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

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

- **Has the measure been tested in a clinical setting with patients before?**
  - **NO**
  - **Has the measure been verified and analytically validated?**
    - **NO**
    - **Assess evidence on verification & analytical validation of a digital measurement**
      - **Evidence captured: Utility & usability outcomes in specific patient population**
      - **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**
    - **Perform clinical validation of a digital measurement**
      - **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**
    - **Congratulations! You have now collected sufficient evidence about the digital measure.**

- **YES**
  - **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**
  - **NO**
    - **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
  - **NO**
    - **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.

**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).

**Digital Measure Development**

**Core Measures of Physical Activity**

**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.