Decision tree supporting **endpoint strategy** for clinical trials utilizing digital measures of physical activity (PA)

CORE MEASURES *of* PHYSICAL ACTIVITY

Digital Measures Development

DATAcc by DiMe

Engage with regulators, early and often

There is a need to use a digital physical activity endpoint in my clinical trial.

Amazing! First, evaluate the existing evidence about each candidate measure from the core set you are considering. For each digital measure, assess the following:

Note: Performance of digital PA endpoint(s) in early phase studies can provide initial evidence of signal detection to inform internal decision-making related to inclusion of novel digital endpoints in later trial phases. In practice, the process of evidence collection may be more circular as continuous evidence is compiled to justify use of new endpoints.

Has the measure been tested in a clinical setting with patients before?

NO

Test a new digital health technology (DHT), its feasibility, usability, & acceptance in patient population

Evidence captured: Utility & usability outcomes in specific patient population; specifications of source data collected from new DHTs; specifications for data operations (collection, storage, & transfer); economic feasibility; operational feasibility; sample data analysis

YES

V3

Has the measure been verified and analytically validated?

NO

Assess evidence on verification & analytical validation of a digital measurement

Evaluate the evidence available related to the performance of a DHT to convert sensor outputs into physiological metrics using a defined data capture protocol in a specific subject population. This process may not be in the scope of pharma companies; data may be made available by manufacturers.

Evidence captured - verification: performance specs of the hardware; sensor level output data; repeatability & reproducibility; firmware & OS specs; data suitability for algorithm development

Evidence captured - analytical validation: specs of algorithmic output metrics; metrics calculations protocol; comparison to reference standard (including protocol & statistical analysis methods); description of the human subjects population; experimental conditions

YES

Has the measure been clinically validated?

NO

Perform clinical validation of a digital measurement

Evaluate whether the physiological metric acceptably identifies, measures, or predicts a meaningful clinical, biological, physical, and functional state or experience, in the stated context of use and specified population.

Evidence captured: definition and concept of the measure; clinical meaningfulness of the digital clinical measure; measured concept of interest (COI); context of use (COU); measured outcomes; assessing a true correlation between the digital clinical measure and the clinical meaningfulness to the patients and their disease indication.

YES

Digital Measure Use

Study phase	Endpoint
Pilot study	Primary, Secondary
Non-pivotal study	Secondary, Exploratory

Digital Measure Use

Study phase	Endpoint
Pivotal study	Primary, Secondary, Exploratory
Non-pivotal study	Secondary, Exploratory

Note: The V3 process is modular and re-review of previous stages or simultaneous analytical and clinical validation can occur in practice

Congratulations!

You have now collected sufficient evidence about the digital measure.

What would you like to do next?

Qualify my new digital measure as a drug development tool (DDT)

Pursue regulatory qualification via the DDT qualification pathway with the U.S. Food and Drug Administration (FDA).

REMEMBER TO:

- ✔ Start with defining concept of interest and the context of use.
- ✔ Gather information about the digital measure in the evidence dossier: Check out the Structure of evidence dossier to support the use of connected sensor products for clinical outcome assessments in clinical trials.

Use my digital measure to study the disease in real-world or post-market settings

It is assumed that collected data are not intended for submission to health authorities for labeling, post-marketing safety commitment, benefit-risk assessment, or any other purpose.

Read more in *The Playbook:*

- ✔ Post-Market Settings - Safety Surveillance Checklist.
- ✔ Post-Market Settings - Considerations for Digital Companion Checklist.

Use my digital measure to generate evidence supporting the label claims of a new treatment

Example: use of a fit-for-purpose digital measure in a drug trial to support regulatory label inclusion.

REMEMBER TO:

- ✔ Test the measure and technology early - in non-pivotal studies.
- ✔ Perform additional research and development to ensure acceptance of the measure as an endpoint by regulatory authorities.
- ✔ Document V3 prior to use.
- ✔ Engage with payers alongside regulators as soon as you make the decision to include a digital endpoint. You can use this decision tool to help determine whether you are ready to implement an integrated evidence plan to ensure your digital endpoints are suitable for regulators **and** payers.