European Federation of Pharmaceutical Industries and Associations

Current references on clinical endpoints derived from Digital Health Technologies

This document lists current relevant references for the development, validation, and deployment of Digital Health Technologies to collect clinical measures and derive (novel) clinical endpoints in drug development. It has been established by the EFPIA working group on Digital Endpoints and can be used as an introduction into the field.

Last update: October 2022

Documents applicable in the European Union (issued by or related to the EMA)

Medical Device Regulation (MDR) and In-vitro Diagnostics Regulation (IVDR)

EMA webpage on Medical Devices

Medical Device Coordination Group[1]: MDCG 2021-24 (on classification of medical devices) / MDCG 2020-16 rev 1 (on classification of IVD) / MDCG 2020-1 (on Clinical Evaluation (MDR) / Performance Evaluation (IVDR) of Medical Device Software) / MDCG 2019-11 (on Qualification and Classification of Software in MDR and IVDR) / MDCG 2021-6 (on Q&A clinical investigations (MDR)) / MDCG 2022-10 (Q&A on the interface between CTR and IVDR)

Complex Clinical Trials – Q&A

EMA Guideline on computerised systems and electronic data in clinical trials (draft)

Q&A for applicants, marketing authorisation holders of medicinal products and notified bodies with respect to the implementation of the MDR and IVDR

On Qualification Programs

EMA's Q&A - Qualification of digital technology-based methodologies to support approval of medicinal products

[1] The Medical Device Coordination Group (MDCG) deals with key issues from the medical devices sector, from Notified Body oversight or standardization to market surveillance, passing by international matters, new technologies and clinical investigation.


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EMA Qualification of novel methodologies for drug development: guidance to applicants

EMA essential considerations for successful qualification of novel methodologies

On Specific Use Cases – Qualifications Opinions and Letters of support

EMA Opinions and Letters of support on the qualification of novel methodologies for medicine development

EMA Letter of Support for Mobilise-D digital mobility outcomes as monitoring biomarkers – 2020

EMA Letter of Support for Mobilise-D digital mobility outcomes as monitoring biomarkers – 2021 (FUP)

EMA Qualification opinion on stride velocity 95th centile as a secondary endpoint in Duchenne Muscular Dystrophy measured by a valid and suitable wearable device – 2019

EMA Qualification opinion on PROactive in COPD – 2018

EMA IDEA-FAST qualification advice request submitted to EMA – IDEA-FAST - 2021

Documents applicable in the United States (issued by or related to the US FDA)

FDA's Draft Guidance Document on Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

FDA's BEST (Biomarkers, EndpointS, and other Tools) Resource - FDA-NIH Biomarker Working Group

FDA's Roadmap to Patient-Focused Outcome Measurement in Clinical Trials

FDA Patient-Focused Drug Development Guidance Series for Enhancing the Incorporation of the Patient's Voice in Medical Product Development and Regulatory Decision Making

FDA Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments (draft)

FDA's Guidance on Computerized Systems used in Clinical Trials

On Qualification Programs

FDA's Drug Development Tool (DDT) Qualification Programs

FDA's Biomarker Qualification Program

FDA's Clinical Outcome Assessment (COA) Qualification Program

FDA's Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program

See also: FDA Digital Health Center of Excellence


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Initiatives from organizations and consortiums

Innovative Medicines Initiatives: IDEA-FAST / Mobilise-D / Radar-CNS / Radar- AD

Digital Medicine Society (DiMe): The Playbook: Digital Clinical Measures , the DiMe's Library of Digital Endpoints and more resources from DiMe

ICH: Reflection Paper on Patient Focused Drug Development / ICH E6 R3 draft principles on Good Clinical Practices / ICH E8 (R1) – Harmonized Guideline on General Considerations for Clinical Studies

Clinical Trials Transformation Initiative (CTTI): Developing Novel Endpoints Generated by Digital Health Technology for Use in Clinical Trials and more resources from CTTI

TransCelerate Biopharma Inc.: focus on Patient Technology / Implementation Framework / Regulatory Landscape Tool.

Patient Focused Medicine Development (PFMD)

Critical Path Institute: Active programs / Applying Digital Technologies to Developing Endpoints for Neonatal Trials

Health XL: Digital Health Vendor Assessment for Clinical Trials

NESTcc: Data Quality Framework

Relevant publications in the field

Vasudevan S. et al. - Digital biomarkers: Convergence of digital health technologies and biomarkers - 2022 [FDA CDRH / Digital Health Center of Excellence]

Mori et al. - Quantifying the Benefits of Digital Biomarkers and Technology-Based Study Endpoints in Clinical Trials: Project Moneyball – 2022

Crouthamel *et al.* – Developing a Novel Measurement of Sleep in Rheumatoid Arthritis: Study Proposal for Approach and Considerations - 2021 [supported by Transcelerate]

Goldsack J. *et al.* - Evaluation, Acceptance, and Qualification of Digital Measures: From Proof of Concept to Endpoint – 2021 [supported by DiMe]

Servais et al. - First Regulatory Qualification of a Novel Digital Endpoint in Duchenne Muscular Dystrophy: A Multi-Stakeholder Perspective on the Impact for Patients and for Drug Development in Neuromuscular Diseases - 2021

Stephenson et al. - Digital Progression Biomarkers as Novel Endpoints in Clinical Trials: A Multistakeholder Perspective – 2021 [supported by Critical Path Institute]

Goldsack et al. - Verification, analytical validation, and clinical validation (V3): the foundation of determining fit-for-purpose for Biometric Monitoring Technologies (BioMeTs) - 2020 [supported by DiMe]


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Kruizinga *et al.* - Development of Novel, Value-Based, Digital Endpoints for Clinical Trials: A Structured Approach Toward Fit-for-Purpose Validation - 2020

Walton *et al.* - Considerations for development of an evidence dossier to support the use of mobile sensor technology for clinical outcome assessments in clinical trials - 2020

Manta *et al.* - Digital Measures That Matter to Patients: A Framework to Guide the Selection and Development of Digital Measures of Health - 2020

Taylor et al. - Outcome measures based on digital health technology sensor data: data- and patient-centric approaches - 2020

Cerreta et al. – Digital technologies for medicines: shaping a framework for success - 2020

Coravos et al. - Developing and adopting safe and effective digital biomarkers to improve patient outcomes - 2019

Polhemus et al - Accelerating Adoption of Patient-Facing Technologies in Clinical Trials: A Pharmaceutical Industry Perspective on Opportunities and Challenges - 2018 [supported by Transcelerate]

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