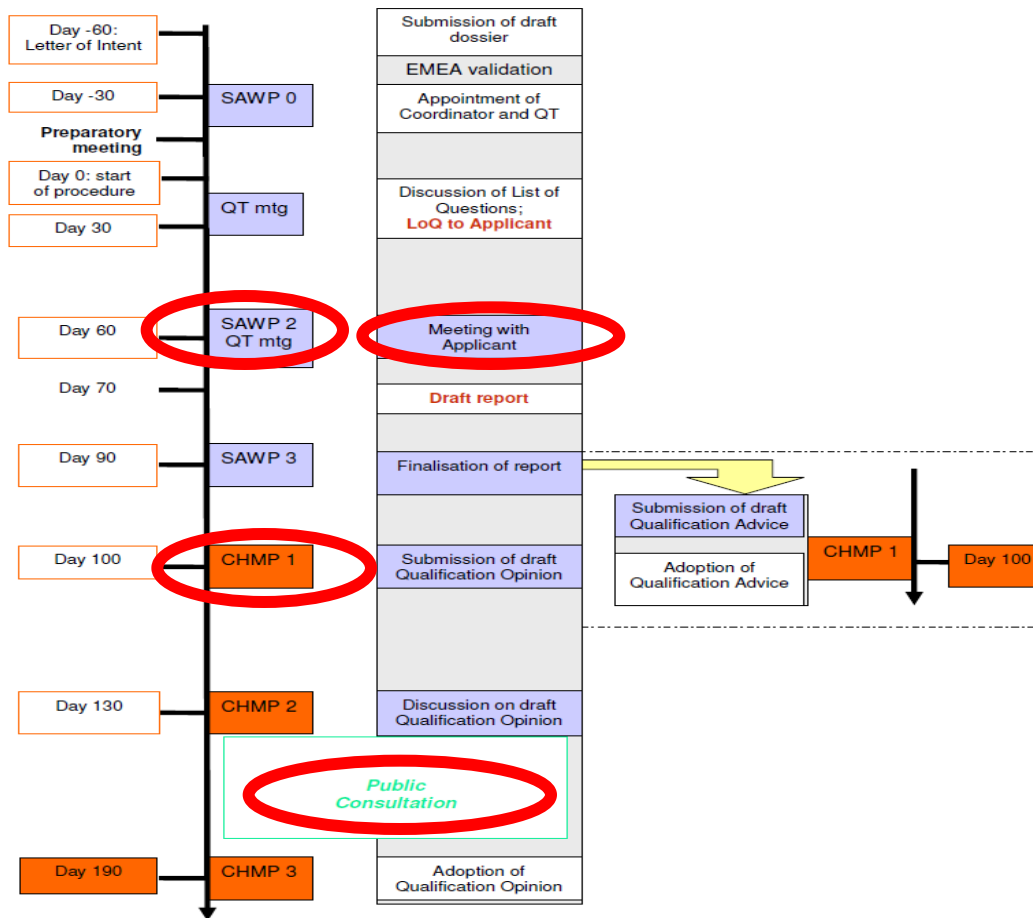
Scientific Advice Working Party (SAWP) –

Serves as primary scientific group, allows extensive networking within the Agency (Committees, other working parties and expert groups will be involved as appropriate)

Committee for Medicinal Products for Human Use (CHMP) involvement -

- CHMP member can be team member, peer review, discussion and adoption of final responses (Advice Letter or Qualification Opinion) by CHMP plenary
- SAWP/CHMP **commitment** to evaluate the data obtained from studies agreed during Qualification Advice and to provide a Qualification Opinion regarding the use of the method in R&D.
- Helpful for future CHMP interactions

Process timelines



What are the differences vs. SA?



<u>Scientific advice/Protocol assistance</u>	<u>Qualification advice/opinion</u>
Product and indication specific	Broad scope – may concern several indications or products, novel methodologies for specific R&D requirements, safety signal detection tools, etc.
Fixed timelines – 40 or 70 days	Flexible timelines and proceedings
Applicant can intervene only if requested by the SAWP, mainly in case of disagreement with the proposal	Always face-to-face meetings, applicant can raise issues for discussion during the procedure, can provide additional data/analyses
SAWP “looks” into the data but focuses on methodology	Assessment of the data!
Always confidential until drug approved	Public if a positive opinion is issued (after public consultation and check for commercially relevant information)



- **Applicants:** Consortia, Networks, Public/ Private Partnerships, Learned societies, Academia, Pharmaceutical industry
- **Fee incentives:** Same fee reductions as in scientific advice for paediatric use, orphan conditions and SMEs (small and medium-sized enterprises)
- **Initiation, Consultation and Qualification Advice:** Confidential
- **Qualification Opinion:** Public consultation prior to final publication ensuring scrutiny of and alignment with scientific community and external stakeholders


Final conclusions on the pilot joint European Medicines Agency / Food and Drug Administration VXDS experience on qualification of nephrotoxicity biomarkers

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Document(s)	Language	Status	First published	Last updated	Effective Date
 Final conclusions on the pilot joint European Medicines Agency / Food and Drug Administration VXDS experience on qualification of nephrotoxicity biomarkers	(English only)		22/01/2009		

Total kidney volume (TKV) as a prognostic biomarker for use in clinical trials evaluating patients with autosomal dominant polycystic kidney disease (ADPKD)

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Document(s)	Language	Status	First published	Last updated	Effective Date
 Draft qualification opinion total kidney volume (TKV) as a prognostic biomarker for use in clinical trials evaluating patients with autosomal dominant polycystic kidney disease (ADPKD)	(English only)	draft: consultation open	22/07/2015		



- [Paediatric Ulcerative Colitis activity index \(PUCAI\)](#)
- [Ingestible sensor system for medication adherence testing in clinical trials](#)
- [Total kidney volume \(TKV\) as a prognostic biomarker for use in clinical trials evaluating patients with autosomal dominant polycystic kidney disease \(ADPKD\)](#)
- [Qualification of exacerbations of chronic pulmonary disease tool \(EXACT\), and EXACT-respiratory symptoms measure \(E-RS\) for evaluating treatment outcomes in clinical trials in COPD](#)
- [In-vitro hollow fiber system model of tuberculosis \(HFS-TB\)](#)
- [MCP-Mod as an efficient statistical methodology for model-based design and analysis of phase-II dose-finding studies under model uncertainty](#)



- [A novel data-driven model of disease progression and trial evaluation in mild and moderate Alzheimer's disease](#)
- [Alzheimer's disease novel methodologies / biomarkers for the use of cerebrospinal-fluid amyloid beta 1-42 and t-tau and / or positron-emission-tomography amyloid imaging \(positive / negative\) as biomarkers for enrichment, for use in regulatory clinical trials in mild and moderate Alzheimer's disease](#)
- [Low hippocampal volume \(atrophy\) by magnetic-resonance imaging for use in clinical trials for regulatory purpose in predementia stage of Alzheimer's disease](#)
- [Novel methodologies in the predementia stage of Alzheimer's disease: cerebrospinal-fluid-related biomarkers for drugs affecting amyloid burden](#)
- [Alzheimer's disease novel methodologies / biomarkers for BMS-708163](#)
- [ILSI / HESI submission of novel renal biomarkers for toxicity](#)



The screenshot shows the FDA website header with the logo and tagline "U.S. Food and Drug Administration Protecting and Promoting Your Health". It includes a search bar and navigation tabs for Home, Food, Drugs, Medical Devices, Radiation-Emitting Products, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, and Tobacco Products. The main content area is titled "Drugs" and features a breadcrumb trail: Home > Drugs > Development & Approval Process (Drugs) > Drug Development Tools Qualification Programs. A blue sidebar on the left lists "Development & Approval Process (Drugs)", "Drug Development Tools Qualification Programs", and "Animal Model Qualification Program". The main heading is "Joint FDA/ EMA Letter of Intent (LOI) Submissions for Biomarker and Clinical Outcome Assessment Qualification Programs". Below the heading is a paragraph: "A [Joint Letter-of-intent \(LOI\) template](#) to enable efficient parallel submissions to the US FDA and EMA for Drug Biomarker Qualification or Clinical Outcome Assessment Qualification."

Update: Letter of intent

To facilitate parallel submissions of applications for drug [biomarker qualification](#) or clinical outcome assessment to EMA and to the United States Food and Drug Administration (FDA), the two agencies launched a joint [letter of intent](#) (LOI) in December 2014.

The joint LOI allows the two agencies to share scientific perspectives and advice. The agencies are also able to provide the same response to submitters.

With the joint LOI, the agencies intend to reduce the time taken by applicants to prepare LOIs. However, applicants do not have to submit jointly to EMA and the FDA - they can send EMA or FDA-specific LOIs separately if they wish.

Some sections of the LOI are specific for EMA or the FDA. See the template for details.



- 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: preparatory interactions with both 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

Letters 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.

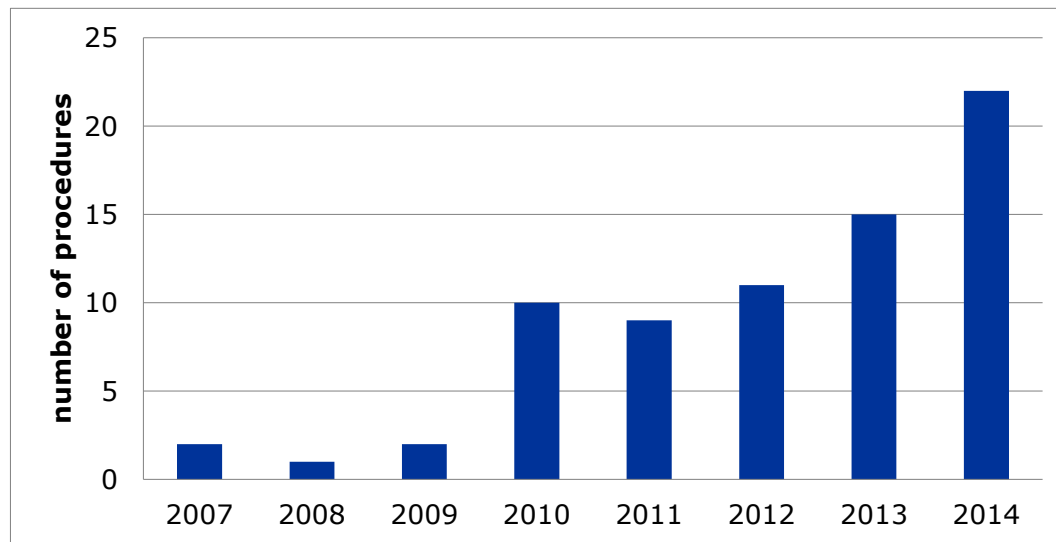
Letters of support

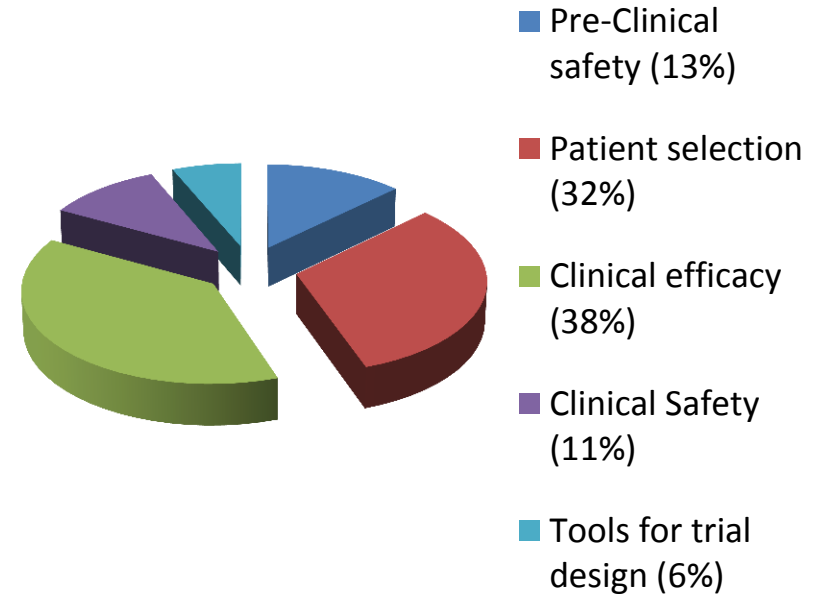
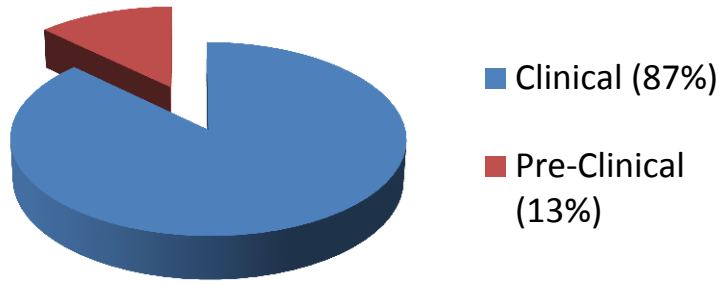
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Document(s)	Language	Status	First published	Last updated	Effective Date
 Letter of support for skeletal muscle injury biomarkers	(English only)		19/03/2015		
 Letter of support for micro-aneurysm formation rate (MAFR) biomarker	(English only)		21/01/2015		
 Letter of support for Predictive Safety Testing Consortium translational drug-induced kidney injury biomarkers	(English only)		07/11/2014		



Novel Methodologies procedure numbers







Thank you for your attention

Further information

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