Challenges in Validating Digital Biomarkers from an Academic Perspective

ACT EU multi-stakeholder methodology workshop

23rd November, Amsterdam

Martin Daumer
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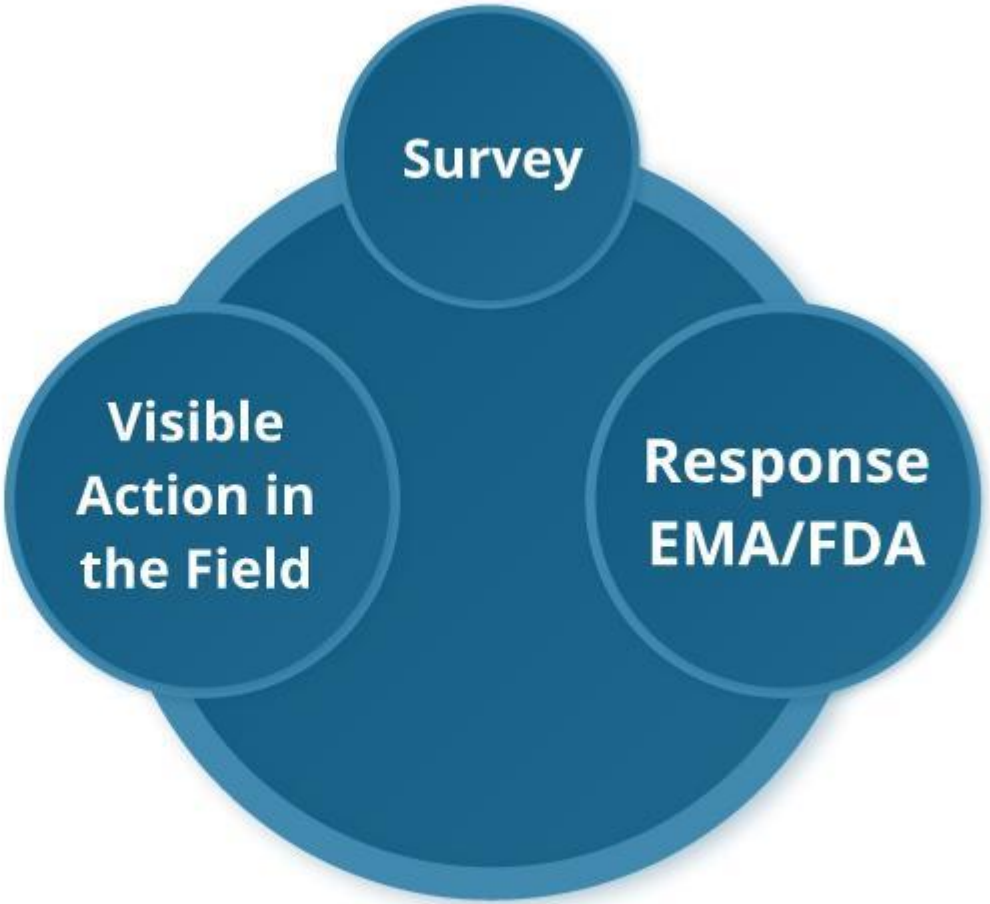


Survey

Regulatory Acceptance of Digital Biomarker Survey: perception of the field

This survey - based on Google Forms - is a cooperative effort of the University of Oxford - MDUK Oxford, Neuromuscular Center, Department of Pediatrics, the TUM - School of Computation, Information and Technology, the Friedrich-Baur-Institute, Neurologische Klinik und Poliklinik, LMU Munich, Else Kröner Fresenius Center for Digital Health, Technische Universität Dresden, The Critical Path Institute and the SLC e.V. - The Human Motion Institute, Munich. The aim is to get a snapshot of the perception in the field of the status and the expectations about the development of the field of digital biomarkers, with a particular focus on the path toward regulatory acceptance of novel endpoints based on data from wearables in clinical trials. A milestone in the field is the positive qualification opinion of the CHMP, July 20 2023 "Qualification Opinion for Stride velocity 95th centile as primary endpoint in studies in ambulatory Duchenne Muscular Dystrophy studies". It is planned to make the results publicly available at conferences and peer-reviewed journals. We hope to contribute to be able to inform the field about perceived importance and barriers. Overcoming these barriers requires collaboration among researchers, clinicians, regulatory agencies, technology companies, and patients. As the field of digital biomarkers continues to evolve, addressing these challenges will be essential to harness the full potential of remote monitoring and real-world data in clinical research.

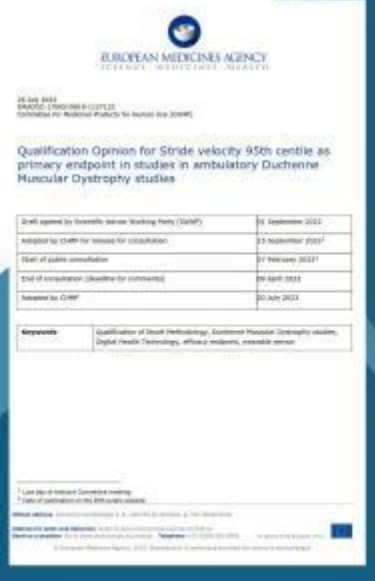
We assume that by filling in the survey, you give your consent. The survey is anonymous. Thank you for your support, the organizers. Martin Daumer and Benedikt Schoser

How do you rate the importance of the following typical barriers for using digital biomarkers as outcome in clinical trials?

Top 2:

Regulatory approval and validation (lack of established standards)
> 79% very high or high

Endpoint Validation (establishing clinical relevance, endpoint variability)
>76% very high or high



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Qualification Opinion for Stride velocity 95th centile as primary endpoint in studies in ambulatory Duchenne Muscular Dystrophy studies

34 respondents (9.10-30.10.2023)
58% Uni, 21% pharma, 21% other

85% Prof or PhD/MD

Overall, how important is the usage of digital biomarkers as outcome measure in phase 3 clinical trials - trials aiming at the approval of medicines in the future?
> 91% very important or important

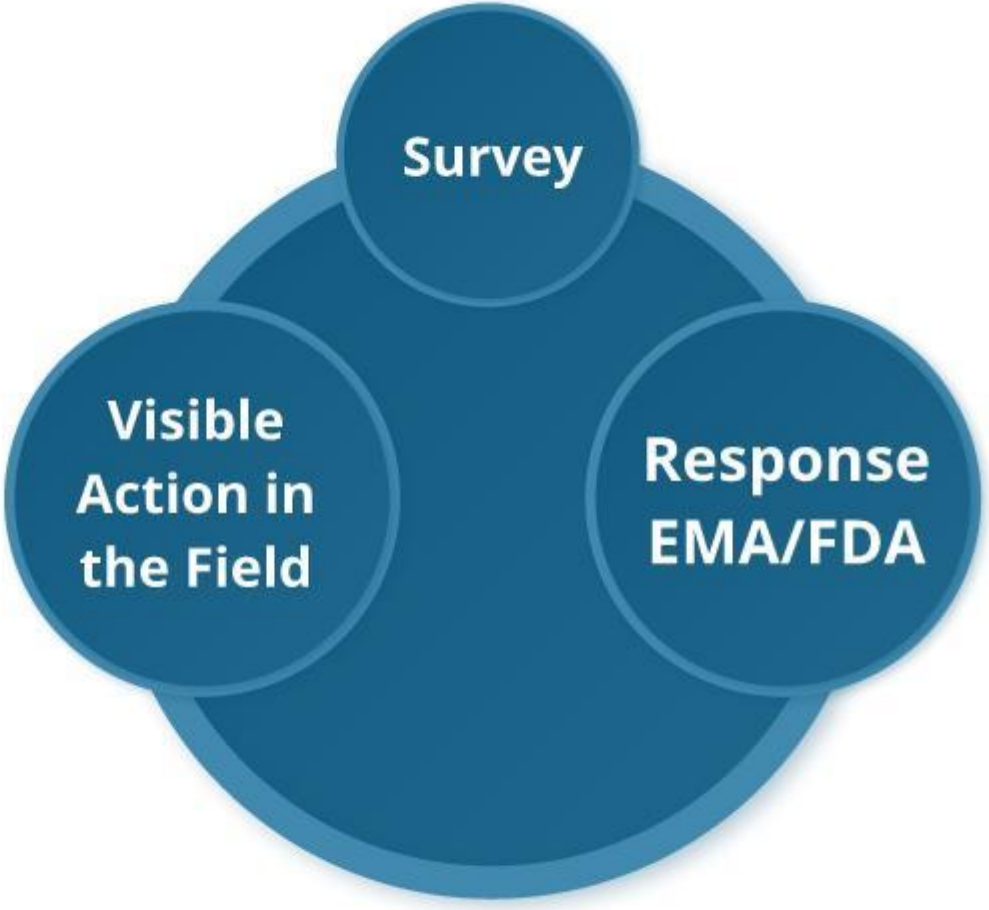
How promising is the concept of the digital biomarker "real world walking speed" as outcome measure in phase 3 clinical trials for diseases other than Duchenne muscular dystrophy?
>79% very important or important

scale from 1 negligible to 5 very important

It has been discussed for MS studies. However, I'm not aware that it has been implemented.

As per relevant EMA and FDA guidance, collaborative groups such as consortia and industry trade associations are encouraged to initiate qualification of new measures as endpoints. This is mainly due to the efforts and amount of data needed for a successful qualification. Accordingly, activities as led by the IMI consortia are ongoing to qualify mobility outcome in different indications, e.g. COPD, HF, and MS (e.g. IMI consortium Mobilise-D).

Yes, this is the work done by the Mobilise-D consortium


Survey
Visible Action in the Field
Response EMA/FDA

nature medicine

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Correspondence | Published: 09 October 2023

First regulatory qualification of a digital primary endpoint to measure treatment efficacy in DMD

Laurent Servais ✉, Damien Eggenspieler, Margaux Poleur, Marc Grelet, Francesco Muntoni, Paul Strijbos & Mélanie Annoussamy

Jean-Yves Hogrel, Institute of Myology, Paris

Nature Medicine **29**, 2391–2392 (2023) | Cite this article

IMI2 call 13, Topic 7: Linking digital assessment of mobility to clinical endpoints to support regulatory acceptance and clinical practice

Topic 7: Linking digital assessment of mobility to clinical endpoints to support regulatory acceptance and clinical practice

Duration 60 months

Budget: EUR 50,2 Mio.

- "We believe that physical activity monitoring using inertial sensors is the most advanced technology relevant to pharmaceutical development, and that RWS is the most advanced endpoint that could be validated within a 2-3 year period."
- "Devices that capture data from the body centre of mass or lower extremities are preferred to those positioned at the wrist."

- Evaluation Summary Report:

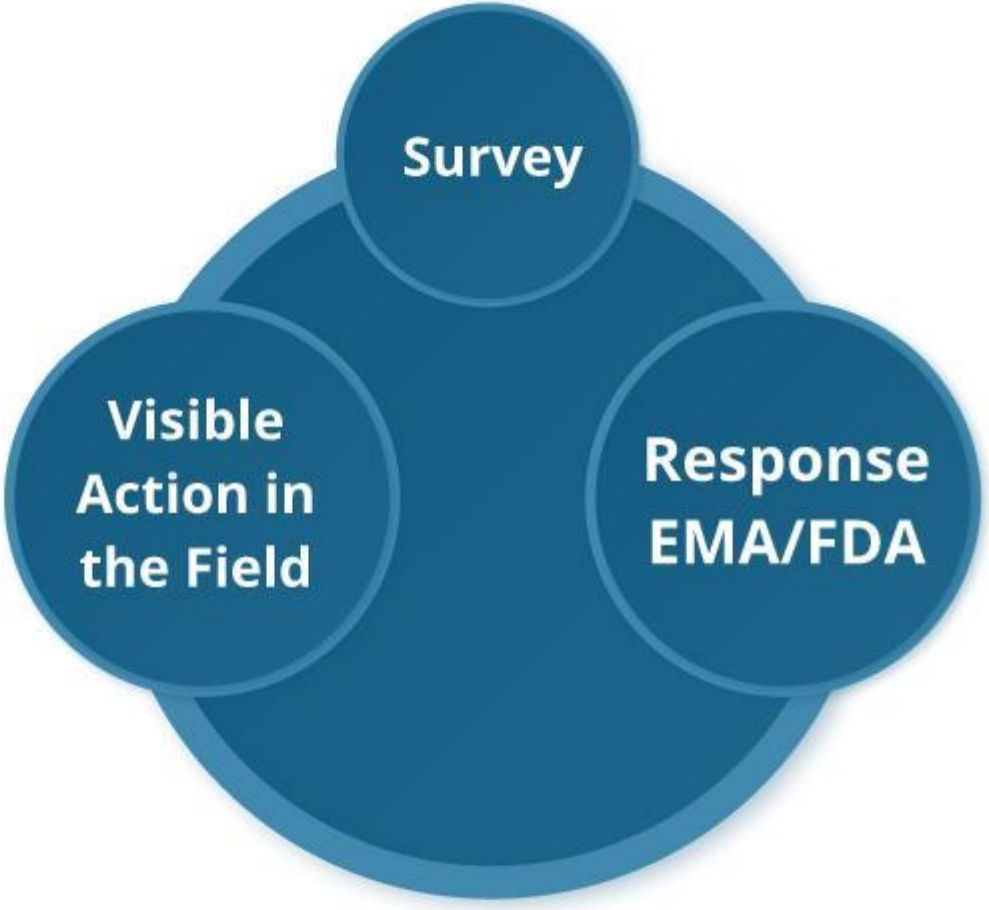
"The concept is sound and benefits from the availability of a large dataset in the required clinical conditions. However, the ambition is low since most of the activities either have been completed or are already ongoing. The consortium plans only to refine their already existing solutions limiting the step beyond the state of the art."

Mobilise-D

MOBILISE-D DATA

Data Sharing Commitment

Data Sharing Policy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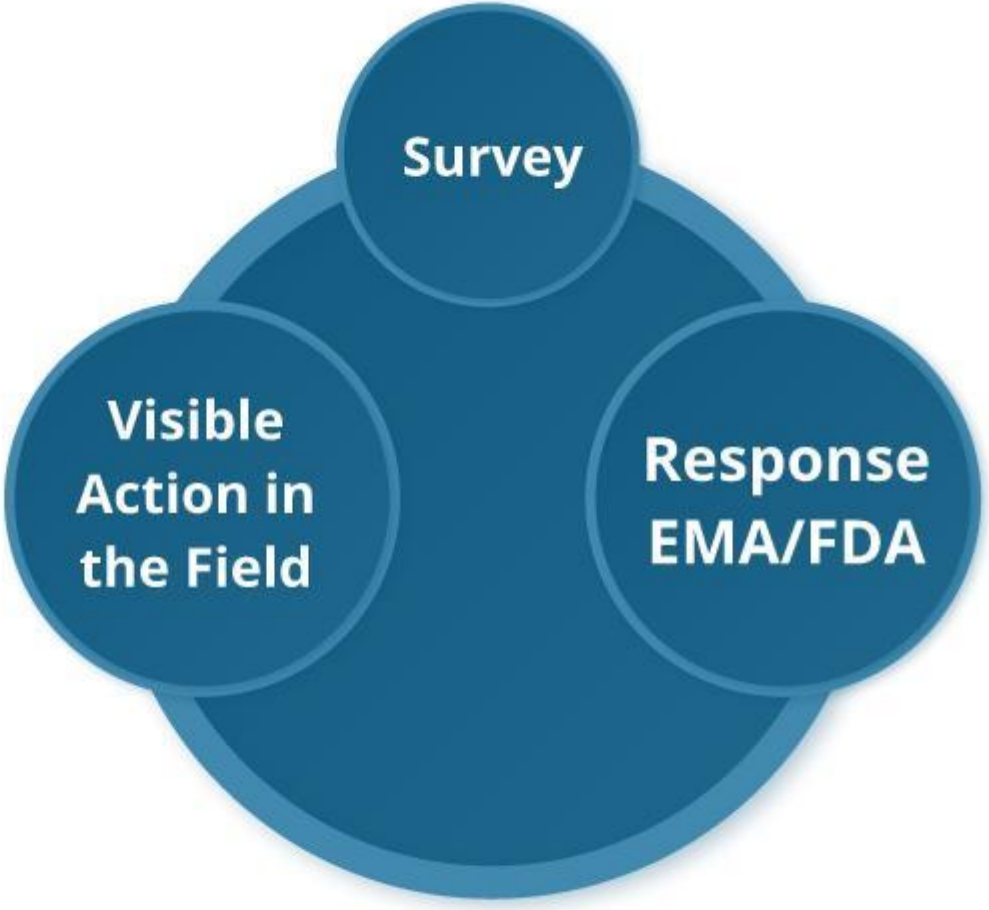
EUROPEAN MEDICINES AGENCY
Letter of support for Mobilise-D digital mobility outcomes as monitoring biomarkers
Drug Regulatory Affairs
actibelt®
Briefing Book
for the EMA Qualification of novel methodologies for drug development
EUROPEAN MEDICINES AGENCY
Qualification advice
Actibelt (Real World Walking Behaviour)
FDA
DDT COA #000106: Actibelt® in Multiple Sclerosis
U.S. FOOD & DRUG
REQUEST FOR QUALIFICATION PLAN
DDT COA #000105: Actibelt® in Sarcopenia
U.S. FOOD & DRUG
DDT COA #000103: ActiMyo®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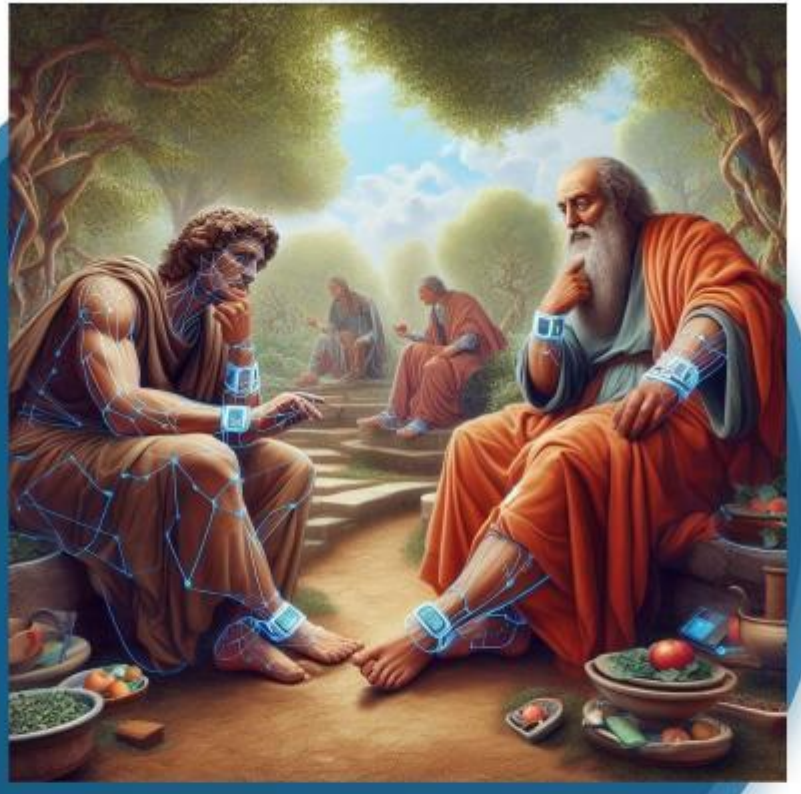
Open Callaborative Platform for Digtial Biomarkers

algorithms and raw data

disease agnostic

device agnostic



Initial focus on human motion - walking speed? MS? Hip/ankle? 6MWT?

"acceleromics"

The International Federation of Multiple Sclerosis Societies is pleased to announce funding for an exciting new research initiative:

International Multiple Sclerosis Trials, Research and Resource Center (IMSTRaRC)

The Sylvia Lawry Centre for Multiple Sclerosis Research (SLCMSR)—Critical review facing the 25 anniversary

Highlights

Abstract

Save the date - 11th **Winter Symposium** of the Human Motion Project - Munich - March 26, 2024
"A philiosophical garden for digital biomarkers"

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