Are Digital Endpoints Fit for Health Technology Assessment?

ISPOR Europe 2024

19th November, 13:45 – 14:45 CET

NICE National Institute for Health and Care Excellence

Introducing the panel

Moderator: Jeanette Kusel

Programme Director – Methods, Research and Health Economics,

NICE

Professor Lynn Rochester

Professor of Human Movement Science,

Newcastle University

Dr Jacoline Bouvy

Programme Director – Medicines Evaluation,

NICE

Dr Lada Leyens

Regulatory Lead,

DEEP Measures

What are digital endpoints?

Endpoints in a clinical trial that are derived using sensor-generated data or other digital technology, often collected outside of the clinical setting

Landers M, Dorsey R, Saria S. 2021. Digital endpoints: definition, benefits and current barriers in accelerating development and adoption. *Digital biomarkers*, 5:216-23

NICE

Questions to be addressed by the panel

What are the benefits and limitations of digital endpoints?

Are there any examples where digital endpoints are at the point where they are ready for use by HTA decision makers?

What further work in this field is needed?

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Poll question 1

1. Do you think digital endpoints will be a key evidence source used by HTA bodies at the current time?
    A. Yes
    B. No
    C. Limited to certain circumstances
    D. Unsure

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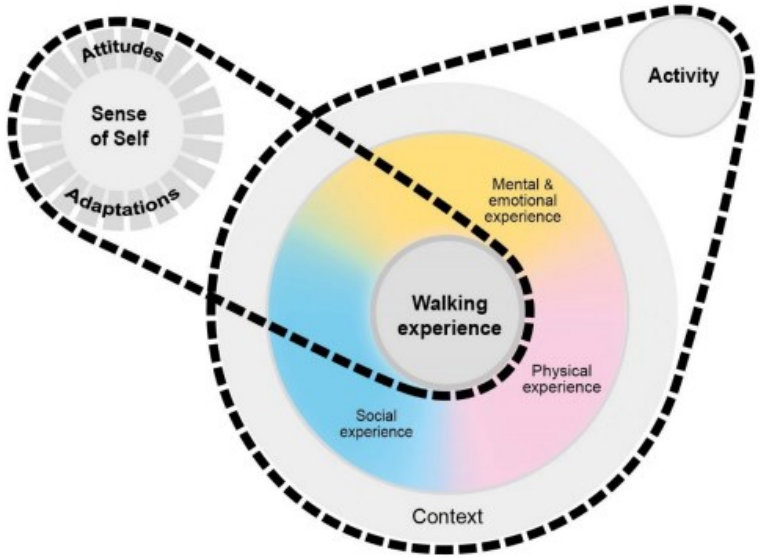
Poll question 2

2. Do you think digital endpoints will be a key evidence source used by HTA bodies in the future?
    A. Yes
    B. No
    C. Limited to certain circumstances
    D. Unsure

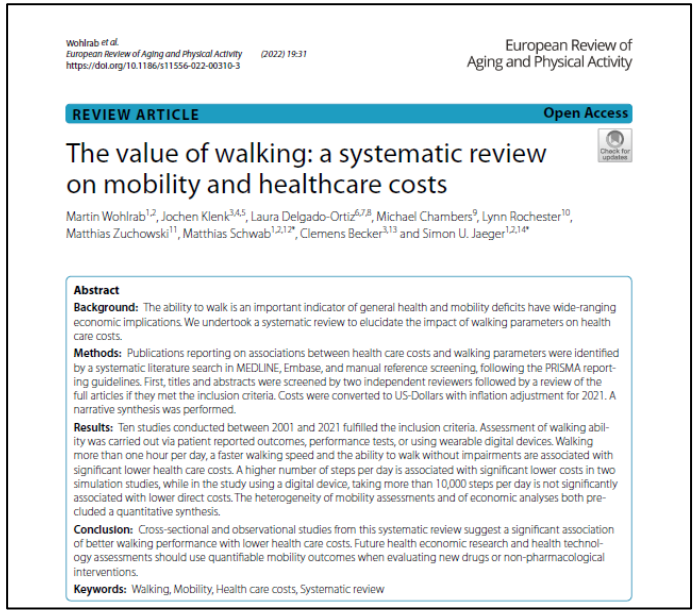
Connecting digital mobility assessment to clinical outcomes for regulatory & clinical endorsement

Professor Lynn Rochester
Newcastle University, UK

Measuring What Matters - Mobility



Delgado-Ortiz et al., 2023



Wohlrab et al.
European Review of Aging and Physical Activity (2022) 19:31
https://doi.org/10.1186/s11556-022-00310-3

European Review of Aging and Physical Activity

REVIEW ARTICLE Open Access

The value of walking: a systematic review on mobility and healthcare costs

Martin Wohlrab[1,2], Jochen Klenk[3,4,5], Laura Delgado-Ortiz[6,7,8], Michael Chambers[9], Lynn Rochester[10], Matthias Zuchowski[11], Matthias Schwab[1,2,12*], Clemens Becker[3,13] and Simon U. Jaeger[1,2,14*]

Abstract

Background: The ability to walk is an important indicator of general health and mobility deficits have wide-ranging economic implications. We undertook a systematic review to elucidate the impact of walking parameters on health care costs.

Methods: Publications reporting on associations between health care costs and walking parameters were identified by a systematic literature search in MEDLINE, Embase, and manual reference screening, following the PRISMA reporting guidelines. First, titles and abstracts were screened by two independent reviewers followed by a review of the full articles if they met the inclusion criteria. Costs were converted to US-Dollars with inflation adjustment for 2021. A narrative synthesis was performed.

Results: Ten studies conducted between 2001 and 2021 fulfilled the inclusion criteria. Assessment of walking ability was carried out via patient reported outcomes, performance tests, or using wearable digital devices. Walking more than one hour per day, a faster walking speed and the ability to walk without impairments are associated with significant lower health care costs. A higher number of steps per day is associated with significant lower costs in two simulation studies, while in the study using a digital device, taking more than 10,000 steps per day is not significantly associated with lower direct costs. The heterogeneity of mobility assessments and of economic analyses both precluded a quantitative synthesis.

Conclusion: Cross-sectional and observational studies from this systematic review suggest a significant association of better walking performance with lower health care costs. Future health economic research and health technology assessments should use quantifiable mobility outcomes when evaluating new drugs or non-pharmacological interventions.

Keywords: Walking, Mobility, Health care costs, Systematic review

Wohlrab et al., 2022

Common	**Important aspect of health**	**Read out of health, QuOL & cost**

Digital technology potential

Mobility assessment **limited**

- Indirect
- Infrequent
- High burden
- Imprecise
- No common standard

PERSPECTIVE Drug Discovery Today • Volume 24, Number 1 • January 2019

ELSEVIER

feature

How soon will digital endpoints become a cornerstone for future drug development?

Philip Boehme[1,2,†], Arne Hansen[2,3,†], Ronenn Roubenoff[4], Joseph Scheeren[5], Maximilian Herrmann[1,2], Thomas Mondritzki[1,2], Jan Ehlers[2] and Hubert Truebel[1,2], hubert.truebel@bayer.com

Digital technologies are transforming healthcare and will provide the basis for more patient-centric innovation in the pharmaceutical industry. Digital endpoints in clinical studies have the potential to drive innovation and reduce costly late-stage failures. This is also currently under consideration by regulatory agencies, such as the US Food and Drug Administration (FDA). The academic–industrial collaboration MOBILISED-D aims to implement and validate real-world walking speed (RWS) as a digital endpoint accepted by regulatory authorities as a first of its class. Previous work has shown that loss of mobility driven by chronic illness and frailty in older patients can be a relevant readout or effect of different diseases and various organ systems.

Features • PERSPECTIVE

- **Direct measurement**
- **Ecologically valid**
- **Inclusive**
- **Patient centric**

Digital mobility outcomes as endpoints in clinical trials/care

Mobilise-D

imi innovative medicines initiative

efpia

>300 experts

12 countries

34

universities, pharmaceutical, technology, CROs

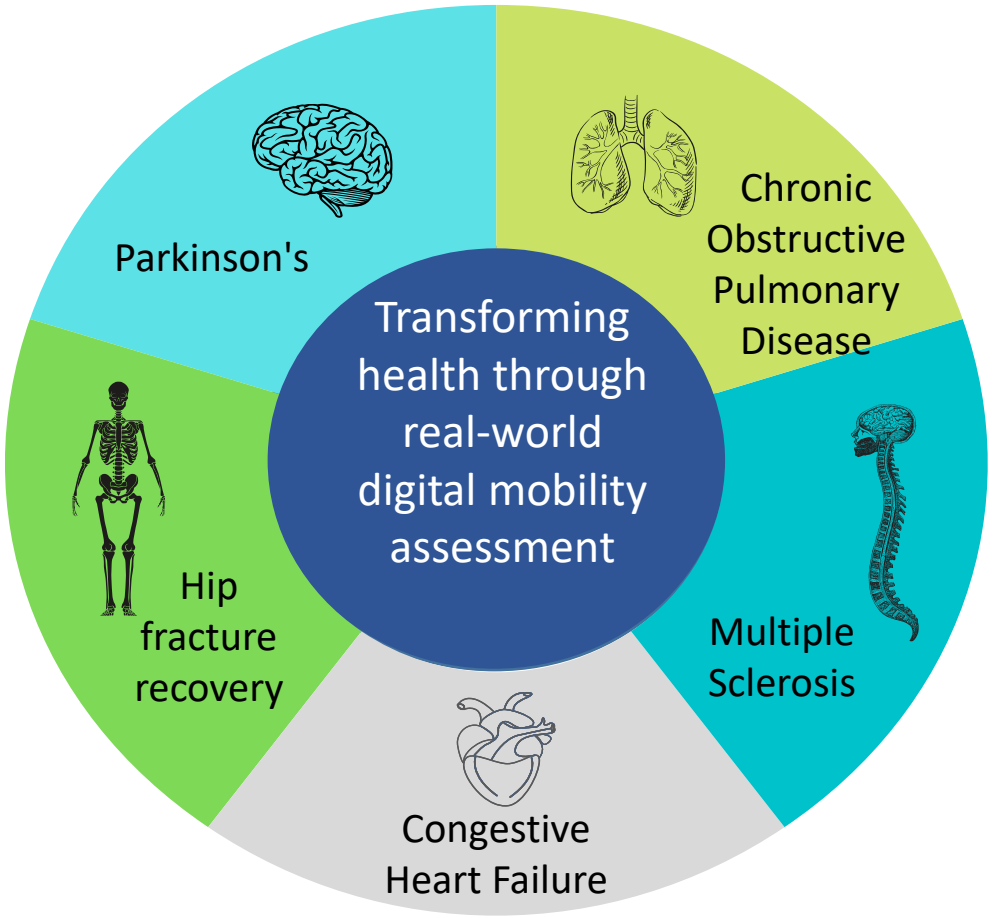
patients & public

€ 50 m

2019-2024

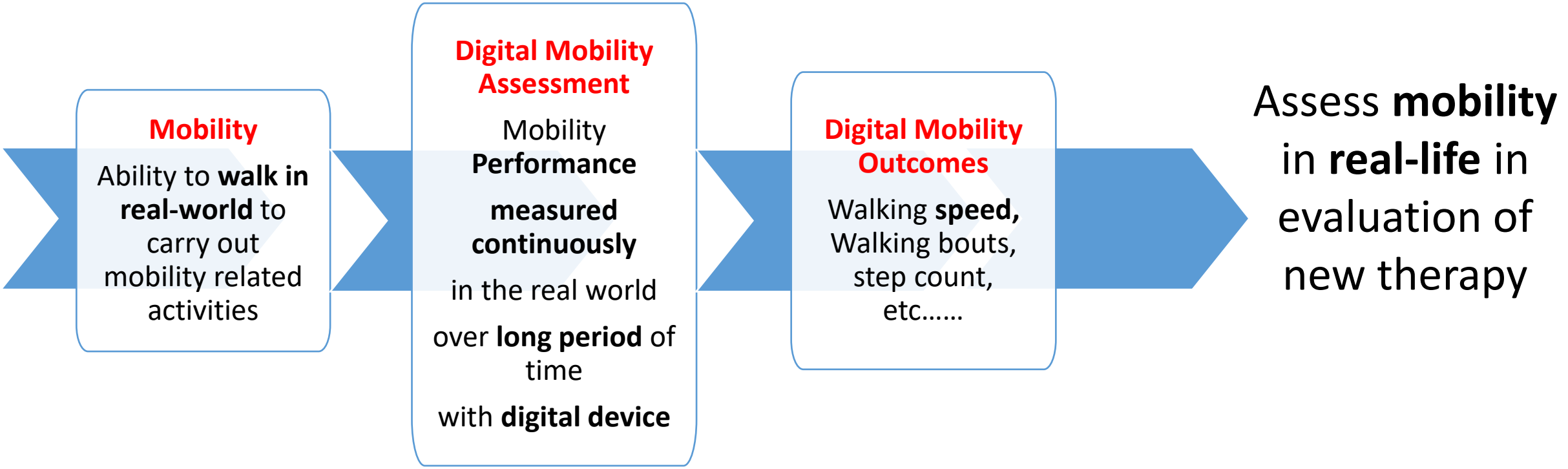
Are digital endpoints fit for health technology assessment? Rochester_ISPOR 2024

Aim - Comprehensive **digital technology solution** to **continuously** assess **real-world mobility**



Primary Objective - qualification of new method by **regulatory authorities**

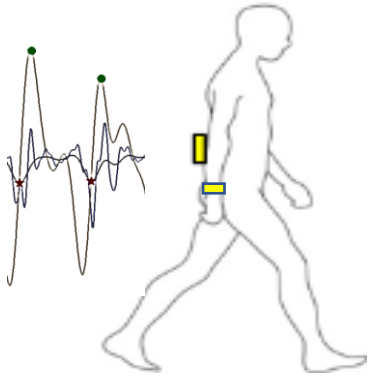
Digital Mobility Assessment & Outcomes



Rochester et al., 2020; Viceconti et al., 2020, 2022

Overall plan

Technical Validation Study	Clinical Validation Study
from device to digital mobility outcomes	*from digital mobility outcomes to health status*



Digital data from wearable device

→ Digital mobility outcome(s) (DMO) →

Health status

Patient groups

Regulatory authorities

Rochester et al., 2020

Clinical Validity of Digital Mobility Outcomes

- **N = 2400**
- **PD, MS, COPD, Hip Fracture**
- 2 years – 6 month FU
- 2021-2024
- Detailed clinical & mobility characterisation
- Digital mobility assessment
  - 7 days/24 DMOs

- 16 sites/10 countries
- 80,000+ days
- 120Tb multimodal data
- 90%+ compliance
- Generalisable

- Reliable
- Minimum wear time
  - **3 days@12 hours/day**
- Acceptable
- High compliance
- Clinically validity (**construct** & ability to detect **change; predictive**)

Methods | **Scalability** | **Findings**

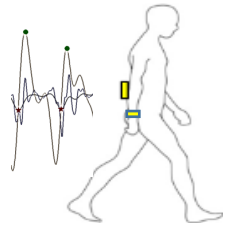
Mikolaizak et al., PLOS ONE, 2022

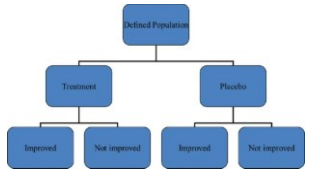
Development pathway of a DMO - regulatory

2019 — Mobilise-D — 2024 — SUSTAIN — Mobilise-D

Development | **Adoption**

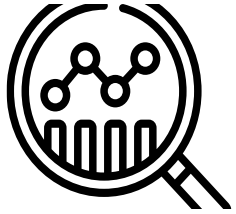
Technical Validation → Clinical Validation → Intervention clinical trial → Health Authorities → Qualification of DMO → More therapies to improve mobility

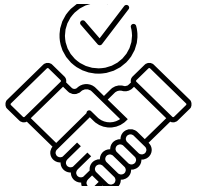




✓ | ✓ Observational | ⊗ Randomized controlled trial | ✓ 2 x QA LoI meetings | ⊗

Impact





- Validated, open-access **algorithms** & reference **data**
- Digital mobility assessment **feasible** in clinical trials
- **Guidelines** for technology & clinical trial application
- Integrated **patient voice** in all steps
- Foundational knowledge of DMOs
- **Next generation** of academic, research, & clinical leaders
- **Regulatory discussions** on digital mobility outcomes
- **Digital mobility** outcome development **roadmap**

Looking forward

- Address gaps for regulatory approval (clinical trials) (SUSTAIN + others)
- Share data/learning & build networks
- Repurpose for multiple use cases
- Extend evidence for HTA

Are digital endpoints fit for HTA?

Dr Jacoline Bouvy
Programme Director Medicines Evaluation

NICE National Institute for Health and Care Excellence

What should endpoints capture for them to be useful for HTA?

- Diseases can be complex and impact the person with the condition in many different ways
    - How much of the entirety of the condition and how it impacts the patient is captured by the endpoint?
- For a digital endpoint to be useful for HTA, it needs to:
    - Measure a clinically relevant component of the condition (e.g. functioning/mobility)
    - It needs to be well-established what the association is between the digital endpoint and health-related quality of life and/or survival
    - Crucially, evidence to support the assumption that an improvement in the digital endpoint also has a corresponding impact on other outcomes is required

What does that mean for new digital endpoints?

- If this is an indication with existing technologies as part of standard of care, can you still do an indirect treatment comparison using your clinical trial?
- What does the natural history of the disease look like when measured by the digital endpoint?
- Is the endpoint also usable in clinical practice (will it generate real-world evidence?)
- For HTA that involves cost-effectiveness modelling: how is the endpoint going to define your economic model?

NICE National Institute for Health and Care Excellence

Thank you.

DEEP | Building Digital Measures

ISPOR 2024

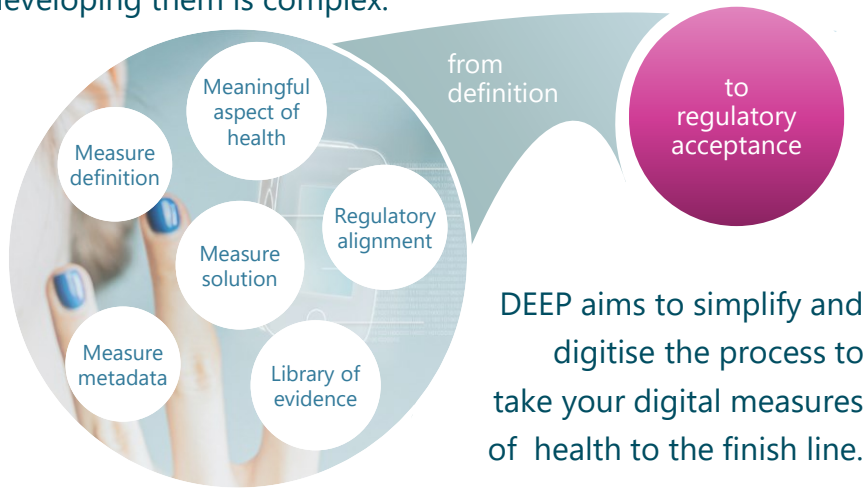
Are Digital Endpoints fit for Health Technology Assessment?

Importance of collaboration, simplification, structured content, sustainability and reliance across stakeholders

DEEP Measures OY
19 November 2024
www.deepmeasures.health

Introduction to DEEP

Digital Measures unlock insights into human health but developing them is complex.



DEEP aims to simplify and digitise the process to take your digital measures of health to the finish line.

We collaborate to unlock digital measures to transform patient health.

We seek to connect, not to compete with an ecosystem to collaborate

How DEEP supports digital measure development

Digital Measure Builder

A structured way to construct your digital measure

Private & Public Catalogs

Find components to build your digital measure.

Development Platform

Co-create digital measures & gain acceptance

Services Marketplace

Specialists help you complete your measure

DEEP supports drug development from discovery to post-approval.

Exploratory Phase

Explore, test & plan new ways to measure your asset.

Early Development Phase

Find digital solutions, improve validation work and collaborate to develop new measures.

Late Development Phase

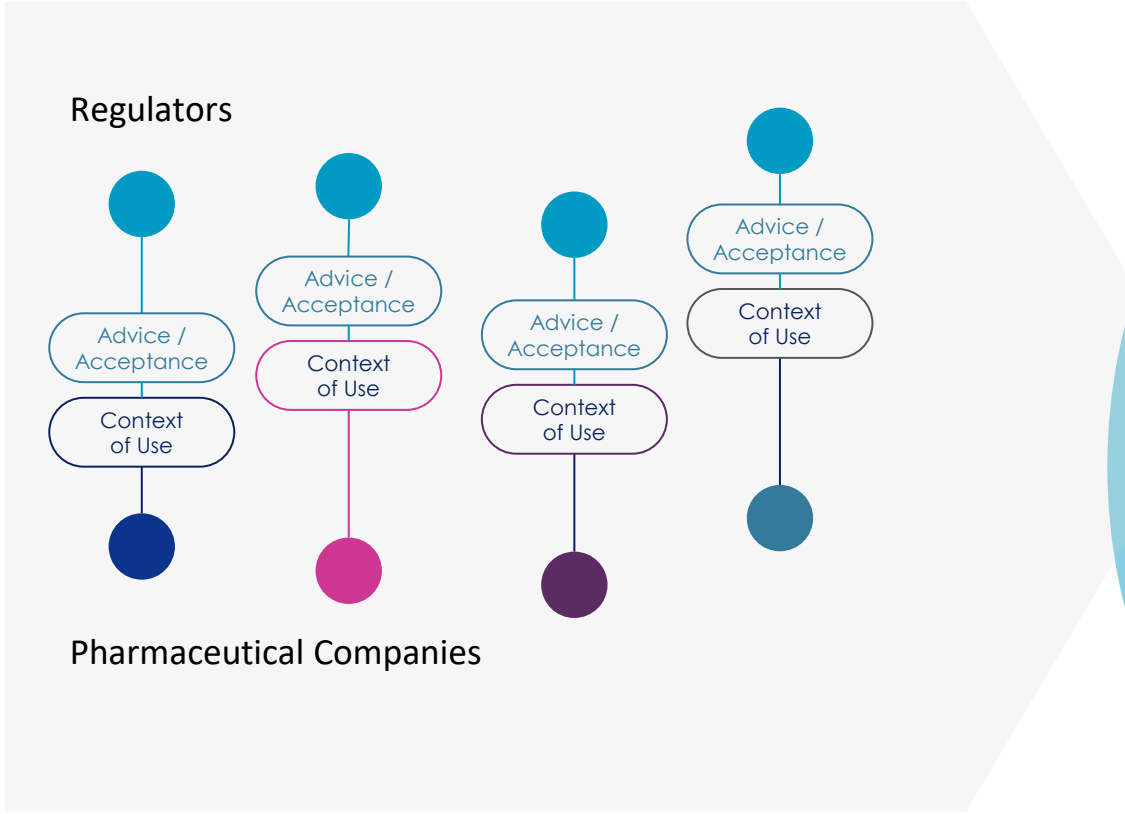
Get regulatory acceptance to use new measures in pivotal trials.

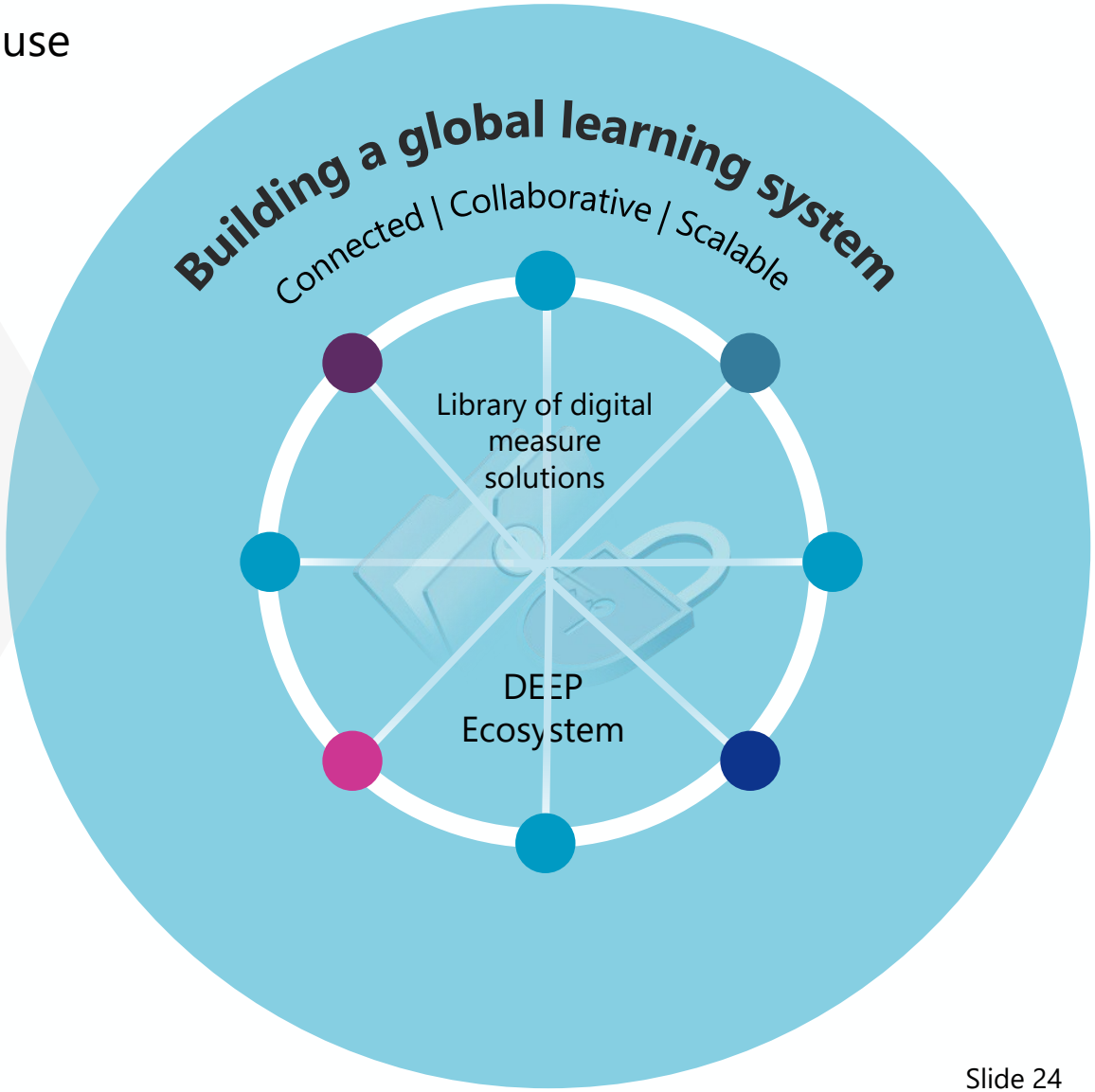
Post Approval & Marketing

Adapt and re-use your measures in clinical practice and post-approval settings.

Today's model does not scale

One-on-one engagements with specific contexts of use





A complex environment for global sponsors: At the interface of drug and technology regulatory frameworks as well as global development

	The DHT: Regulatory identity and documentation?	**The Data:** Quality and clinical operations?	**The digital endpoint:** Meaningful, relevant and robust?
Multiple components and evidence with distinct regulatory considerations	Regulatory identity: Is it a medical device? Is the computerised system validated?	Does it comply with privacy, security, GDPR, safety & environmental requirements? Has it been collected according to GxP principles?	Does it represent an outcome that is relevant for patients or is linked to the pathophysiology of the disease and can inform a regulatory decision? Is it sensitive to change?
Regulatory Stakeholders	Notified Bodies; NCAs; EMA; Ethics Committees	Ethics Committees; NCAs; EMA	EMA; HTA
Relevant Regulatory guidances EU	Medical Device Regulation Product specific EU legislation (Radio Equipment Directive EMA guideline on Computerised Systems and Electronic Data in Clinical Trials Draft RP on the use of artificial intelligence in the lifecycle of medicines	General Data Protection Regulation Clinical Trial Regulation ICH E6: Good Clinical Practice EU recommendation paper on decentralised elements in clinical trials	EMA Q&A: Qualification of digital technology-based methodologies to support approval of medicinal products ICH E9: Statistical principles for CTs Disease specific guidances for endpoints HTA guidances on endpoints
Relevant Regulatory guidances USA	FDA U.S. FOOD & DRUG ADMINISTRATION Overview of Device Regulation Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers Using Artificial Intelligence & Machine Learning in the Development of Drug & Biological Products Discussion Paper	Regulations: Good Clinical Practice and Clinical Trials ICH E6: Good Clinical Practice trials Conducting Clinical Trials With Decentralized Elements	Digital Health Technologies for Remote Data Acquisition in Clinical Investigations ICH E9: Statistical principles for CTs Disease specific guidances for endpoints

BM= Biomarker COA = Clinical Outcome Assessment; DHT = Digital Health Technology; EC= Ethic Committees; EMA= European Medicines Agency; HTA= Health Technology Assessment Body; NCA= National Competent Authority; CT= Clinical Trial

*Digital Endpoint = precisely defined variable intended to reflect an outcome of interest that is statistically analysed to address a particular research question, that is derived from or includes a digital measurement (Definition in EMA Q&A) . Link to key resources from EFPIA digital endpoints sub-team.

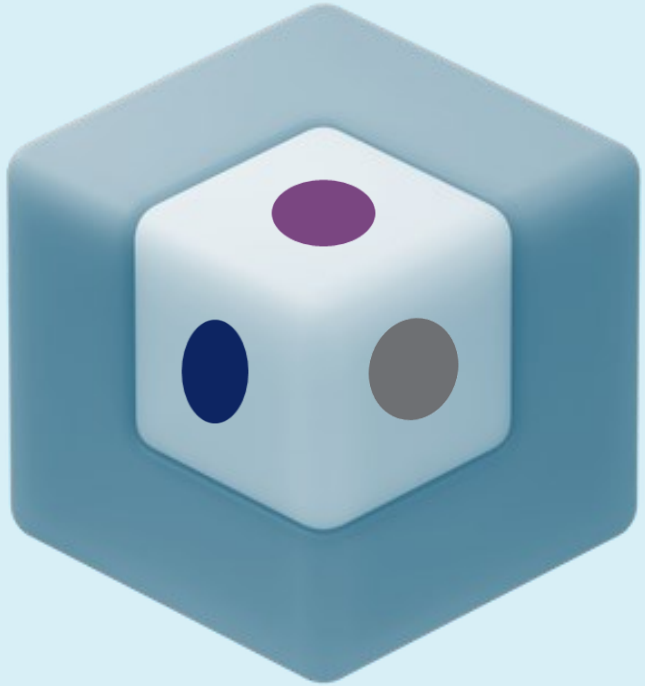
Stack Model

A better way to construct digital measures using a structured model to standardise digitally-derived endpoints

What and why to measure?
Measurement Definition

How to measure?
Device-agnostic Target Solution Profile

What technology?
Digital Measurement Solutions



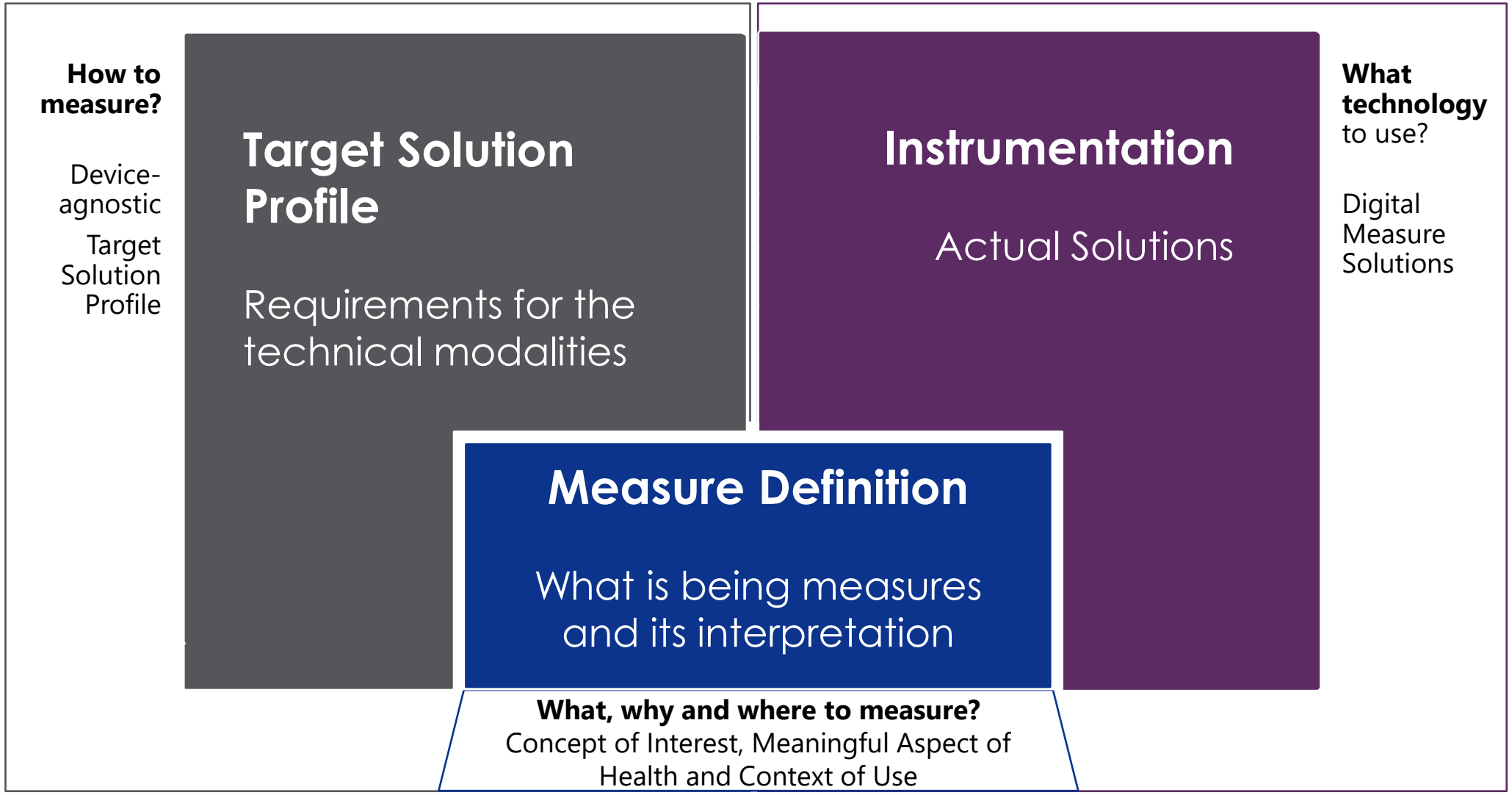
Keep data current with lifecycle management and version control.

Quickly find missing data to build a complete solution.

Create structured information and evidence for submission to regulators.

Adapt and re-use measures in other contexts.

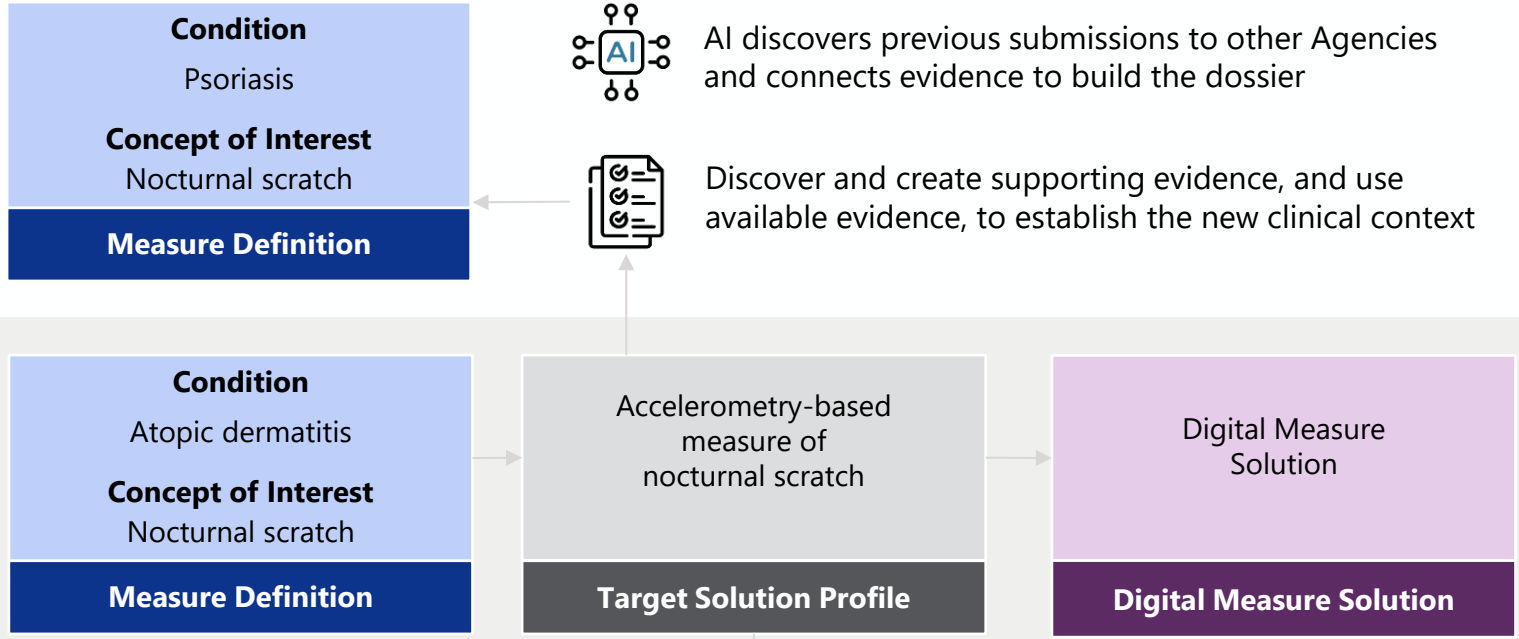
The Stack Model: Structured Content and Evidence



Target Solution Profile enables Device-Agnostic Development of Measures

Scenario 1

Extending the Measure to another Condition with the same Concept of Interest

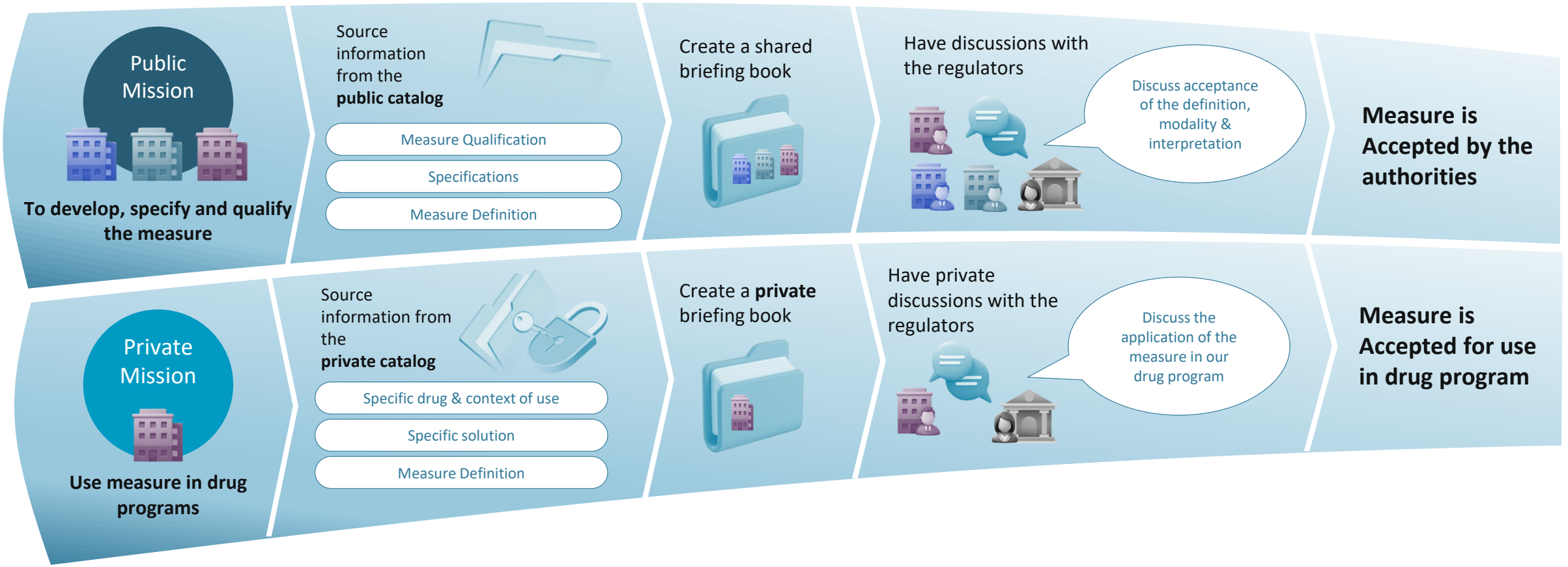


Scenario 2

Developing a new Digital Measurement Solution for current Target Solution Profile

Public & Private Regulatory Pathways

DEEP helps gain acceptance for novel digital measures and to integrate them into drug programs.



What our customers and partners say

The platform provided a neutral and accessible collaboration space to all member companies”

The support, clear understanding of our needs and quick turnaround has been impressive.

About our platform & missions

The platform improves collaboration with the Agency and between the applicant companies

The platform provided a single location for all evidence and materials which allowed easy referencing and viewing of the materials that supported the claims

The platform facilitated the sharing of questions and materials ahead of the meeting and provided grounds for clarification.

DEEP | Building Digital Measures

For more information, browse our website at:

www.deepmeaures.health

Lada Leyens
Founder, Regulatory Lead
Lada@deepmeasures.health

Kai Langel
Founder, CEO
Kai@deepmeasures.health

Poll question 3

3. Given what you've heard, how are you feeling about digital endpoints being used in HTA?

NICE

Poll question 4

4. Do you think digital endpoints will be a key evidence source used by HTA bodies at the current time?
    A. Yes
    B. No
    C. Limited to certain circumstances
    D. Unsure

NICE

Poll question 5

5. Do you think digital endpoints will be a key evidence source used by HTA bodies in the future?
    A. Yes
    B. No
    C. Limited to certain circumstances
    D. Unsure