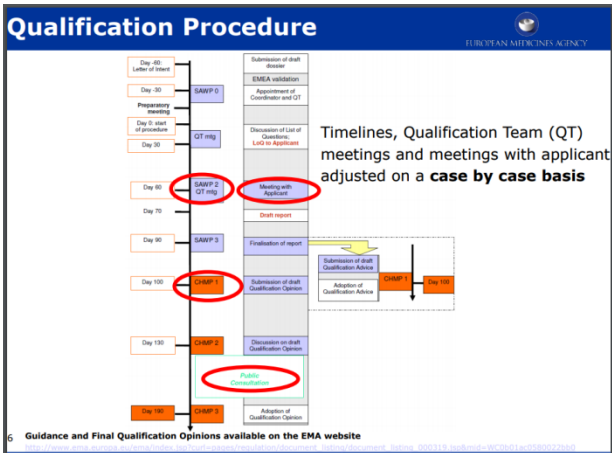
IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Orphan Drug Development Guidebook

Building Block E110

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	EMA qualification of novel methodologies for medicine development (EMA-Qualification)
References	https://www.ema.europa.eu/human-regulatory/research-development/scientific-advice-protocol-assistance/qualification-novel-methodologies-medicine-development https://www.ema.europa.eu/documents/presentation/presentation-chmp-qualification-novel-methodologies-efthymios-manolis_en.pdf https://www.ema.europa.eu/en/human-regulatory/overview/fees-payable-european-medicines-agency
Description	The EMA qualification process is a voluntary, scientific pathway leading to either a CHMP (Committee for Medicinal Products for Human Use) 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. The development of medicines for rare diseases is often hampered by the scarcity of data available, the lack of Natural History Studies and the difficulties to collect existing data,

	aggregate and analyze it in a way that would be suitable for a regulatory assessment, e.g. acceptance of a surrogate endpoint, robust grounds to demonstrate Major Contribution to Patient Care/Significant benefit. The use of new, non-conventional or infrequently used methods during drug development for rare diseases may find regulatory reluctance and become a major issue at the time of marketing authorization application assessment. Qualification process may avoid such issues if done early in the development process. 
Category	Regulatory Building Block
Geographical scope	European Union
Availability	Applicants developing medicines for rare and non-rare diseases using innovative/novel methodologies. This qualification process addresses qualification of biomarkers or other tools such as PROMs, developed by consortia, networks, public/private partnerships, learned societies or pharmaceutical industry for a specific intended use in pharmaceuticals R&D.
Scope of use	The existing scientific advice/protocol assistance procedure is prospective advice related to a specific product(s), indication(s) or technology within a development programme. The existing scientific advice/protocol assistance procedure is not affected by the qualification procedure. To facilitate parallel submissions of applications for drug biomarker qualification or clinical outcome assessment to EMA and to the 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.
Stakeholders	• CHMP • Consortia • Networks • Public/Private Partnerships • Expert societies • Pharma • CROs • Software developers, etc…
Enablers / Requirements	Submit an application: Letter of intent for request of Qualification of Biomarkers/Clinical Outcome Assessments (COAs) in a joint FDA-EMA Submission
Output	• CHMP qualification opinion and scientific assessment 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; the CHMP makes its evaluation open for public consultation, and is open to scientific scrutiny and discussion (public document). • 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 (confidential document shared only with the applicant). • Based on the qualification advice a letter of support may be proposed by EMA as an option, when the novel methodology under evaluation cannot yet be qualified but is shown to be promising based on preliminary data. This letter includes a high level summary of the novel methodology, context of use, available data and on-going/future investigations. Letters of support will be made publicly available on the EMA website subject to sponsor's agreement. The objective of the letter of support is to encourage the efforts for data sharing and facilitate studies towards qualification for the novel methodology under evaluation.
Best time to apply and time window	Early in the development – before the design of clinical trials so that the methodologies can be embedded into the design once qualified.

Expert tips	PROs: • Having this process of Qualification of the Methodologies used ahead of the assessment phase is a strong asset because it ensures that the data submitted to the regulators (here the EMA) would fit the requirements. • The publication of qualification opinions in open access allows advancement in research methods and improves efficiency of the procedure. CONs: • Keeping qualification advices confidential may decrease efficiencies and may difficult the dissemination of best practices to groups sharing similar research objectives.