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2026 US Interchange

THE FUTURE IS CONNECTED: STANDARDS AND AI POWERING DIGITAL TRANSFORMATION



From Wearables to Regulatory Submissions: Digital Health Technologies in Clinical Research

Varun Sethuraman,
Venkata Suresh Babu Bondu,
Lifesciences Practice & Solutions, Hexaware Technologies

Speakers



Varun Sethuraman
Practice Manager,

Lifesciences Practice & Solutions
Hexaware Technologies



Venkata Suresh Babu Bondu
Associate Vice President,

Lifesciences Practice & Solutions
Hexaware Technologies

The adoption - acceptance gap

- DHTs are now routine in trials: wearables, eCOA, mobile apps and remote sensors
- Regulators accept endpoints, not devices
  - Every digital endpoint needs a validated derivation, traceable data and a submission-ready structure
- That last mile is a data standards problem and it is where this community comes in

1,021 drug trials used wearables through 2025.

Zero sensor-derived endpoints fully qualified through FDA's DDT program.

Source: Brain Trials analysis of registered studies, 2026

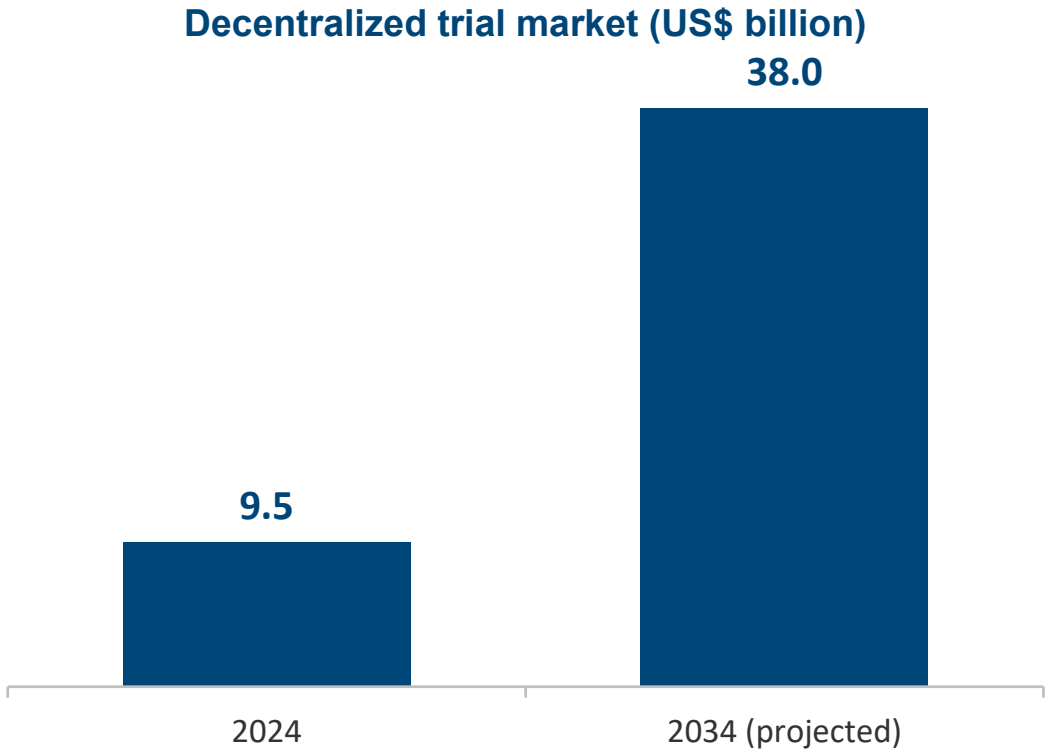
Agenda

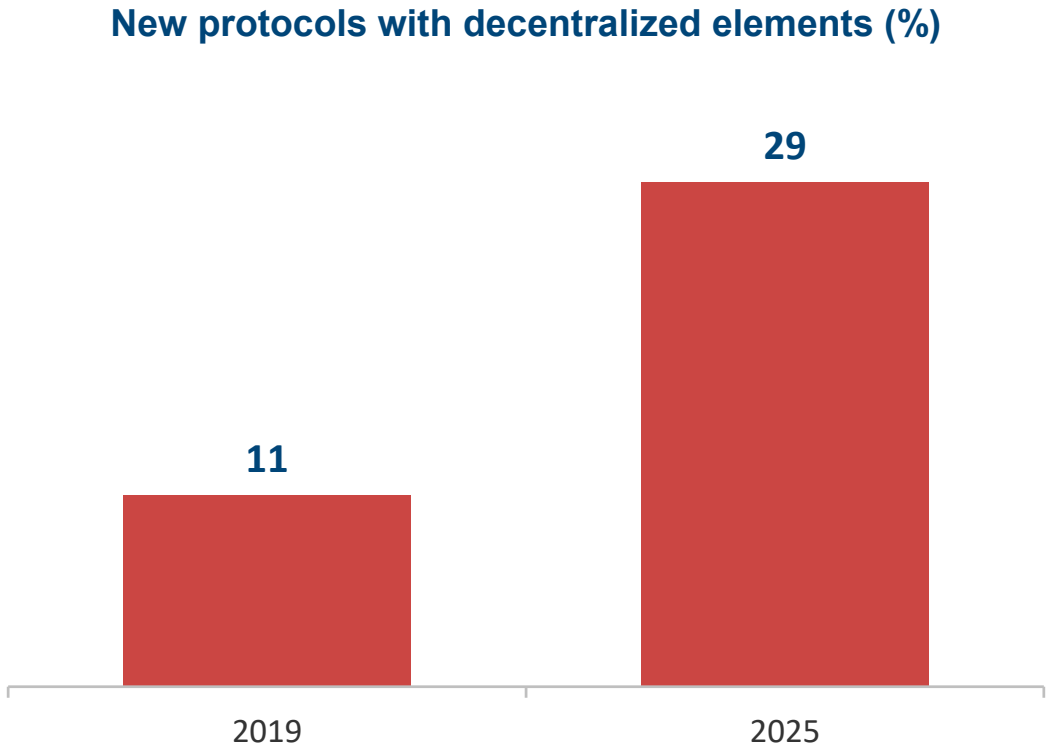
1. Why DHTs, why now
2. Wearables that reached regulators
3. Worked examples: SV95C and Eversense CGM
4. Toward a CDISC-aligned DHT architecture
5. Key takeaways

Why DHTs, Why Now

Adoption, momentum and the 2024–2025 regulatory reset

DHTs have moved from experiment to mainstream





DHT use in registered trials: under 1% (2010) → over 11% (2020). **Early adopters:** up to 50% faster enrollment and 10–25% lower costs.

What changed in 2024-2025

- **FDA DCT final guidance (Sept 2024)**
  - DHT validation and reliability expectations; sponsor oversight of remote activities
- **FDA DHT guidance for remote data acquisition**
  - Fit-for-purpose verification and validation, data security, endpoint justification
- **ICH E6(R3) GCP (Jan 2025)**
  - eSource, eCOA and DHT data accepted as primary trial data, with audit trails
- **21 CFR Part 11 / EU Annex 11**
  - Audit trails, e-signatures and data integrity for every DHT platform

What it means for data teams

Device, firmware and algorithm versions become regulated metadata.

Traceability from sensor to endpoint is now an expectation, not a nice-to-have.

Wearables That Reached Regulators

Four real-world cases, four different outcomes

Four real-world cases

Case	Regulator & pathway	Context of use	Outcome & lesson
SV95C *ankle-worn inertial sensor*	EMA qualification: secondary endpoint (2019), primary endpoint (2023)	Ambulant DMD patients aged ≥4; passive capture over 50–180 hours of daily life	First digital primary endpoint qualified by a regulator; under FDA COA review
Apple Watch AFib History *wrist PPG sensor*	FDA MDDT (Medical Device Development Tools) qualification (May 2024)	Weekly AFib burden as a secondary effectiveness endpoint in cardiac ablation device trials	First DHT qualified as an MDDT; clinically meaningful change not yet defined
Actigraphy MVPA Moderate-to-Vigorous Physical Activity *Bellerophon REBUILD*	FDA-agreed primary endpoint in a pivotal Phase 3 trial	Physical activity in fibrotic interstitial lung disease (INOpulse)	Trial did not meet its primary endpoint: acceptance does not guarantee success
Eversense CGM *Implanted fluorescence sensor*	FDA PMA approval, P160048 (June 2018); Class III device	Adults with diabetes; glucose every 5 min for up to 90 days, adjunctive to fingersticks	Approved after 8–0 panel vote; algorithm updated after trials by re-processing stored raw data

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What the cases teach us

1

Context of use is narrow

Each qualification covers one population, one device placement and one endpoint role. Reuse outside that scope needs new evidence.

2

The evidence bar is high

SV95C required reliability, validity, responsiveness, clinically meaningful change and patient relevance data.

3

Acceptance ≠ success

REBUILD shows an accepted digital endpoint still needs a real treatment effect and robust, complete data capture.

Common thread: regulators must be able to trace every endpoint value back to the device, the algorithm and the raw signal.

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Worked Example 1: SV95C

From ankle sensor to submission-ready datasets

Preface: what is Duchenne muscular dystrophy?

1 in 3,500

male births worldwide are affected by DMD

- **Cause:** A mutation in the DMD gene means muscles make no dystrophin, a protein muscle fibres need.
- **Inheritance:** X-linked recessive, so it mainly affects boys. About a third of cases are new mutations with no family history.
- **Course:** Progressive weakness that starts in the legs and pelvis: a waddling gait and difficulty climbing stairs come first.

How ambulation is lost

Age 1–6
First symptoms; motor milestones delayed

Age 6–11
Steady decline in muscle strength

By ~10
Braces may be needed to walk

By ~12
Most boys use a wheelchair

Teens onward
Heart and breathing complications

Source: NHGRI, genome.gov – About Duchenne Muscular Dystrophy

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How SV95C is captured and calculated



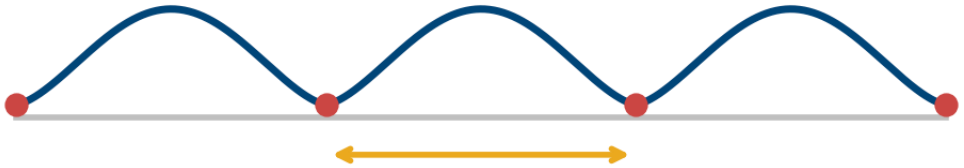
Inside each sensor

Accelerometer
linear acceleration

Gyroscope
angular velocity

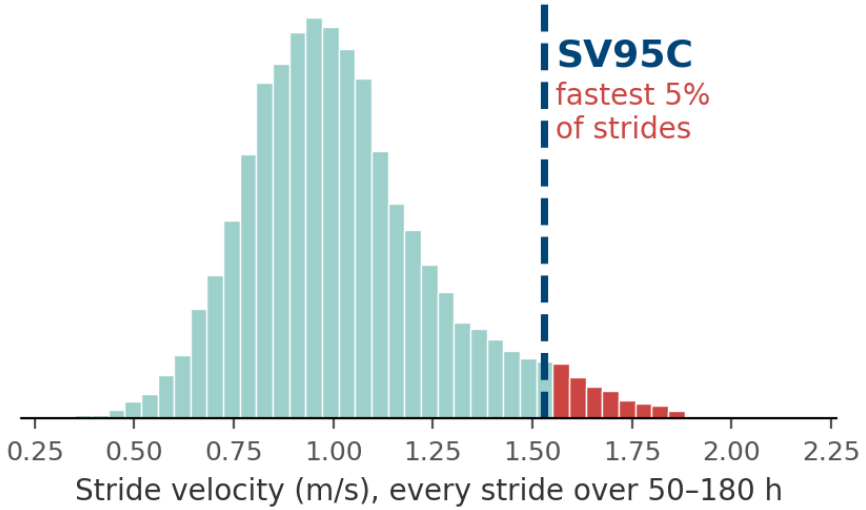
Magnetometer
orientation in all directions

Barometer
altitude change, e.g. stairs



one stride: length + speed

Illustrative, not patient data



Morning: put on → **Day: passive capture** → **Night: dock and charge** → **Upload: secure cloud, no patient ID**

The sensors behind SV95C

a) ActiMyo wearable sensors (third generation)



b) ActiMyo docking station (third generation)



c) Syde wearable sensors (new generation)



d) Syde docking station (new generation)



ActiMyo® and Syde® wearable sensors and docking stations (SYSNAV)

ActiMyo® (third generation)

CE-marked Class I medical device. All data in the EMA qualification packages were recorded with it.

Syde® (new generation)

Smaller successor. SYSNAV states it captures SV95C to the same regulatory standard.

How it is used

Two watch-sized sensors (ankle plus ankle or wrist) worn by day; docked at night to charge and upload, without patient ID.

Regulators qualified the endpoint, not the device: any ankle sensor meeting EMA's precision requirements can capture SV95C.

The SV95C data pipeline



1. Capture	2. Raw signal	3. Quality	4. Tabulate	5. Analyze
Ankle-worn inertial sensor records 50–180 h of daily life	Stride-level velocity and length	Wear-time and compliance checks	SDTM findings plus device domains	SV95C derived per assessment window
Device / vendor platform	**Source archive, traceable**	**Data review rules**	**SDTM**	**ADaM + define.xml**

Key principle: keep raw data traceable, tabulate once in SDTM, and derive the endpoint in ADaM with the algorithm version documented.

How the evidence was built

Validation followed the three-part V3 approach: verify the algorithm, prove it measures strides accurately, then prove the number behaves like a good endpoint.

ANALYTICAL

Lab accuracy

8 healthy volunteers walked set paths at three speeds in a motion-capture room; cameras were the reference.

98.7% of strides detected; speed error ≈ 1 cm/s

ANALYTICAL

Patient accuracy

23 DMD patients did the 6-minute walk while a physiotherapist measured distance alongside the wearable.

Difference < 1 m on ≈ 308 m walked

CLINICAL

Reliability

Two recording periods one month apart in 52 patients; variability tested by hours of recording.

ICC 0.970; variability jumps below 50 h → 50 h minimum

CLINICAL

Validity

Compared with 6MWD, North Star and 4-stair climb; 125 patients vs 66 healthy controls.

Correlated at every visit; median 1.56 vs 2.71 m/s

CLINICAL

Responsiveness

Followed patients on stable steroids for 12 months, and 11 patients starting steroids.

Decline seen at 3 months vs 9 for older tests; rise after steroids

PATIENT VOICE

Meaningfulness

Surveys of patients, caregivers and 52 clinicians; anchors such as clinician global impression.

Meaningful change ≈ 0.10–0.20 m/s; >70% favor a wearable

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Digital endpoint to regulatory evidence: SV95C

CDISC standards from ankle sensor to qualified endpoint

EMA-QUALIFIED EXAMPLE

SV95C

SYSNAV (ActiMyo® / Syde®) • EMA qualified: secondary 2019, primary 2023 • Ambulant DMD, age 4+ • FDA DDT COA #000103 in review

Evidence plan: regulatory question, DMD trial population, endpoint role, wear-time rules and statistical analysis

Device data

ActiMyo® / Syde®

Ankle sensor
Docking station
Cloud platform

Stride speed + length + time, device IDs

50–180 h of daily life at home

Capture & curate

Direct device feed

Stride-level data and device metadata

CDASH

Planned forms for device assignment, wear, events

Link subject and device
Check wear ≥ 50 h, gaps
Retain raw + algorithm ver.

SDTM

Device domains, as applicable

DI	Device Identifiers
DO	Device Properties: firmware, algorithm
DU	Device-In-Use: ankle, wear period
DE	Device Events
DT	Device Tracking and Disposition
DR	Device-Subject Relationships

FT*

Stride metrics per period + device link

ADaM

ADSL

Subjects, populations, baseline ambulation

BDS datasets

SV95C per window
Baseline and change
Wear-time sufficiency flag

Prespecified derivations and source traceability

Regulatory evidence

Analyze & interpret

Effect, consistent with 6MWT / North Star

Package & submit

Datasets + Define-XML[1]
Reviewer guides + algorithm
Device precision evidence

Sponsor submission

and agency review

TRACEABILITY Raw strides + device ID ↔ FT + device domains ↔ ADaM SV95C ↔ reported endpoint

EMA qualification opinion
SV95C: 2019 secondary, 2023 primary

FDA DDT COA #000103
COA qualification in progress

ICH E6(R3)
DHT data as GCP trial data (2025)

EU 2017/745
MDR, device conformity for EU scope

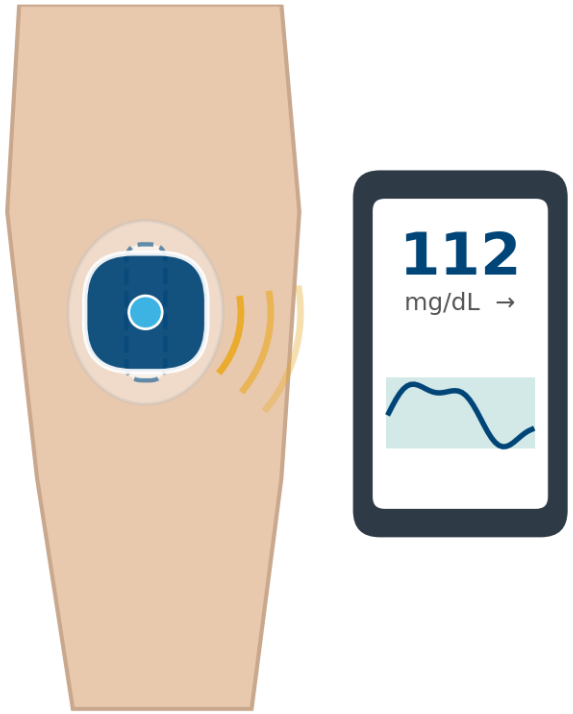
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*Illustrative flow, not a sponsor submission. *FT vs custom findings domain is a proposed choice.*

Worked Example 2: CGM

Eversense: from implanted sensor to FDA approval

How Eversense CGM works

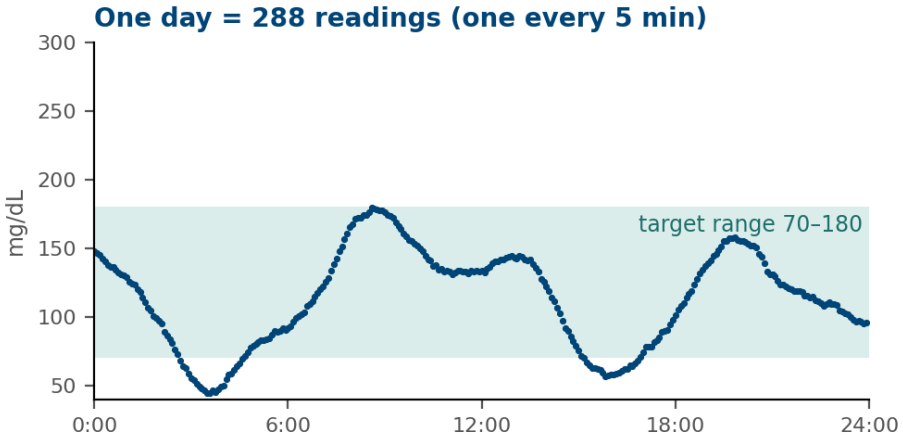


Sensor
Implanted under the skin of the upper arm; fluorescence measures interstitial glucose every 5 min for up to 90 days

Smart transmitter
Worn over the sensor; powers it, calculates glucose in firmware, vibrates for alerts

Mobile app
Displays readings, trends and alerts; takes fingerstick calibrations; uploads data

Insertion tools
Used by a physician to place and later remove the sensor



Illustrative, not patient data

≈ 26,000 readings

per sensor over 90 days, measuring range 40–400 mg/dL

Physician inserts → **Sensor measures** → **Transmitter calculates** → **App displays and alerts** → **Upload to data system**

Source: FDA SSED, PMA P160048

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How the CGM evidence was built

A device approval follows a different playbook: bench and safety testing, human factors, then clinical accuracy against a laboratory reference.

BENCH

Device safety

Electrical safety, EMC, home-use, battery and IP67 water-ingress testing of the transmitter.

All pre-set acceptance criteria met

BENCH

Biocompatibility

ISO 10993 tests of sensor, transmitter and tools, incl. a 26-week implant study in rats.

Passed all tests

HUMAN FACTORS

Usability

Patient users on iOS and Android; 16 physicians inserting sensors in simulated tissue.

Android alert gap found → banner alerts added

CLINICAL

PRECISE II (pivotal)

90 adults at 8 US sites; blinded, single-arm; CGM vs lab analyzer on days 1, 30, 60 and 90.

15,753 paired readings; MARD 8.5%

CLINICAL

PRECISION

35 adults, unblinded; added day 7 and 14 checks and accuracy during sleep.

15,170 paired readings; MARD 9.6%

REAL WORLD

EU patient registry

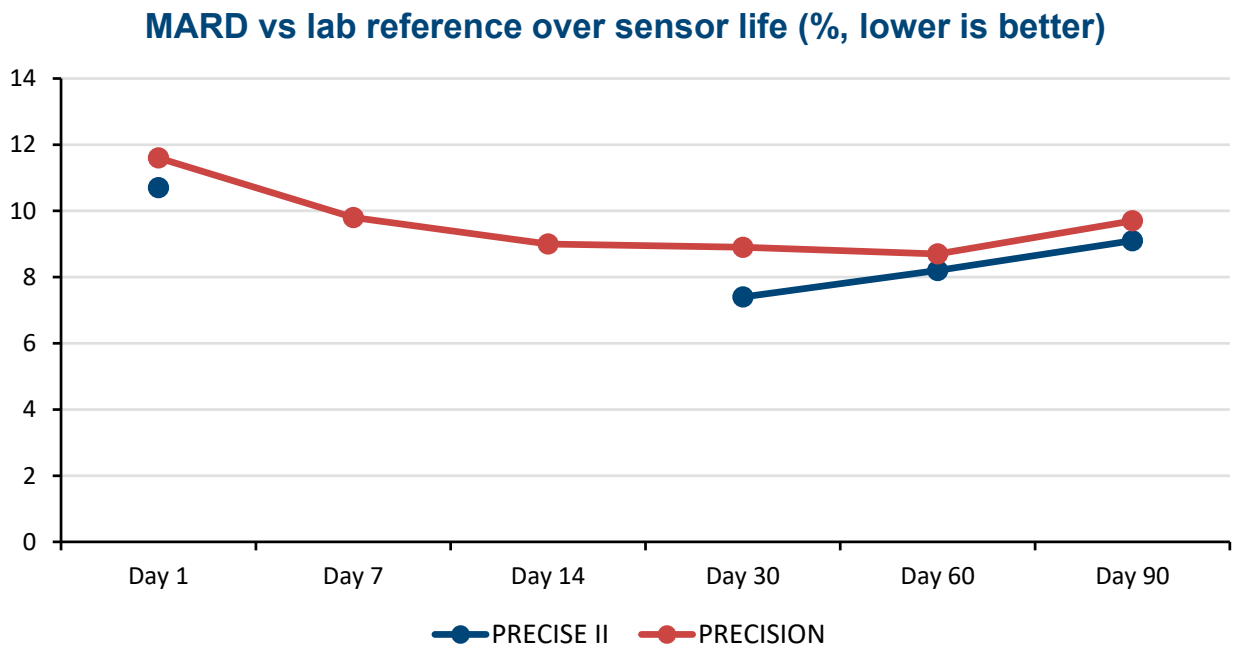
Every EU patient enrolled after CE mark; long-term safety of repeat insertions.

1,686 patients, 2,386 insertions; 0 related SAEs

Source: FDA SSED, PMA P160048

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What the CGM studies showed, and where it led



8.5%

overall MARD, PRECISE II

92%

of sensors working at day 90

0

device-related serious adverse events

Sources: FDA SSED P160048; FDA PMA database (S006, S016)

Regulatory path

- **May 2016** CE mark (EU, earlier version)
- **Mar 2018** FDA panel votes 8–0 on safety, effectiveness, benefit-risk
- **Jun 2018** PMA P160048 approved: adults, 90 days, adjunctive; post-approval study required
- **Jun 2019** Non-adjunctive use approved (S006)
- **Feb 2022** Eversense E3: 180-day sensor (S016)

Data lesson: the algorithm changed after the trials. FDA reviewed results from re-processing the stored raw sensor data with the new version.

Digital health data to regulatory evidence

CDISC standards across the real-world evidence lifecycle

FDA-APPROVED EXAMPLE

Eversense CGM

Senseonics • Original PMA P160048 • Approved 21 June 2018 • Product code QCD

Evidence plan: regulatory question, routine-care cohort, endpoints, data quality and statistical analysis

Device data

Eversense CGM

Sensor
Transmitter
Mobile app

Glucose + time
Device identifiers

Linked routine-care
clinical context

Capture & curate

Direct device feed

Glucose readings
and device metadata

CDASH

Planned forms for
device use and events

Link subject and device
Check gaps, units, timing
Retain source + versions

SDTM

Device domains, as applicable

DI	Device Identifiers
DO	Device Properties
DU	Device-In-Use
DX	Device Exposure
DE	Device Events
DT	Device Tracking and Disposition
DR	Device-Subject Relationships

LB

Glucose observations + device link

ADaM

ADSL

Subjects and populations

BDS datasets

Mean glucose
Time in range
Baseline and change

Prespecified derivations
and source traceability

Regulatory RWE

Analyze & interpret

Effects, uncertainty
and bias assessment

Package & submit

Datasets + Define-XML[1]
Reviewer guides + report
Device / quality evidence

Sponsor approval

and agency review

TRACEABILITY Source + device ID ↔ LB + device domains ↔ ADaM endpoints ↔ reported evidence

21 CFR Part 820
QMSR / ISO 13485:2016

21 CFR Part 814
PMA pathway: P160048

21 CFR Part 812
IDE, when applicable

EU 2017/745
MDR, for EU scope

Illustrative flow, not the Eversense FDA dossier. Use domains relevant to collected data.

Open gaps for the standards community

- No standard SDTM structure for continuous, high-frequency data
- Most digital endpoints lack CDISC controlled terminology
- Algorithm or firmware updates mid-study: how are derived values versioned?
- Where passively collected measures belong (FT vs. custom domain) is still a design decision
- Wear-time and compliance rules are not harmonized across sponsors

The mapping you just saw is a proposed approach, not settled guidance.

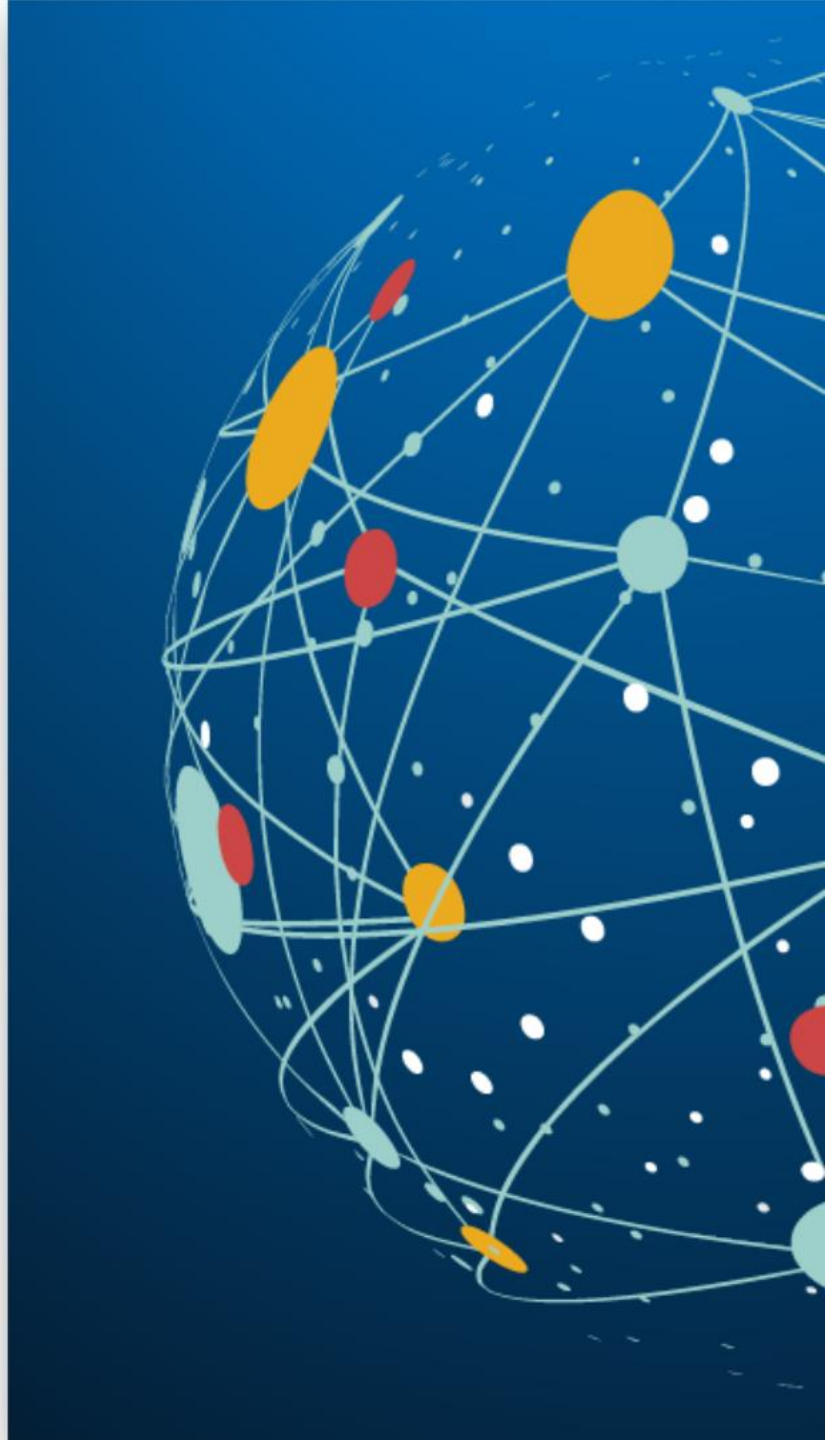
These gaps are where CDISC teams, sponsors and regulators can move together.

Toward a CDISC-aligned DHT architecture

1	**CDASH first**	Define collection fields up front, then engineer device outputs to map to them
2	**COA-ready eCOA**	Map ePRO/eCOA to QS, FT or RS with documented paper-to-electronic equivalence
3	**Endpoint qualification plans**	Therapeutic-area plans aligned with FDA DDT and EMA qualification pathways
4	**Device metadata governance**	Capture device ID, firmware and calibration in SDTMIG-MD domains
5	**FHIR as a bridge**	FHIR Observation as an intermediate layer before SDTM, enabling EHR integration

Key takeaways

- **Regulators are ready:** FDA, EMA and ICH E6(R3) now give a clear framework for DHT data
- **Real endpoints exist:** SV95C and Apple AFib History show qualification is achievable, within a narrow context of use
- **Standards are the bottleneck:** continuous data, device metadata and algorithm versioning need CDISC-aligned patterns
- **Design for submission from day one:** CDASH-first collection, SDTMIG-MD device domains and ADaM-derived endpoints



Questions?

varuns8@hexaware.com
VenkataSureshBabuB@hexaware.com

