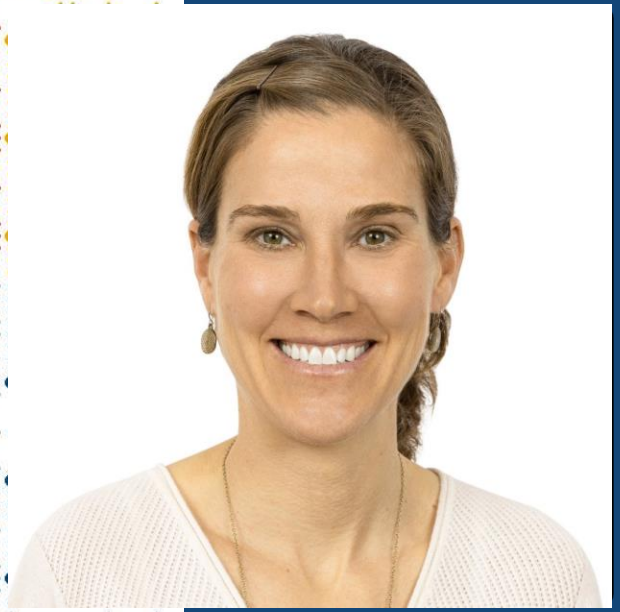
Considerations for driving high quality DHT datasets and aligning with CDISC standards

Kate Lyden and Tayana Pierre-Louis



Meet the Speaker

Kate Lyden

Title: Chief Science Officer

Organization: VivoSense, Inc

Kate Lyden, PhD is the Chief Science Officer for VivoSense, a science and analytics company that develops and validates digital clinical measures and provides end-to-end services for their delivery in regulated clinical trials. In this role, Kate leads a team of scientists dedicate to developing and delivering real-world digital measures that are trusted and valued by all stakeholders. Kate has an extensive and diverse background in the development and implementation of wearable sensor methodologies across clinical, academic, and industry settings

Meet the Speakers

Vanessa Sarrechia

Title: Data Standards Lead

Organization: argenx

Vanessa has more than 10 years of experience in the field of Clinical Data Management and Data Standards development. She is leading a group of Data Standards Managers, supporting the clinical Data Management team at argenx.

Tayana Pierre-Louis

Title: Clinical Data Manager

Organization: argenx

Tayana has more than 20 years of experience in the field of Data Management and more than 6 years in Data Standard. She is working at Clinical Data Management at argenx.

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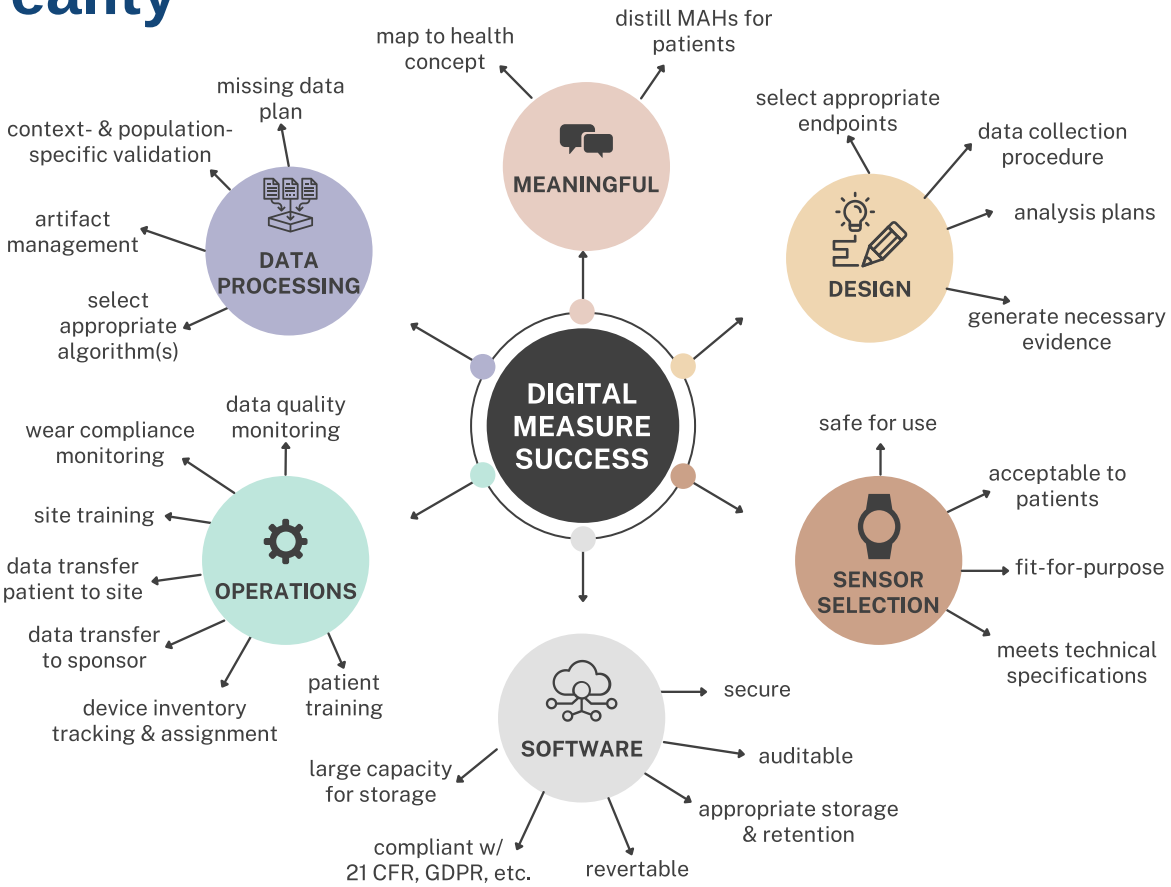
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

- *{Please disclose any financial relationship or conflict of interest relevant to this presentation here OR}*
- *The author(s) have no real or apparent conflicts of interest to report.*

Agenda

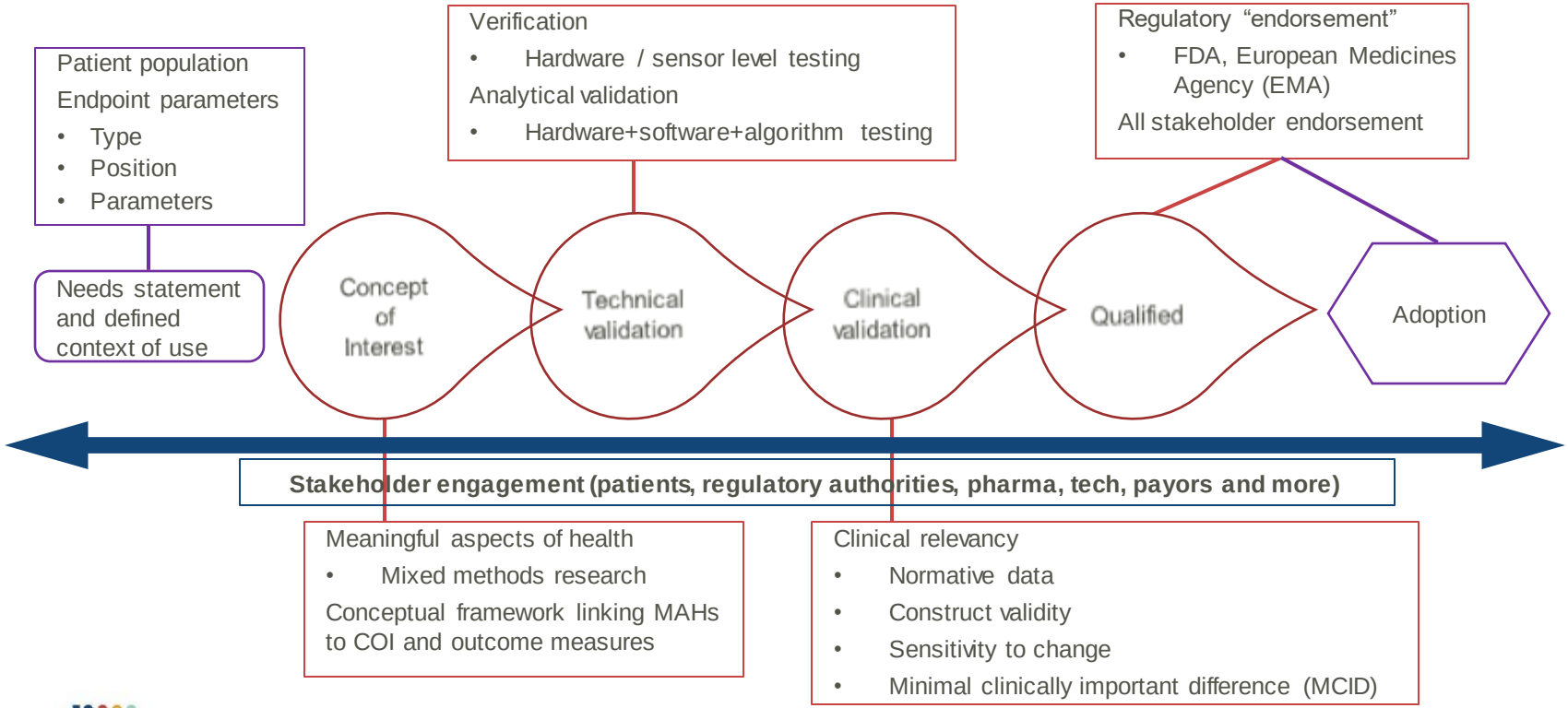
1. **Considerations when using DHT in clinical investigations**
2. SDTM mapping: Use case
3. Key Learnings

DHT reality


DIGITAL MEASURE SUCCESS
MEANINGFUL
map to health concept
distill MAHs for patients
DATA PROCESSING
missing data plan
context- & population-specific validation
artifact management
select appropriate algorithm(s)
DESIGN
select appropriate endpoints
data collection procedure
analysis plans
generate necessary evidence
OPERATIONS
data quality monitoring
wear compliance monitoring
site training
data transfer patient to site
data transfer to sponsor
device inventory tracking & assignment
patient training
SENSOR SELECTION
safe for use
acceptable to patients
fit-for-purpose
meets technical specifications
SOFTWARE
secure
auditable
appropriate storage & retention
revertable
compliant w/ 21 CFR, GDPR, etc.
large capacity for storage

Validation: Establish fit-for-purpose digital endpoints

From exploratory research to efficacy endpoints



Validation: Establish fit-for-purpose digital endpoints

From exploratory research to efficacy endpoints

Measure what you intend to measure

- **Analytical Validity** – Evidence demonstrating the underlying algorithms and data processing techniques derive outcomes that are accurate and reliable in the specific context of use

- **The Problem:** Many different methods to derive measures of wake and sleep behavior from wearable actigraphy sensors
  - No consensus on which are "correct"
  - Most methods have been developed on healthy populations

MVPA

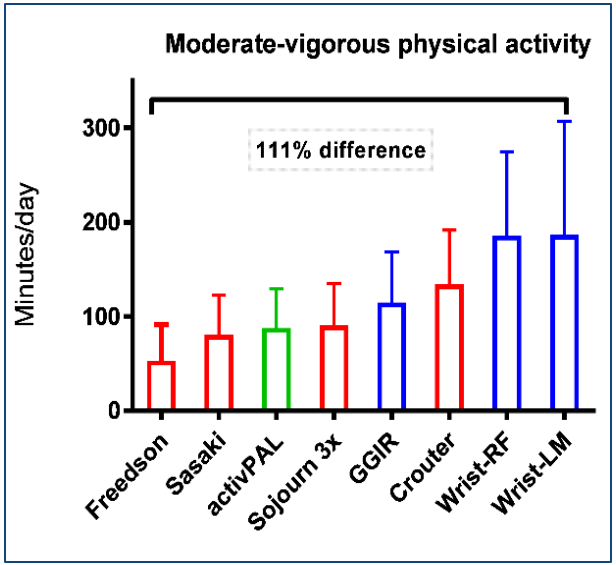


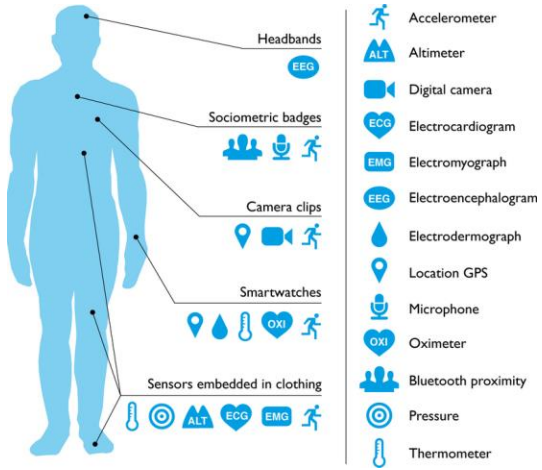
FIGURE *4.* Mean (SEM) estimates of MVPA across hip (red) thigh (green) and wrist (blue) methods over 7-days of wear.

Unpublished data courtesy of Sarah Keadle skeadle@calpoly.edu

Study Design: Select technology and define measurement protocol

Patient preferences and acceptability

Remote. Passive. Continuous.



1. **Fit-for-purpose**
   - Meaningful, clinically relevant, valid, reliable, sensitive to change
2. **User experience**
   - Comfort – sizing, wear location, unobtrusive
   - Interaction – charging protocol, visibility to data, active tests
3. **Data access**
   - Raw data – auditable
   - Remote uploads – near-real-time access
4. **Compliant and secure**
   - 510k, CE
   - GDPR, HIPAA, GCP
5. **Other**
   - Cost
   - Support

Operationalization: Produce precise datasets with minimal missing data

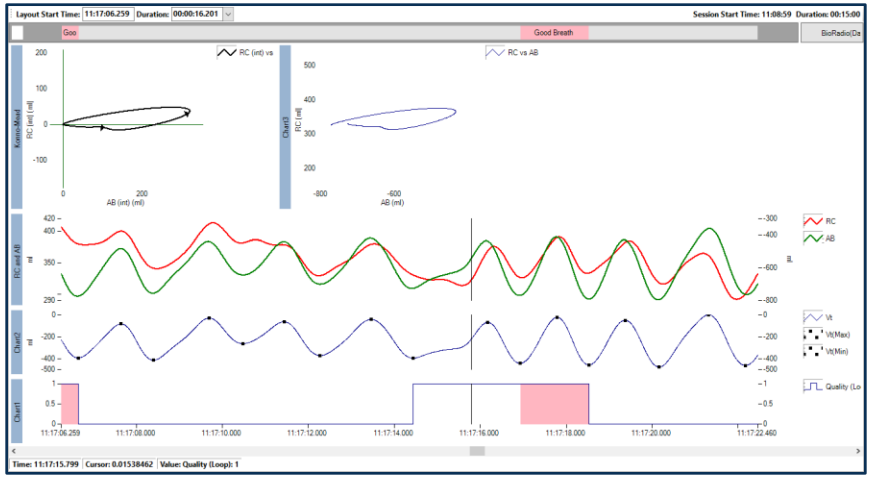
Near-real time compliance monitoring, technology oversight, and artifact detection

Data Cleaning: Actigraphy non-wear example

Regulatory Compliant: Ensure secure, reproducible datasets

Compliant software and auditable data derivations

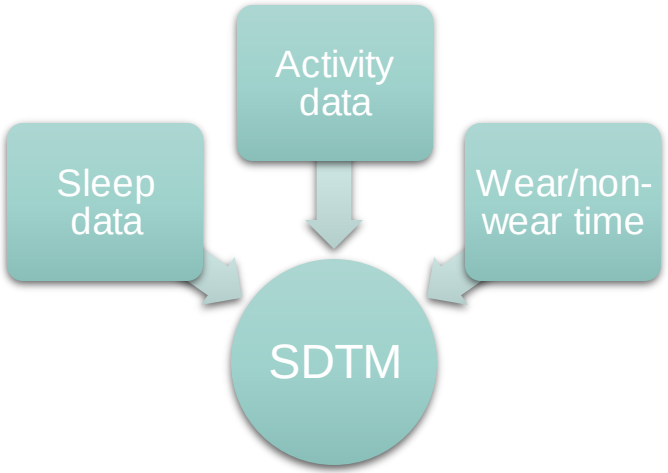
- Annotate wearable sensor(s) data with subjective data like ePRO or eCOA
- Human-augmented AI ensures algorithms are applied appropriately
- Compliant with FDA (21 CFR), EMA, GDPR, HIPAA
- Plug-and-play software allows quick scaling, multiple sensors, easy changes
- Fully auditable and revertible



Agenda

1. Considerations when using DHT in clinical investigations
2. **SDTM mapping: argenx use case (ongoing study)**
3. Key Learnings

Understand WHICH DATA is collected



Understand the ENDPOINTS and how to get there...

Clinical Study Protocol:

Monitor Actigraphy

Participants will be instructed to wear an actigraph (a physical activity monitor) at the times specified in the SoA. The actigraph will record step counts, cadence, vector magnitude, and time spent in different levels of daily activities (mild, moderate, to strenuous activity, and sedentary activity)

Statistical Analysis Plan:

The exploratory actigraphy endpoints are:

- The change from baseline at week x in weekly MVPA
- The change from baseline at week x in weekly vector magnitude.
- The change from baseline at week x in weekly cadence.
- The change from baseline at week x in weekly number of steps.

Additional endpoints:

- The change from baseline to week x in weekly time spent in sedentary level
- The change from baseline to week x in weekly time spent in light level.
- The change from baseline to week x in weekly time spent in moderate level.
- The change from baseline to week x in weekly time spent in vigorous level.
- The change from baseline to week x in weekly time spent in non-sedentary activity

Understand the ENDPOINTS and how to get there...

Data Transfer Agreement:

- *minute level data* -> too detailed, so not used
- *subject sleep metrics* -> no endpoints about sleep metrics, so not used
- *daily summaries* -> 40+ measures can be provided ('out of the box summaries')

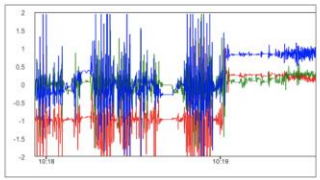
Awake Minutes
Wear Minutes
Awake Wear Filtered Steps
Awake Wear Filtered Light Activity
Awake Wear Filtered Moderate Activity
Awake Wear Filtered Viggorous Activity
Awake Wear Filtered Total Axis X Counts
Awake Wear Filtered Total Axis Y Counts
Awake Wear Filtered Total Axis Z Counts
Average Cadence
...
...

Understand possibilities of DERIVED MEASURES

Derived Measure: data points derived from raw sensor data

Wrist-worn actigraphy sensors

Raw, unprocessed triaxial accelerometer data



Data cleaning and processing

Derived measures

Daily summaries
Total minutes of Light activity
Total minutes of Moderate activity
Total minutes of Vigorous activity
Total detected non-wear time
Total detected wear time

!! Problem with these derivations= many variants & no consensus...

Problems with DERIVED MEASURES

Subject	Derived Measure	Result	Unit	Date
xxxxxxxx	Total minutes of Light activity	1354.00	min	2024-01-26
xxxxxxxx	Total minutes of Locomotion	11.75	min	2024-01-26
xxxxxxxx	Total minutes of Moderate activity	86.00	min	2024-01-26
xxxxxxxx	Total Moderate/higher physical activity	86.00	min	2024-01-26
xxxxxxxx	Total minutes of Non-Locomotion	1428.25	min	2024-01-26
xxxxxxxx	Total minutes of Non-Sedentary Behavior	543.25	min	2024-01-26
xxxxxxxx	Total minutes of Sedentary Behavior	896.75	min	2024-01-26
xxxxxxxx	Total detected awake time	966	min	2024-01-26
xxxxxxxx	Total wear time excluding sleep period	966	min	2024-01-26
xxxxxxxx	Total detected non-wear time	0	min	2024-01-26
xxxxxxxx	Total detected sleep time	474	min	2024-01-26
xxxxxxxx	Total detected wear time	1440	min	2024-01-26
xxxxxxxx	Total minute epochs for the given day	1440	min	2024-01-26

Are the derived measures CORRECT?

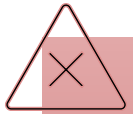
Endpoint:

"The change from baseline at week x in weekly cadence."

Cadence =

number of steps / time spent in non-sedentary activity (min)

Subject	Derived Measures	Result	Unit	Date
xxxxxxxx	Total minutes of Light activity	1134.50	min	2024-01-26
xxxxxxxx	Total minutes of Moderate activity	55.25	min	2024-01-26
xxxxxxxx	Total Moderate/higher physical activity	56.50	min	2024-01-26
xxxxxxxx	Total minutes of Vigorous activity	1.25	min	2024-01-26
xxxxxxxx	Total minutes of Non-Sedentary Behavior	487.00	min	2024-01-26
xxxxxxxx	Total minutes of Sedentary Behavior	704.00	min	2024-01-26
xxxxxxxx	Total estimated steps	1685		2024-01-26
xxxxxxxx	Total detected awake time	1191	min	2024-01-26
xxxxxxxx	Total detected sleep time	0	min	2024-01-26
xxxxxxxx	Total wear time excluding sleep period	818	min	2024-01-26



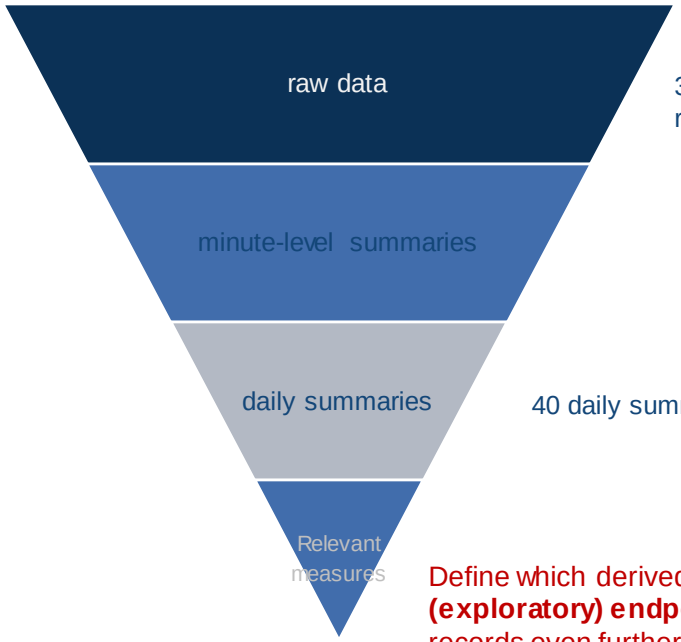
Calculate Cadence based on daily summaries:

Assumption that *all non-sedentary time* is spent stepping

Cadence is calculated across all types of stepping (e.g., random incidental stepping vs. continuous stepping bouts)

Understand SIZE of the data

Use Case: continuous data collection over 2 periods of 'only' 7 days per patient, for 240 patients...



32 X 3 records per sec x 2 x 7 days x 240 patients = 27.869.184.000 records

40 daily summaries x 2 x 7 days x 240 patients = 134.400 records

Define which derived measures are **required for (exploratory) endpoints** to reduce the number of records even further

SDTM: Custom findings domain XA

STUDYID	DOMAIN	USUBJID	XASEQ	XAGRPID	XATESTCD	XATEST	XACAT	XAORRES	XAORRESU	XASTRESC	XASTRESN	XASTRESU	XAMETHOD	EPOCH	XADTC	XADY
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	1	PERIOD1	AWMIN	Awake Minutes	DAILY SUMMARY	720	min	720	720	min		TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	2	PERIOD1	WRMIN	Wear Minutes	DAILY AVERAGE	1100	min	1100	1100	min		TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	3	PERIOD1	STEPS	Awake Wear Filtered Steps	DAILY AVERAGE	4000		4000	4000			TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	4	PERIOD1	LITACT	Awake Wear Filtered Light Activity	DAILY AVERAGE	200	min	200	200	min		TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	5	PERIOD1	MODACT	Awake Wear Filtered Moderate Activity	DAILY AVERAGE	200	min	200	200	min		TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	6	PERIOD1	VIGACT	Awake Wear Filtered Viggorous Activity	DAILY AVERAGE	20	min	20	20	min		TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	7	PERIOD1	TOTXCT	Awake Wear Filtered Total Axis X Counts	DAILY AVERAGE	6892		6892	6892			TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	8	PERIOD1	TOTYCT	Awake Wear Filtered Total Axis Y Counts	DAILY AVERAGE	8797		8797	8797			TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	9	PERIOD1	TOTZCT	Awake Wear Filtered Total Axis Z Counts	DAILY AVERAGE	8582		8582	8582			TREATMENT	01/01/2024	1
ARGX-XXX-XXXX	XA	ARGX-XXX-XXXX-nnnnnnn	10	PERIOD1	MVPA	Total Moderate/Higher Physical Activity	DAILY AVERAGE	0.00	min	0.00	0	min	STAUDENMAYER 15	TREATMENT	01/01/2024	1

DHT - Data Flow

ActiGraph

Activity monitor

ActiGraph

- wrist-worn
- continuous collection of tri-axial acceleration data

VivoSense

Platform

vivoSENSE

- raw data remains accessible to argenx
- data cleaning

VivoSense

Aggregate data/ derived measures

vivoSENSE

- VivoSense proprietary algorithms used to aggregate data & derive measures
- Data Processing Specs (derivation methods)
- data transfer (SDTM-like) to DM CRO

argenx DM-CRO

Clinical Database & SDTM

- Derived measures are included in custom XA domain in SDTM

argenx QS-CRO

ADaM TLF's

- ADaM creation from SDTM data

Agenda

1. Considerations when using DHT in clinical investigations
2. SDTM mapping: argenx use case
3. **Key Learnings**

Key Learnings

✓ **ENSURE FIT FOR PURPOSE**

- Meaningful to patients, valid and reliable

✓ **START WITH THE END IN MIND**

- Ensure right expertise is available to select appropriate endpoints
- Standards team to be involved before finalization of protocol

✓ **OPERATIONAL EXPERTISE**

- DHT Vendor Selection: Regulatory compliance of the vendor QMS and processes, for GCP
- Technology assignment and oversight, data collection, compliance monitoring, data cleaning

✓ **CO-CREATION: Argonauts – stronger together**

- Onboard VivoSense as specialized partner
- Development of DHT Strategy & Framework
- Potential partnering on industry initiatives: CDISC + DiME; DEEP; ...

Thank You!

Kate Lyden,

Vanessa Sarrechia,

Tayana Pierre-Louis,

Stijn Rogiers