

# **Eversense<sup>®</sup> Continuous Glucose Monitoring (CGM) System**

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**March 29, 2018**

Senseonics, Inc.

Clinical Chemistry and Clinical Toxicology Device Panel

# Introduction

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**Mukul Jain, PhD**

Chief Operating Officer

Senseonics, Inc.

# Eversense Continuous Glucose Monitoring (CGM) System

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**90-day Implantable  
Sensor**  
subcutaneous



**Removable  
Transmitter**  
worn over skin



**Mobile  
Application**  
handheld device



# Proposed Indication for Use

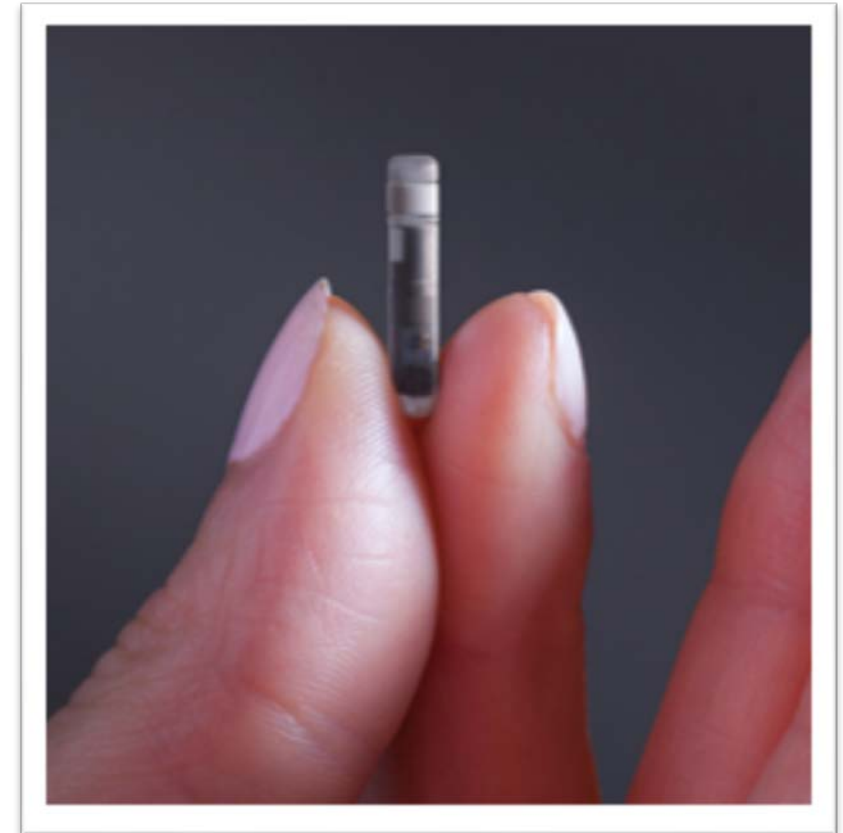
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- For continually measuring glucose levels in adults (age  $\geq 18$ ) with diabetes for operating life of sensor
- System provides:
  - Real-time glucose readings
  - Glucose trend information
  - Alerts for detection and prediction of episodes of low blood glucose (hypoglycemia) and high blood glucose (hyperglycemia)
- Adjunctive device to complement, not replace, information obtained from standard home blood glucose monitoring devices

# System Components: Sensor

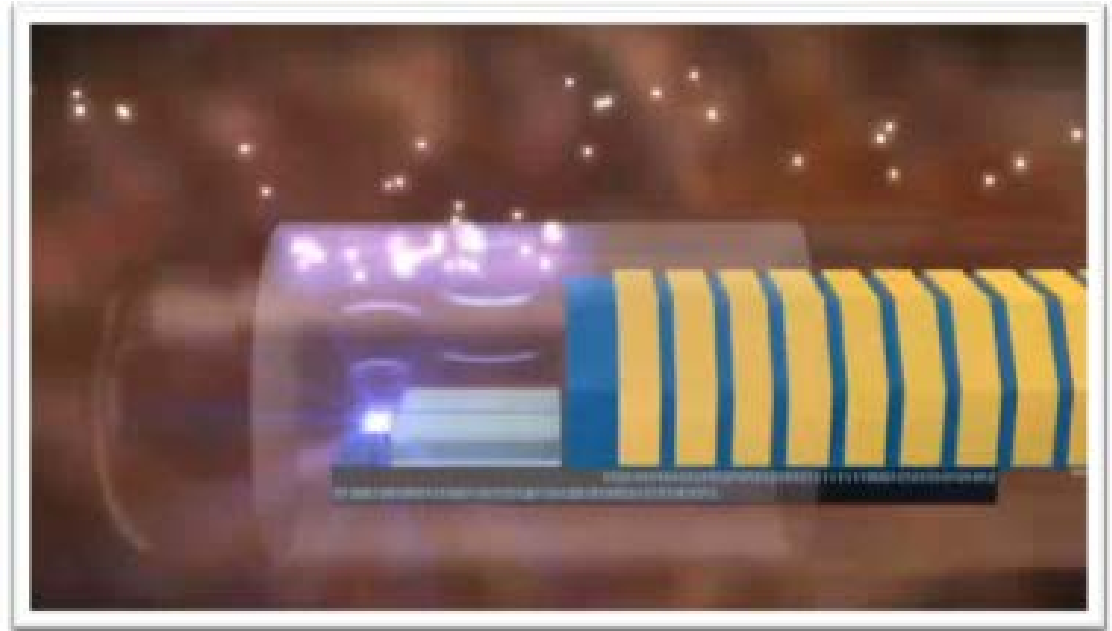
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- Inserted into upper arm
- Lasts up to 90 days
- Measures glucose every 5 min
- Silicone collar containing 1.75 mg dexamethasone acetate (DXA)
  - Reduce inflammation around sensor



# Sensor Technology Based on Fluorescence

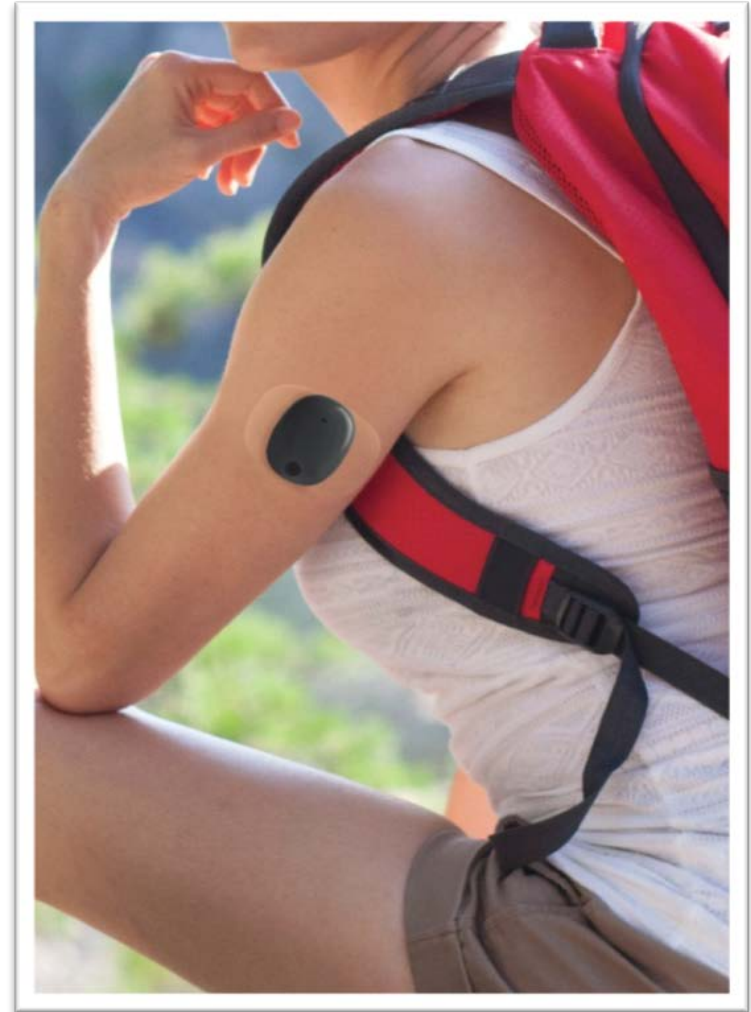
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# System Components: Transmitter

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- Calculates glucose values and trends
- Worn externally over inserted sensor
- Secured with adhesive patch
- Vibrates for alerts and notifications
- Rechargeable



# System Components: Mobile Medical Application

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- Displays glucose information from transmitter
  - Values and trends
  - Alerts and notifications
- Runs on smartphone
- Reminds user to calibrate (2x/day)
- Option to upload data to Senseonics' Data Management System



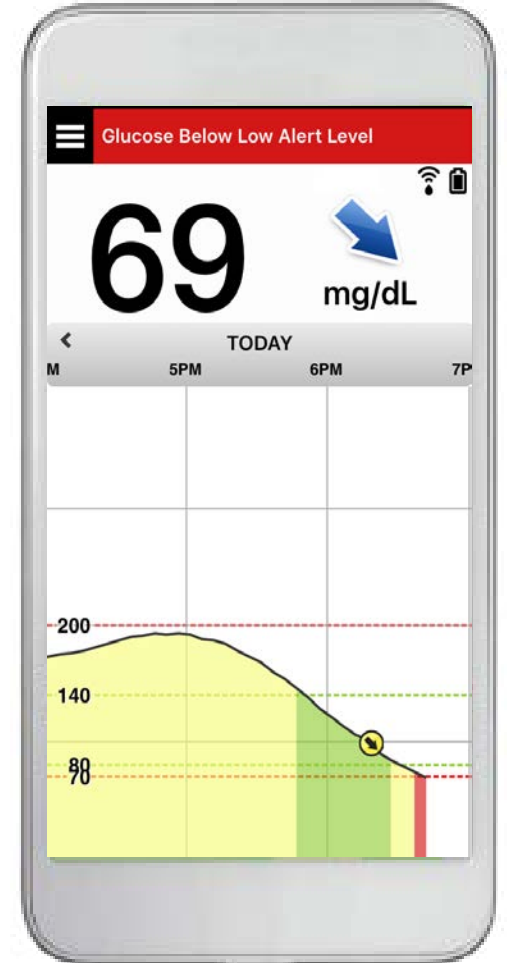
# Multiple Alert Types to Ensure Safety

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- **Threshold**
  - Identify glucose levels below or above pre-set values
- **Predictive**
  - Signal when alert level is expected to be crossed in immediate future (e.g. 10 minutes prior)
- **Rate of change**
  - Identify rising or falling glucose exceeding pre-set rate of change

# Vibratory, Visual, and Audio Alerts

- Transmitter vibrates whether mobile app is active or in vicinity
- Unique vibration patterns
- Audible alert AND visual message on handheld device



# Sensor Inserted in Upper Arm During Simple, Office-Based Procedure

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- Sensor inserted/removed by HCP
- Brief, office-based procedure
- Custom insertion tools
- Procedure:
  - Skin anesthetized and disinfected
  - Small incision in upper arm
  - Blunt dissector creates subcutaneous pocket
  - Sensor transferred to pocket
  - Similar removal procedure

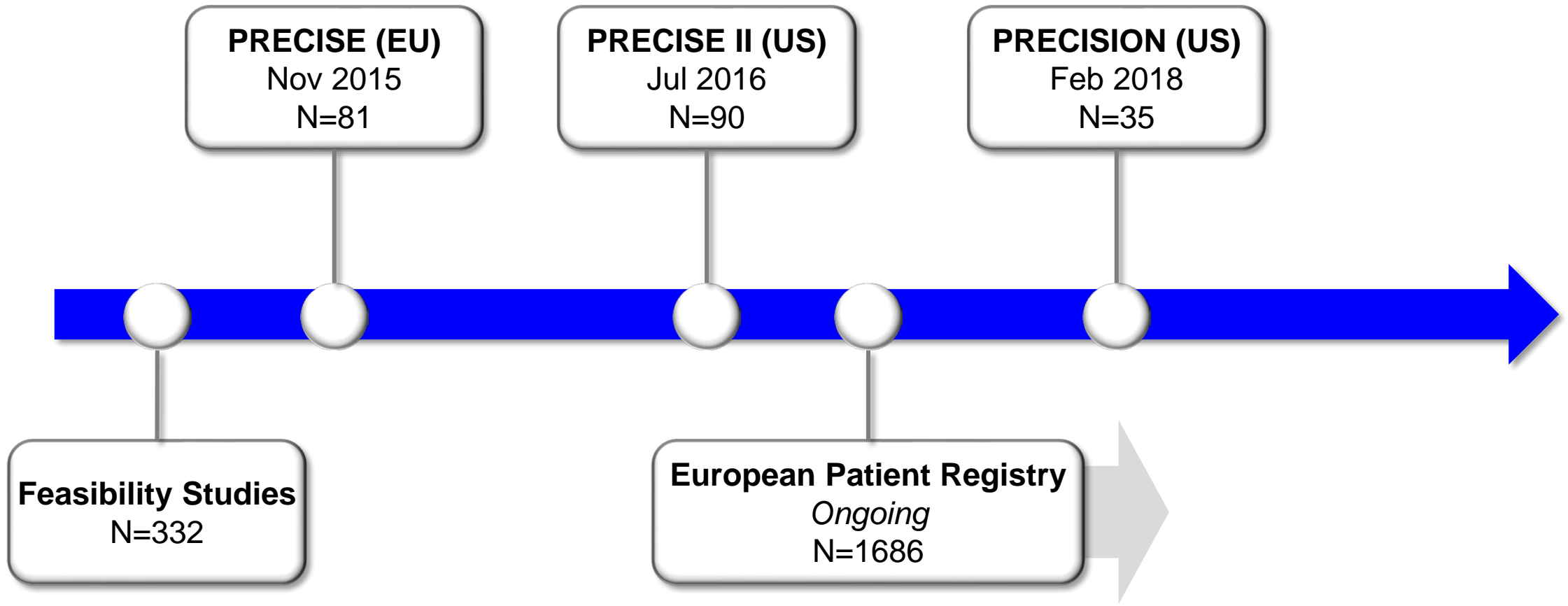


# Eversense System Regulatory Status

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- CE Mark received May 2016
- Available in 14 countries
- 1686 patients commercially
  - 2386 insertions
  - Up to 7 sequential sensors
- PMA submitted to FDA in October 2016

# Clinical Program: 2224 Patients



# FDA Discussion Topics: Design Changes

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- Design changes since PRECISE II
  - Transmitter
  - Glucose algorithm
  - Sensor end cap
  - Blunt dissector tool
- Study results establish Eversense is safe and effective
- Changes are incremental in nature
  - Continuous improvement in design

# Design Changes: Transmitter

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**Generation 1  
PRECISE II + PRECISION**

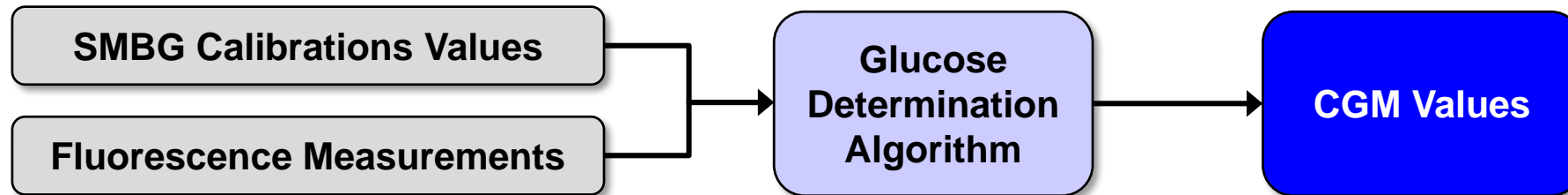
**Generation 2  
PRECISION**

- More ergonomic design
  - Thinner
  - Lighter
  - Less obtrusive
- Water-resistant
- Passed verification and validation testing
- Extensive EU commercial experience

# Design Changes: Glucose Algorithm

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- Glucose algorithm updated to improve performance in
  - Early sensor wear
  - Hypoglycemic range
- Raw sensor data independent of algorithm in transmitter



- Algorithm developed with data from EU pivotal study (PRECISE)
- Post hoc processing of US data collected with SW 602
- Eversense performance accurate and reliable with Study SW and SW 602



# FDA Discussion Topics: Sensor Accuracy

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- Amount of data relative to sensor life (90 days)
- Accuracy in early wear period

# PRECISE II: Eversense System is Highly Accurate

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- Demonstrated accuracy
  - 8.5% mean absolute relative difference (MARD)
  - 87% of readings within 15 mg/dL or 15% of reference
- Excursions consistently detected
  - 96% of hypoglycemic excursions\*
  - 98% of hyperglycemic excursions\*
- Duration of use
  - 91% of sensors functioned for 90 days

# Eversense System is Safe

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- No device-related SAEs
  - 1 procedure-related SAE through 90 days post-insertion
- No unanticipated AEs
- Low rate of infections and adhesive patch skin reactions
- AEs consistent with other CGMs and subcutaneous implants

# Repeat Sensor Use is Safe

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- Risk analysis
  - Risks are consistent, predictable, can be mitigated
  - Single insertion characterizes impact, 90-day use, removal, and healing
- Clinical study results
  - Device and insertion/removal procedure are safe
  - Nominal/complete healing following sensor removal
- Post-marketing studies of repeat use
  - EU Registry (1686 patients, up to 7 sequential sensors)
  - Repeat sensor not associated with increased AEs

# Agenda

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**Unmet Need**

**Jeremy H. Pettus, MD**  
University of California at San Diego

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**Study Design**

**Tim Goodnow, PhD**  
Senseonics, Inc.

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**Effectiveness**

**Safety**

**Lynne Kelley, MD, FACS**  
Senseonics, Inc.

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**Post-approval / Training**

**Clinical Perspective**

**Steven J. Russell, MD, PhD**  
Harvard Medical School

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# Additional Experts

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- *Clinical Pharmacology*  
**Nicholas Fleischer, RPh PhD**  
Vice President  
Clinical Pharmacology and Biopharmaceutics  
The Weinberg Group
- *Statistics*  
**Richard Holcomb, PhD**  
Consultant
- *Study Conduct*  
**Katherine Tweden, PhD**  
Senseonics, Inc.
- *Dermatology*  
**Howard I. Maibach, MD**  
Dermatologist  
Professor of Dermatology  
University of California, San Francisco
- *Pathology*  
**Renu Virmani, MD FACC**  
President  
CVPath Institute

# Unmet Need

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**Jeremy H. Pettus, MD**

Assistant Professor of Medicine

Endocrinology, Diabetes and Metabolism

University of California, San Diego (UCSD)

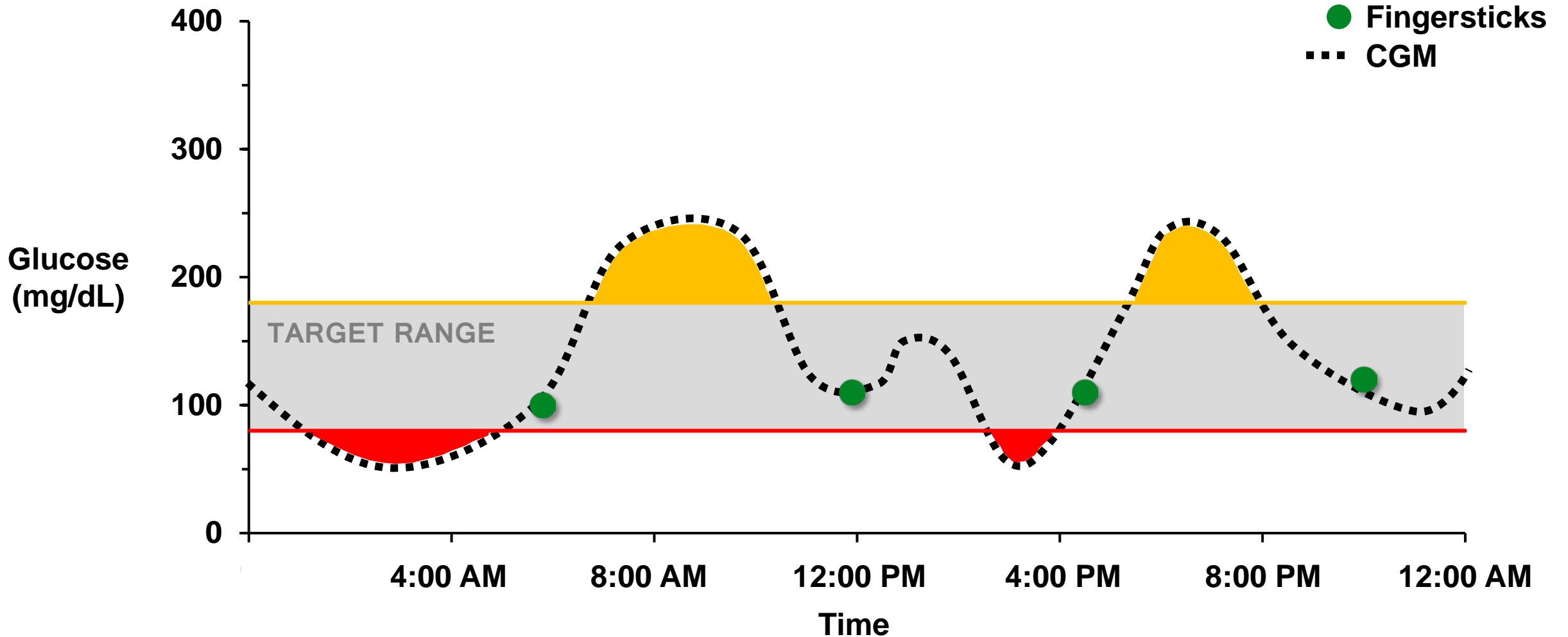
# CGM Overview

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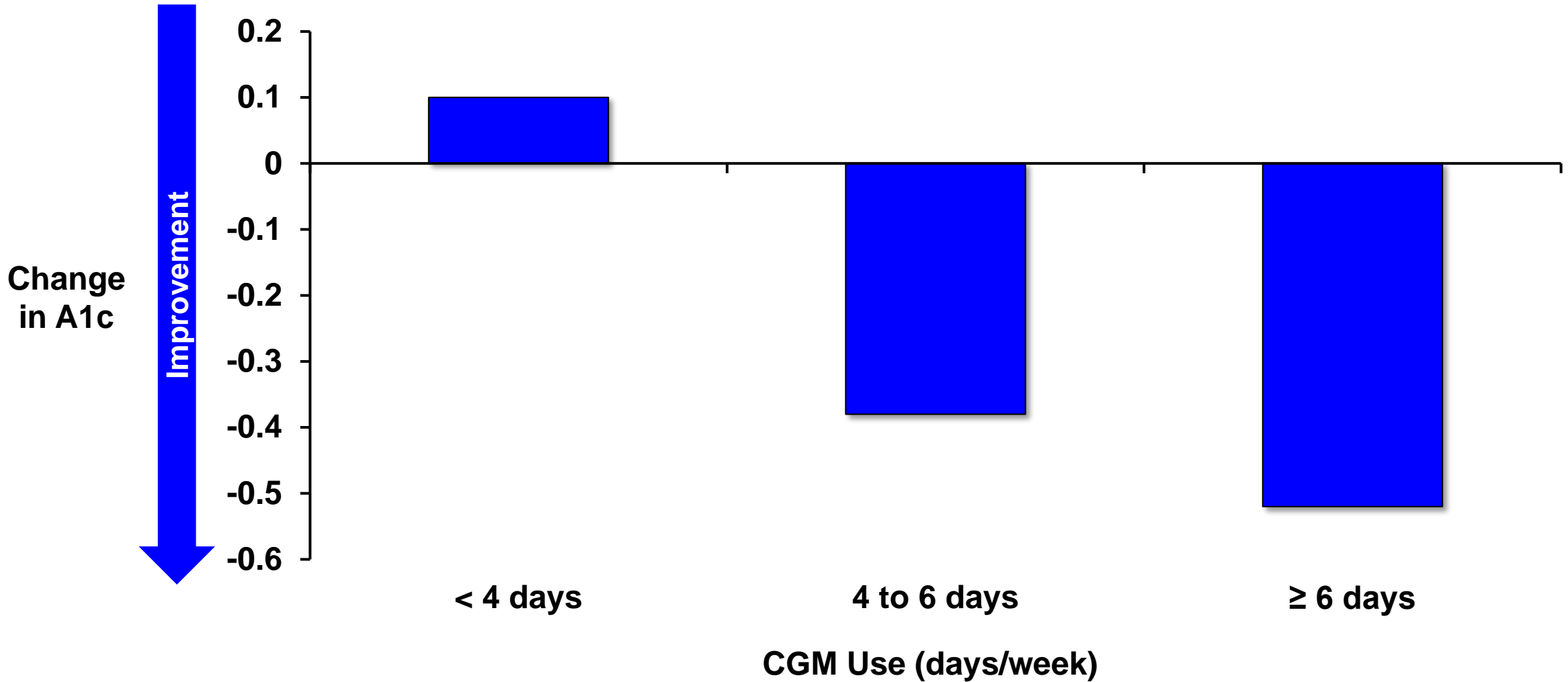
- CGM benefits
  - Improved overall glucose control → lower HbA1c levels
  - Increased time spent within normal glucose range
  - Improved quality of life
- CGM use supported by society guidelines\*
- Greatly underutilized



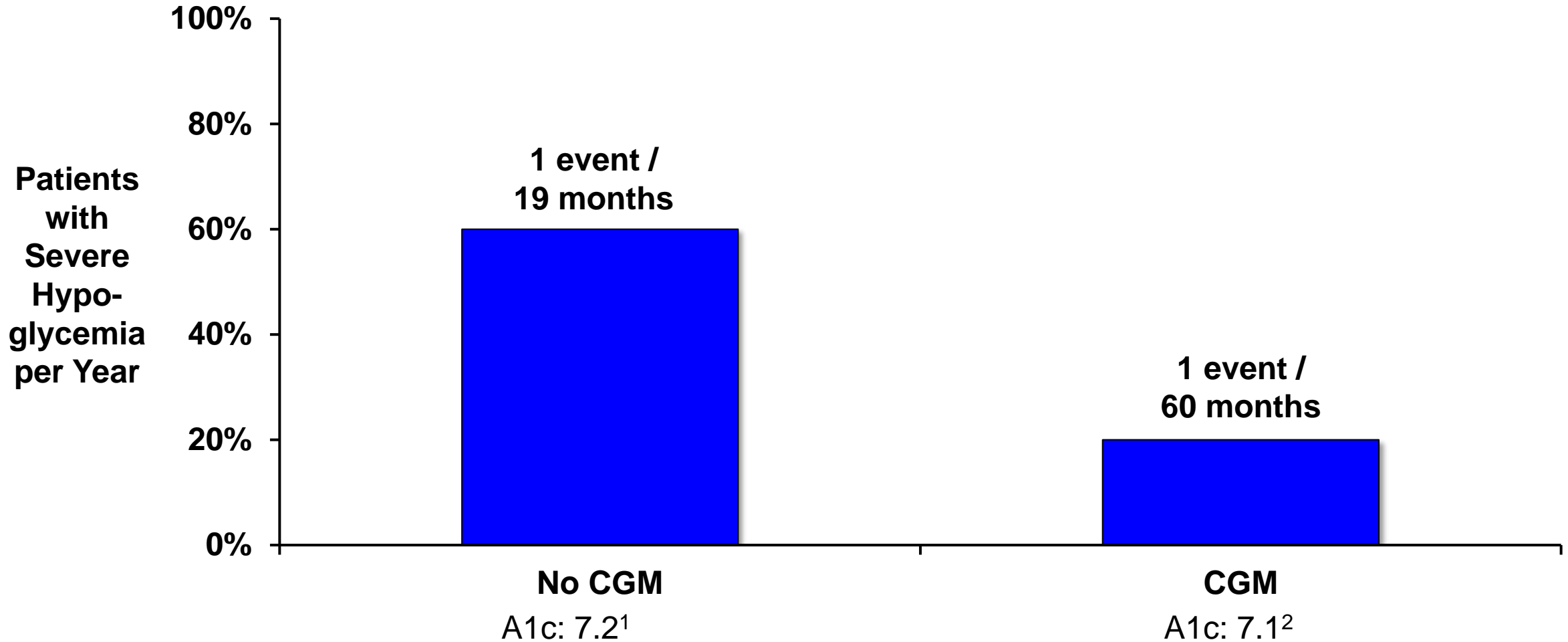
# Intermittent Monitoring with Home Blood Glucose Meter Leads to Unnoticed Highs and Lows



# Maximum A1c Improvement with Regular CGM Use

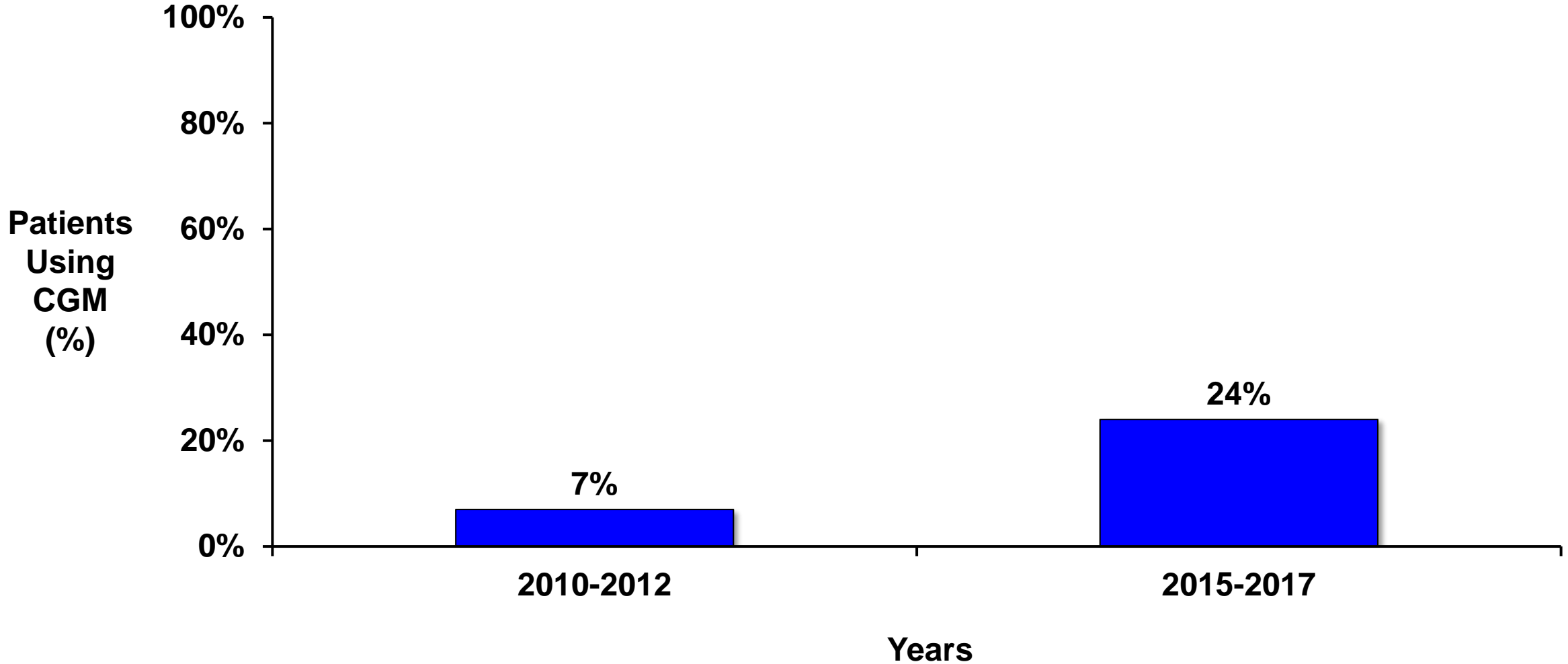


# CGM Protects Against Severe Hypoglycemia



# CGM Systems Are Underutilized: 76% of Patients Do Not Use CGM

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# 27% of Patients Discontinue CGM Use Within 1 Year

<b>Reason</b>	<b>N=262</b>
<b>CGM not working properly / accurate enough</b>	<b>71%</b>
<b>Problems with adhesive/insertion</b>	<b>61%</b>
<b>Too expensive / not covered by insurance</b>	<b>58%</b>
<b>Uncomfortable to wear</b>	<b>41%</b>
<b>Using pump / don't want two sites on body</b>	<b>33%</b>
<b>CGM too big</b>	<b>28%</b>

# Advancements Needed in CGM Systems

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- Longer sensor life
- Less frequent sensor insertions
  - Current systems require 25–50 replacements/year
- Easy to wear and easily removed
  - For physical activities or discretion

# Natural Evolution of Sensor Technology: Longer-Lasting, Less Intrusive

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- Proven clinical benefit
- Many patients have not adopted CGM technology or quickly abandon it
- Patients missing opportunity to improve diabetes status and quality of life
- Need more CGM options to increase patient access

# Study Design and Effectiveness

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**Tim Goodnow, PhD**

Chief Executive Officer

Senseonics, Inc.



# Eversense Clinical Program

<b>Study</b>	<b>Duration</b>	<b>Patients</b>	<b>Sites</b>	<b>Role</b>
<b>PRECISE II</b>	<b>90 days</b>	<b>90</b>	<b>8 US</b>	<b>Pivotal</b>
<b>PRECISION</b>	<b>90 days</b>	<b>35</b>	<b>3 US</b>	<b>Supportive</b>
<b>PRECISE</b>	<b>180 days</b>	<b>81</b>	<b>7 EU</b>	<b>Supportive</b>
<b>European Patient Registry (ongoing)</b>	<b>2 years</b>	<b>1686</b>	<b>350 EU</b>	<b>Post-market</b>
<b>Feasibility Studies</b>	<b>Varied</b>	<b>332</b>	<b>10</b>	<b>Pilot</b>
<b>Total</b>		<b>2224</b>		

# PRECISE II: Pivotal Study Design

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- Non-randomized, single-arm, multi-center study
- N=90 patients
  - n=75 one sensor inserted
  - n=15 two sensors inserted (one in each arm)
- Sensors calibrated 2x/day using home glucose meter
- Glucose readings and high/low alerts were blinded during study

# PRECISE II: Pivotal Study Schedule

Clinic Visit	1	2	3	4	5	6	7
Day	-30	0	1	30	60	90	100
Screening / Follow-up	✓	Insertion					✓
Accuracy (in-clinic)			✓	✓	✓	✓	
Challenges*					✓	✓	✓

Removal



At-home wear  
for 90 days

\*Meal, exercise, compression challenges

# PRECISE II: Primary Endpoint Based on MARD

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- Mean absolute relative difference (MARD)
  - Compares sensor reading with reference glucose
  - Smaller MARD = higher accuracy
- Percent of sensor values within 15 mg/dL or 15% of reference

# PRECISE II:

## Additional Effectiveness Characterization

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- Sensor accuracy across 90 days of use
- Agreement of sensor readings within accuracy limits
- High and low glucose alert performance
- Impact of compression
- Paired precision
- Kaplan-Meier analysis of sensor life
- Method comparison, bias analysis, Clarke & Consensus Error Analysis

## PRECISE II: Key Enrollment Criteria

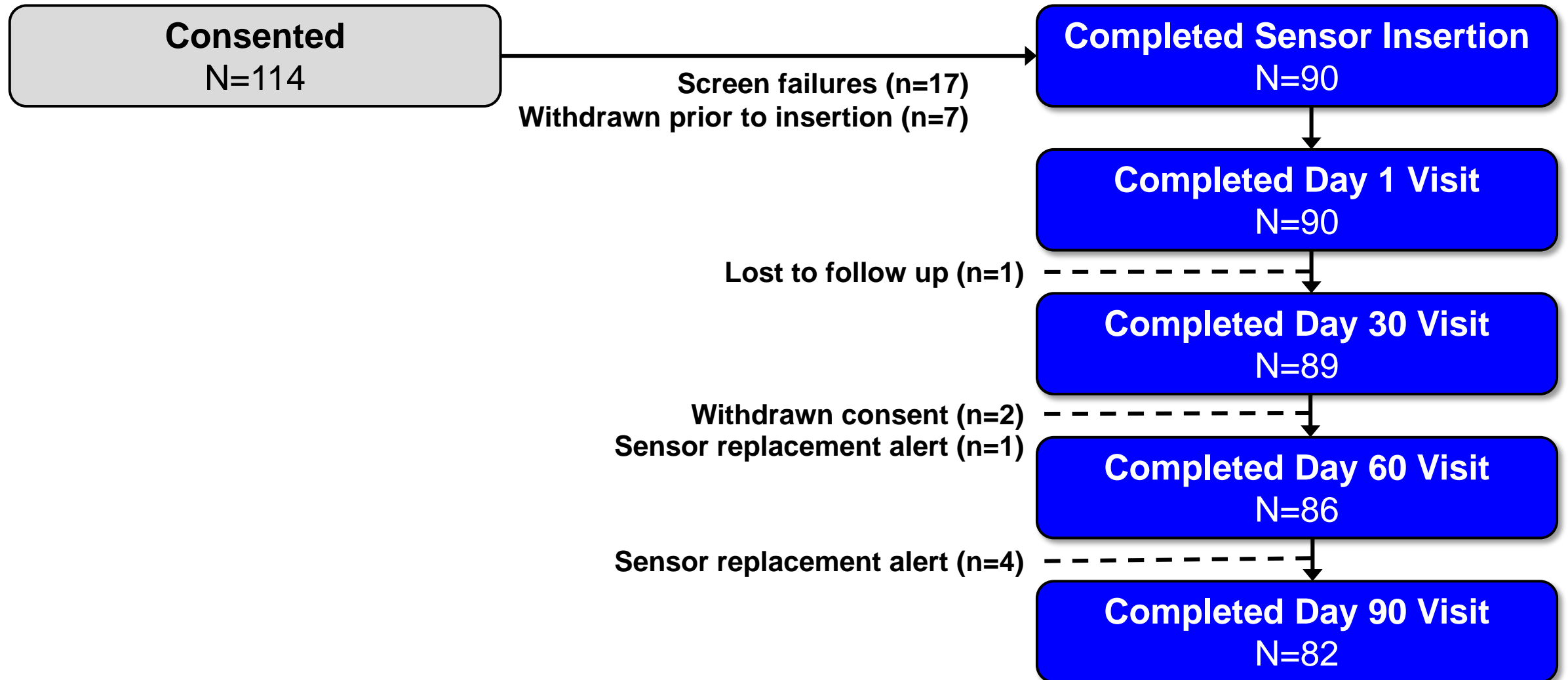
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- Adults diagnosed with diabetes mellitus for at least 1 year
- No severe hypoglycemia within last 6 months
- No diabetic ketoacidosis requiring hospitalization within 6 months

# PRECISE II Demographics: Representative Study Sample

Parameter		N=90
Sex	Male	60%
	Female	40%
Age	Mean	45 years
Race	Caucasian	86%
	Black or African American	8%
	Asian	3%
	Other	3%
Body Mass Index	Mean	29 kg/m <sup>2</sup>
Glycosylated Hemoglobin (HbA1c)	Mean	7.6%
Time since diabetes diagnosis	Mean	20 years
Diabetes type	Type 1	68%
	Type 2	32%
Type of insulin therapy	Continuous insulin infusion pump	48%
	Multiple daily injections	27%
	None (Type 2, not on insulin)	22%
	Other (long-acting insulin only)	3%

# PRECISE II: Disposition





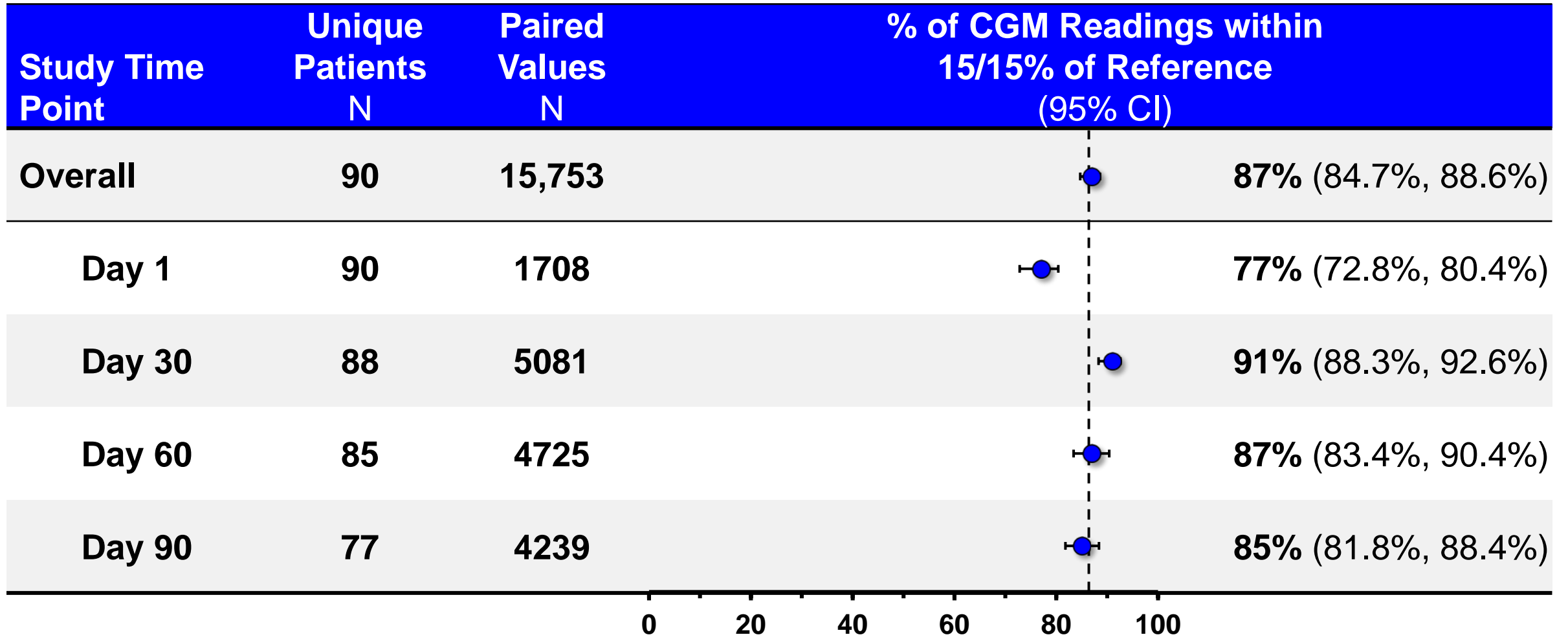
# PRECISE II: Primary Effectiveness Endpoint Met Using Study Software

Software Version	Unique Patients N	Paired Values N	Mean Absolute Relative Difference (95% CI)	p-value
Study SW	90	15,704	8.8% (8.3%, 9.4%)	< 0.0001

# PRECISE II: Primary Effectiveness Endpoint Met Using SW 602

Software Version	Unique Patients N	Paired Values N	Mean Absolute Relative Difference (95% CI)	p-value
SW 602	90	15,753	8.5% (8.0%, 9.1%)	< 0.0001

# PRECISE II: Sensor Accurate through 90 Days of Use



# Eversense Clinical Program

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<b>Total</b>		<b>2224</b>		

# PRECISION Study Design

Clinic Visit	1	2	3	4	5	6	7	8	9
Day	-30	0	1	7	14	30	60	90	100
Screening/Follow-up	✓								✓
Accuracy (in-clinic)			✓	✓	✓	✓	✓	✓	
Challenges*			✓	✓	✓	✓	✓	✓	

At-home wear for 90 days

\*Meal challenges; Overnight challenges were performed on Days 7 and 14

# PRECISION Differences from PRECISE II

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- 3 US sites
- 35 patients with sensors inserted
  - 27 patients had 2 sensors inserted
- Unblinded sensor glucose values and active high/low alerts

# PRECISION:

## Sensor Accurate over 90 Days of Use

Study Time Point	Unique Patients N	Paired Values N	% of CGM Readings within 15/15% of Reference (95% CI)
Overall	35	15,170	85% (82.9%, 87.5%)
Day 1	35	2665	79% (74.5%, 83.1%)
Day 7	35	2926	86% (81.5%, 89.7%)
Day 14	35	2997	88% (84.7%, 90.7%)
Day 30	35	2284	88% (81.3%, 92.6%)
Day 60	35	2133	87% (79.7%, 91.8%)
Day 90	35	2165	84% (78.4%, 88.2%)

# Accuracy Comparison with Approved CGMs through Sensor Life

Device	Data Source	Percent of System Readings Within 15/15% of Reference							
		Day 1	Day 3-4	Day 7	Day 10	Day 14	Day 30	Day 60	Day 90
Eversense (SW 602)	PRECISE II	77%	--	--	--	--	91%	87%	85%
	PRECISION	79%	--	86%	--	88%	88%	87%	84%
Dexcom G5*	--	77%	89%	90%	--	--	--	--	--
Medtronic Guardian (3)*‡	--	68%	87%	82%	--	--	--	--	--
FreeStyle Libre*	--	76%	82%	85%	85%	--	--	--	--

\* Summary of Safety and Effectiveness Data (SSED) - Medical Device Databases - <http://www.fda.gov>

‡ Results based on calibration every 12 hours

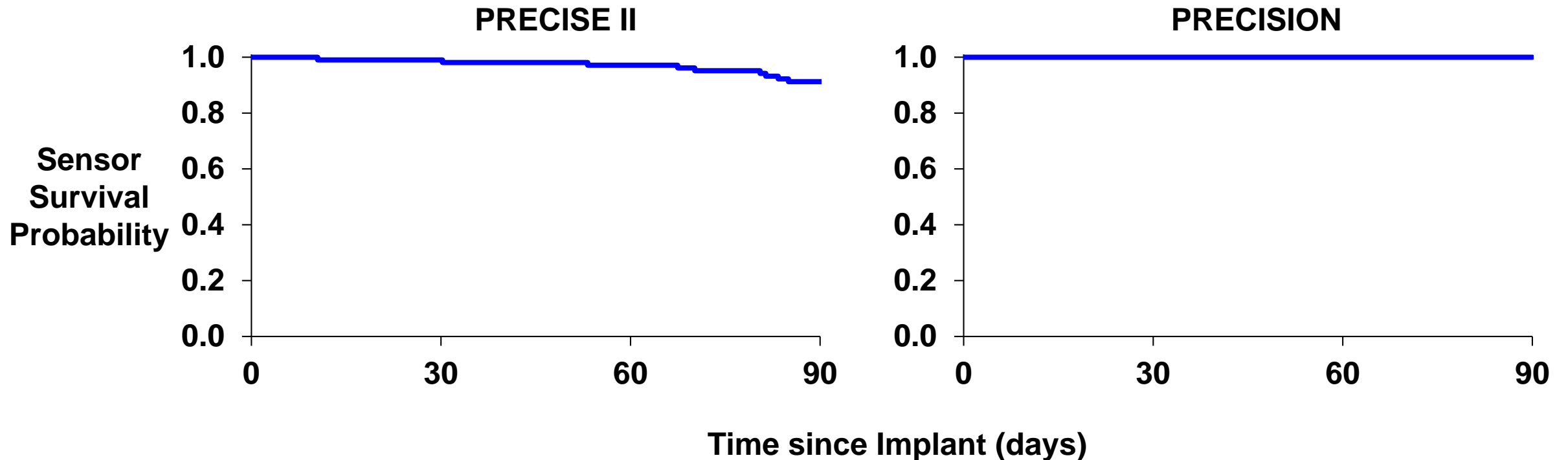


# Accurate Detection of Glucose Excursions

Alert Setting	PRECISE II		PRECISION	
	Detection Rate	False Alert Rate	Detection Rate	False Alert Rate
Low Glucose Alert at 70 mg/dL*	96%	16%	95%	8%
High Glucose Alert at 180 mg/dL*	98%	7%	99%	7%

# PRECISE II and PRECISION: Eversense Sensor Longevity

- PRECISE II: KM survival probability of 91% at Day 90
- PRECISION: All sensors functioned 90 days



# PRECISE II and PRECISION: System Adherence

	PRECISE II	PRECISION
Median wear time	23.4 hours	23.4 hours
% transmitters worn > 20 hours/day	87%	91%

# Effectiveness Summary: Eversense is Accurate for 90 Days

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- PRECISE II: 87% of sensor readings with 15/15% of reference
- PRECISION: 85% of sensor readings with 15/15% of reference
- Accurate at each measured time point
- No degradation of sensor performance
  - 91% of sensors function through 90 days
  - “Sensor Replacement” alert appropriately produced
- Over 95% detection rates for glycemic excursions
  - High (180 mg/dL) and low (70 mg/dL) glucose

# Clinical Safety

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**Lynne Kelley, MD, FACS**

Chief Medical Officer

Senseonics, Inc.

# Overview of Safety Profile

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- Eversense system has acceptable safety profile
  - Similar to other marketed CGM systems
- Procedural risks of implantable sensor mitigated
  - Device design, training, and continued improvements based on post-market surveillance
- Eversense reduces some known risks associated with other CGM systems

# Eversense Clinical Program

<b>Study</b>	<b>Duration</b>	<b>Patients</b>	<b>Sites</b>	<b>Role</b>
<b>PRECISE II</b>	<b>90 days</b>	<b>90</b>	<b>8 US</b>	<b>Pivotal</b>
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# PRECISE II and PRECISION: Device Exposure

	<b>PRECISE II</b>	<b>PRECISION</b>
<b>Sensors inserted and removed</b>	<b>106 sensors</b> (90 patients)	<b>62 sensors</b> (35 patients)
<b>Procedures performed</b>	<b>212 procedures</b>	<b>124 procedures</b>
<b>Sensor use (mean duration)</b>	<b>92.2 days</b>	<b>91 days</b>
<b>Sensor exposure</b>	<b>9,773 days</b>	<b>6,148 days</b>



# PRECISE II and PRECISION: Primary Safety Endpoint

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- Incidence of device-related or insertion/removal procedure-related serious adverse events (SAEs) at any point during sensor use

# PRECISE II and PRECISION: Additional Safety Analyses

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- Non-serious related adverse events
- AEs of special interest
  - e.g. infection, adhesive reactions
- Dexamethasone exposure over time

# PRECISE II and PRECISION: Serious Adverse Events (SAEs)

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## PRECISE II

- No device-related SAEs
- One procedure-related SAE reported
  - Sensor removal sensor unsuccessful (with and without ultrasound)
  - Sensor successfully removed by surgeon under general anesthesia

## PRECISION

- No device- or procedure-related SAEs
  - 3 unrelated SAEs
  - Gastroenteritis, hypoglycemic episode, cellulitis of left foot

# PRECISE II and PRECISION: Device- or Insertion/Removal-Related AEs

Adverse Event	PRECISE II		PRECISION	
	Events	Patients N=90	Events	Patients N=35
All Events	14	7	8	5
Pain/discomfort	4	2	2	2
Bruising	2	2	--	--
Erythema	2	2	--	--
Device fragment not recovered	2	2	--	--
Syncope	1	1	--	--
Tingling	1	1	--	--
Delayed report of pain	1	1	--	--
Secondary procedure to remove sensor	1	1	2	1
Dermatitis at patch location	--	--	2	1
Skin hyperpigmentation	--	--	2	1

# PRECISE II: Two Events Related to Device Fragment

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- All removed sensors returned to sponsor for inspection
- 2 devices did not have cap upon return
- Corrective and preventative action plan implemented
  - Implementing enhanced quality procedures (cap adhesion)
- Cap material: PMMA highly biocompatible, permanent implant
  - Orthopedic, dental, and ophthalmologic
- Cap size: 3.2 mm x 0.8 mm

# PRECISE II and PRECISION: Additional Safety Outcomes

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- No infections
- All related AEs considered expected and common for subcutaneous implant
- All related AEs resolved fully

# Role of Dexamethasone-Eluting Silicone Collar

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- Contains 1.75 mg dexamethasone acetate (DXA)
  - Water-insoluble corticosteroid
  - Reduces local inflammatory response
  - Extends sensor life
- Controlled and slow DXA release
  - $< 3 \mu\text{g/day}$  to local tissue
  - $< 300 \mu\text{g}$  delivered over entire 90 days

# Impact of Dexamethasone Exposure

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- Blood assayed for DXA to 50 pg/mL level
  - No detectable plasma levels of DXA observed
  - No systemic effects
- DXA collars examined after removal
  - Minimal DXA exposure confirmed 3 µg/day
- 2 events of transient hyperpigmentation
  - Resolved upon sensor removal



# Eversense Clinical Program

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# Integrated Device Exposure

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- Three multi-center studies
  - PRECISE II, PRECISION, and PRECISE
- 206 subjects
- 335 sensors
- 670 insertion/removal procedures
- 22,529 patient-days of sensor wear

# Integrated Summary of Related Adverse Events

Adverse Event	Events	Patients N=206
All Events	41	26 (13%)
Pain/discomfort	10	8 (4%)
Redness/erythema	6	6 (3%)
Secondary procedure to remove sensor	4	3 (1%)
Infection	3	3 (1%)
Bruising/hematoma	3	3 (1%)
Device fragment not recovered	2	2 (1%)
Dermatitis at patch location	3	2 (1%)
Skin hyperpigmentation	2	1 (< 1%)

Events occurring once: neuropathy, vertigo, disturbed sleep, headache, paresthesia, syncope, hypertension, and nausea

# Low Rate of Infections Observed in Studies

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- Aggregate infection rate 1%
- Improved incision care instructions
  - PRECISE: leave bandage for 24 hours
  - PRECISE II: leave bandage for 48 hours
- Infection rate observed is below literature reports for similar implants and minor procedures: 2–4%\*

\*Buprenorphine, Braeburn Pharmaceuticals, Inc.

\*<http://www.worldwidewounds.com/2005/september/Gottrup/Surgical-Site-Infections-Overview.html>

# Eversense Clinical Program

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# European Patient Registry

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- All patients inserted commercially enrolled in registry
  - Enrollment completed when 100 patients reach 4 insertions
- All patients enrolled to be followed through 8 insertions and removals

# Low Rate of AEs with Repeat Insertions

Events, n (%)	Post Insertion #						
	1 N=1686	2 N=443	3 N=143	4 N=58	5 N=39	6 N=14	7 N=3
<b>SAEs</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>Device-, procedure-related AEs</b>							
Infection (at sensor site)	<b>8 (0.5%)</b>	<b>4 (1%)</b>	<b>2 (1%)</b>	-	-	-	-
Secondary procedure to remove sensor	<b>7</b>	<b>2</b>	-	-	-	-	-
Adhesive patch site irritation	<b>5</b>	-	<b>2</b>	-	-	-	-
Prolonged wound healing	<b>3</b>	-	-	-	-	-	-
Redness/reaction to dressing	<b>3</b>	-	-	-	-	-	-
Sensor broke during removal	<b>3</b>	-	-	-	-	-	-
Skin atrophy over sensor w/ skin discoloration	<b>2</b>	<b>1</b>	-	-	-	-	-
Skin atrophy over sensor	<b>1</b>	-	-	-	-	-	-
Skin discoloration	<b>1</b>	<b>2</b>	-	-	-	-	-
Sensor site pain/discomfort	<b>1</b>	-	-	-	-	-	-
Bruising	<b>1</b>	<b>1</b>	-	<b>1</b>	-	-	-
Patient fainted during procedure	<b>1</b>	-	-	-	-	-	-
Hematoma	-	-	-	<b>1</b>	-	-	-

# Proposed Post-Approval Study

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# Proposed U.S. Post Approval Study Design

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- Serial sensor insertions and removals for 2 years
- 175 patients in up to 20 clinical sites
- **Primary safety endpoint**
  - Rate of device-related and insertion/removal procedure-related SAEs through 12 months  $\leq 7\%$
- **Primary effectiveness endpoint**
  - Time in range (between 70 mg/dL and 180 mg/dL), 12 months vs. first month

# Proposed U.S. Post Approval Study: Other Outcome Measures

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- All related AEs through 2 years
- Plasma dexamethasone levels every 6 months
- Effectiveness of training program
  - Success rate of insertions/removals
- Diabetes distress scale and CGM satisfaction scale
  - Baseline and annually

# Design Changes

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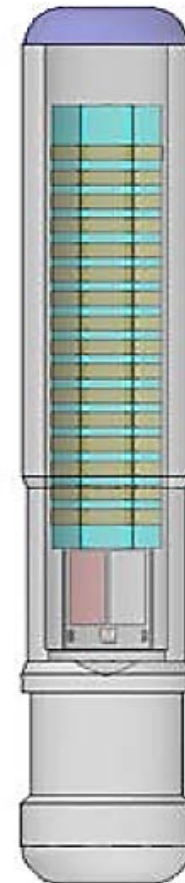
- Sensor end cap
- Blunt dissector tool

# Sensor End Cap Improvement

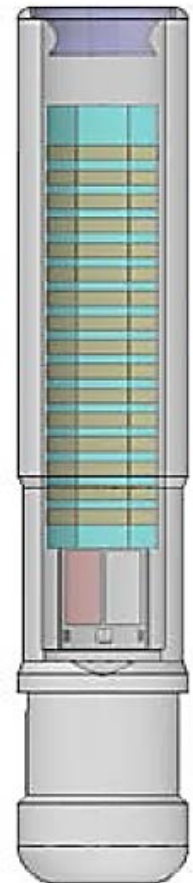
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- End cap redesigned to be flush with end of sensor
- Design verification
  - Compressive forces
  - Torque
  - Maintains functional compatibility with insertion tool

Original Design

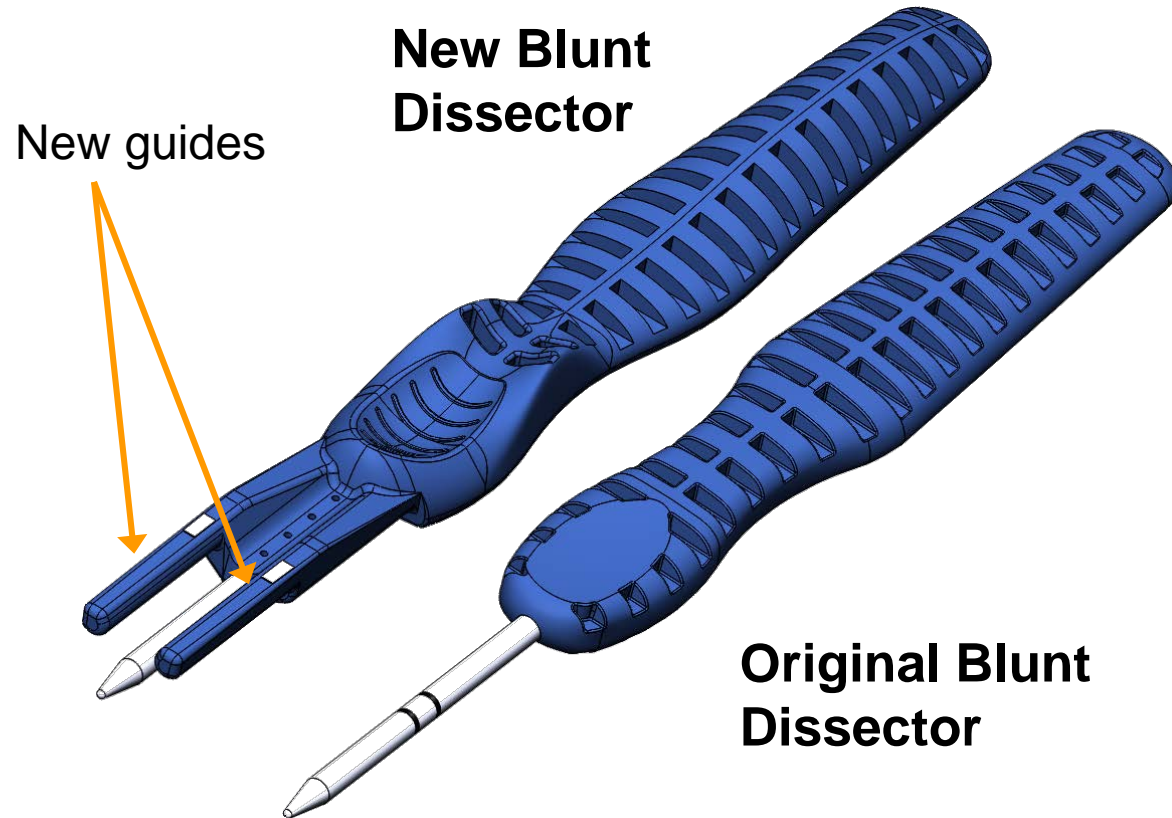


New Design



# Blunt Dissector Design Improvement

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- Same function
- Consistent placement facilitates removal
  - Proper entry angle
  - Pocket depth / length
  - Parallel to skin
- Validated with Human Factors testing

# Training for Clinicians

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# Training Program Overview

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- Mandatory comprehensive training
- Certification process led by Senseonics approved trainers
  - ✓ Didactic session
  - ✓ Practices with simulated skin
  - ✓ Initial insertions and removals are observed

## Training resources:

- *CGM Sensor Insertion and Removal Instructions*
- Insertion videos
- Removal videos
- Simulation station
- Procedure poster
- Take-home instructions

# Training Checklist for Certification

Pre-Work before Simulation Training		Pre-Work before Removal Review	
<p><b>Eversense Certified Physician Checklist</b></p> <p>Instructions: Clinical Training Manager (CTM) will place a check in the space indicating that the physician has independently demonstrated or completed the required skill or step.</p> <p><b>Pre-Work before Simulation Training</b></p> <p>View, Read, or Do:</p> <ol style="list-style-type: none"> <li>1. Video: Insertion and Removal Procedure</li> <li>2. PDF: CGM Sensor Insertion and Removal Instructions</li> <li>3. PDF: Eversense PMCF Adverse Event Form</li> <li>4. Gather all supplies. Check expiration dates on all materials. Do not use expired items.</li> </ol> <p><b>Insertion Simulation Training with CTM</b></p> <ul style="list-style-type: none"> <li>Wipe mayo stand or table clean for sterile field</li> <li>Discuss with patient indications, contraindications, risks, side effects, warnings, and cautions.</li> <li>Decide with patient location of sensor using <i>Things to Consider when Choosing Insertion Location</i> in labeling.</li> <li>Use incision template to mark incision line and position patient.</li> <li>Clean arm in preparation for Lidocaine injection.</li> <li>Inject approximately 2 mL of Lidocaine along the 5 – 8 mm planned incision and approximately 30 mm perpendicular to planned incision.</li> <li>Wash hands, put on sterile gloves, set up sterile field with assistant.</li> <li>Fill well of insertion tool tray with saline.</li> <li>Load sensor into cannula, return to tray, ensuring sensor is in saline for 5 minutes.</li> <li>Place sterile drape over patient's arm.</li> <li>Prepare patient's arm with approved anesthetic agent: chlorhexidine or betadine.</li> <li>Confirm full anesthesia and patient orientation.</li> </ul>	<ul style="list-style-type: none"> <li>Using marking on skin, make 5 – 8 mm long incision, no more than 3 – 5 mm below the skin.</li> <li>Create subcutaneous pocket no more than 3 – 5 mm below the skin with blunt dissector as follows: <ul style="list-style-type: none"> <li>Place the tapered tip of the blunt dissector into the incision at 45 degree angle. Flatten the angle so that the blunt dissector is touching the skin beneath.</li> <li>Ensure finger rests in the finger well, and hand is on top of the blunt dissector. Maintain as shallow an angle as possible and in no case more than 5 – 10 degrees to the exterior arm.</li> <li>Advance blunt dissector until the incision line is between the markings on the blunt dissector. Remove blunt dissector and clean area.</li> </ul> </li> </ul>	<p><b>Eversense Certified Physician Checklist</b></p> <p>Instructions: Clinical Training Manager (CTM) will place a check in the space indicating that the physician has independently demonstrated or completed the required skill or step.</p> <p><b>Pre-Work before Removal Review</b></p> <p>View, Read, or Do:</p> <ol style="list-style-type: none"> <li>1. Video: Insertion and Removal Procedure</li> <li>2. PDF: CGM Sensor Insertion and Removal Instructions</li> </ol> <p><b>Pre-Work before Removal Review</b></p> <ul style="list-style-type: none"> <li>Stabilize sensor by pushing down on the skin over the sensor's proximal end.</li> <li>Create a 5.8 mm incision through the dermis at the location previously marked.</li> </ul>	<p><b>Pre-Work before Removal Review</b></p> <p>View, Read, or Do:</p> <ol style="list-style-type: none"> <li>1. Video: Insertion and Removal Procedure</li> <li>2. PDF: CGM Sensor Insertion and Removal Instructions</li> </ol> <p><b>Pre-Work before Removal Review</b></p> <ul style="list-style-type: none"> <li>Put gentle pressure on the sensor's proximal end through the skin to facilitate grasping and removing it. Rotating the sensor with the clamp may help free the sensor from any attached tissue.</li> <li>Close incision with Steri-Strip™ ensuring sides of the incision are approximated without tension. Dress with sterile gauze and sterile Tegaderm™.</li> </ul>
<p><b>Insertion Simulation Training</b></p> <ul style="list-style-type: none"> <li>With sensor loaded, introduce insertion tool tip into the incision at a 45 degree angle. Immediately flatten tool parallel to the arm. Advance the insertion tool at an angle no more than 5 – 10 degrees until the incision line is between the markings on the insertion tool.</li> <li>Use non dominant hand to gently hold insertion tool in place. With dominant hand, depress and retract thumb slide, ensuring sensor is in saline for 5 minutes.</li> </ul>	<ul style="list-style-type: none"> <li>Skin over the sensor looks like it is thinning, depressed or changing color</li> <li>Ensure sensor is linked with transmitter before patient leaves office.</li> </ul> <p>Physician Name: _____ Physician Email: _____ Clinic Name: _____ City: _____ Country: _____</p>	<p><b>Removal Simulation Training</b></p> <p><b>Removal Simulation Training with CTM</b></p> <ul style="list-style-type: none"> <li>Discuss Potential Complications During Removal Process in labeling with CTM</li> <li>Wipe mayo stand or stable table clean for sterile field.</li> <li>Position patient comfortably.</li> <li>Clean area in preparation for Lidocaine injection.</li> <li>Palpate and mark location of sensor using guide.</li> <li>Incision line only. Excess lidocaine will cause swelling and make finding sensor difficult.</li> <li>Wash hands, put on sterile gloves, set up sterile field with assistant.</li> <li>Place sterile drape over patient's arm.</li> <li>Prepare patient's arm with approved agent: chlorhexidine or betadine.</li> <li>Confirm full anesthesia.</li> </ul>	<p><b>Removal Simulation Training</b></p> <ul style="list-style-type: none"> <li>Replace the Tegaderm™ over Steri-Strip™ after two days with another Tegaderm™ or Sterile bandage.</li> <li>Avoid getting the Tegaderm wet when showering.</li> <li>Change the Tegaderm if it is soiled</li> <li>You can place the transmitter over the Tegaderm after the first day</li> <li>Do not soak in a tub, swim, do strenuous sports, or perspire heavily for five days.</li> </ul> <p>Notify your physician if:</p> <ul style="list-style-type: none"> <li>Your experience any pain, redness, swelling, warmth or drainage at the incision site</li> <li>You develop a fever</li> <li>Skin over the sensor looks like it is thinning, depressed or changing color</li> </ul> <p>State recommended location for new sensor if inserted at same visit.</p> <p>Ensure new sensor is linked with transmitter before patient leaves office.</p> <p>Physician Name: _____ Physician Email: _____ Clinic Name: _____ City: _____ Country: _____</p> <p>Date became Eversense Certified Physician: _____ Physician Printed Name: _____ Physician Signature: _____ CTM Printed Name: _____ CTM Signature: _____</p>
<p><b>Learning curve: ~2 to 3 procedures</b></p> <p><b>3 patients scheduled in same day to familiarize with procedure</b></p>			
<p>CLN – 0002 Rev2</p> <p>By initialing this form, I certify that the trainer provided instruction on, and where applicable, demonstration of, all of the areas covered above. I was given ample opportunity to ask questions, and all of my questions were fully answered to my satisfaction. The instruction and demonstration were sufficient training to fully enable me to safely insert and remove the Eversense CGM sensor from my patients. I am qualified to perform the insertion and removal procedures of the Eversense CGM sensor without further instruction or supervision. I agree to report to the distributor/manufacturer all adverse events related to the device use or procedure.</p>		<p>CLN – 0002 Rev2</p> <p>By initialing this form, I certify that the trainer provided instruction on, and where applicable, demonstration of, all of the areas covered above. I was given ample opportunity to ask questions, and all of my questions were fully answered to my satisfaction. The instruction and demonstration were sufficient training to fully enable me to safely insert and remove the Eversense CGM sensor from my patients. I am qualified to perform the insertion and removal procedures of the Eversense CGM sensor without further instruction or supervision. I agree to report to the distributor/manufacturer all adverse events related to the device use or procedure.</p>	



# Hands-On Practice Session with Simulated Skin, Sterile Field, and Required Supplies

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# Examples of Training Materials

**eversense.**  
Continuous Glucose Monitoring System

## Eversense Insertion Procedure

**Inclusion criteria**  
Adults with diabetes.

**Exclusion criteria**

- Patients who need an MRI, critically ill or hospitalized patients.
- People for whom dexamethasone or dexamethasone acetate are contraindicated.
- People using therapeutics products such as mannitol intravenous and irrigation solutions.
- Women who are pregnant.
- People under the age of 18.

- Position the smart transmitter on skin and mark corners.
- Align incision template and mark the skin for the incision. Put on sterile gloves.

Ask for:

  - Drape for basin
  - Lidocaine
  - Tegaderm\*\* with Pad
  - Sensor
  - Scalpel
  - Gauze
  - Saline in well
  - Chlorhexidine
  - Steri-Strips\*\*

- Remove cap. Align insertion tool cannula with sensor holder making sure slots are aligned. Slide sensor holder over insertion tool so that the two triangles are touching.
- Insert bevel tip of blunt dissector into incision at 45 degrees and until the depth guards are touching the skin. Drop to 5-10 degrees ensuring fingers are not under the tool. Move the blunt dissector towards the shoulder, allowing depth guards to slide over the surface of the skin to create a subdermal pocket that is near parallel. Advance until plastic backstop is reached. Completely retract the blunt dissector and set aside.
- Clean -> Anesthetize.
- Push down here.
- Apply gentle pressure to stop any bleeding. Ensure edges of the incision are closed with Steri-Strips\*\*.

Secure https://hcp.eversensedabetes.com

eversense. Procedure Videos Insertion / Removal Instructions Resources Customer Support Inquiry

## Eversense Procedure Videos

### Insertion of the Eversense CGM Sensor

This video provides step-by-step orientation to the Eversense Insertion Procedure process. The content is designed for a health care provider in training. Topics include patient selection, sensor site considerations, sensor placement technique and patient take home instructions.

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Continuous Glucose Monitoring System

## Advanced Sensor Removal Guidance

Read Sensor Removal Procedure and Potential Complications in the Eversense, CGM Sensor Insertion and Removal Instructions.

- A typical sensor removal takes between 5 and 10 minutes.
- The correct type of clamp must be available before attempting a removal. The 16 cm Crile clamp is the preferred tool. Clamps that are too small can make grasping the sensor difficult.
- Removals done by any provider should be done under local anesthesia, in an exam or procedure room. There is no need for surgical suite or general anesthesia unless there are extenuating circumstances.
- Prior to disinfecting the area, use the transmitter and placement guide to get the best signal possible. Mark the outline of the transmitter. This will define the area of where the sensor is, which will help once the drape is placed.
- If you can palpate the sensor mark both ends or outline it entirely for reference.

# Trained Providers Outside U.S.

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- 461 clinicians trained on insertions
  - 94% certified to do insertions independently
- 258 clinicians trained on removals
  - 86% certified to do removals independently

# Europe: Successful Insertion and Removal Training

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- Procedure easily learned by physicians with no prior Eversense experience
- 99% of removals successful on first attempt
- Low infection rate (0.5%)

# PRECISE II and PRECISION: Successful Insertion and Removal Training

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- 100% of insertions and 99% of removals successful on first attempt
- 91% of insertions and 80% of removals completed in < 5 min

	<b>Insertion</b> N=168	<b>Removal</b> N=168
<b>Mean time</b>	<b>2.3 min</b>	<b>4.5 min</b>

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# Eversense System Has Acceptable Safety Profile

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- No unanticipated adverse events
- Limited AEs related to device or procedure
  - All AEs reported resolved fully
  - No Infections in US clinical trials
  - No detectable blood levels of dexamethasone
- One procedure-related SAE, resolved
- No device-related SAEs
- Eversense is safe for intended use

# Clinical Perspective / Benefit-Risk

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**Steven J Russell, MD, PhD**

Associate Professor of Medicine

Harvard Medical School

# Relevant CGM Experience

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- Experience with all currently approved CGMs (since 2004)
  - Published accuracy comparison studies of CGMs
- Developing bionic pancreas
  - Depends on CGM accuracy and reliability
  - Motivates interest in new CGM technologies
- Clinical investigator in artificial pancreas trials
  - Used Eversense system
  - Inserted and removed sensors
  - Trained quickly



# Current Situation: Majority of Patients Do Not Meet Glycemic Goals

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- 70% not at A1c targets\*
  - Hypoglycemia still very common
- CGM systems are proven to help
  - Improve glucose control
  - Lower risk of hypoglycemia
  - Improve patients' lives

# The Current Situation: Only 3 Out of 10 Patients with T1D Use CGM

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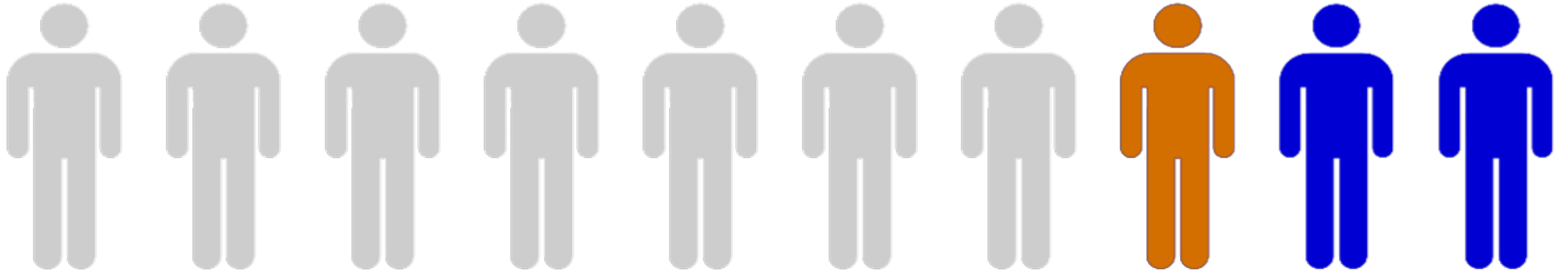


- Perceived burden of repeat insertion
- Fear of pain

# The Current Situation:

## 1 out of 3 CGM Users Discontinue within 1 Year

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- **Problems with adhesive / insertion**
- **Uncomfortable**

# Eversense Addresses Many Barriers to CGM Use

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- Longer sensor life (90 days)
- Less frequent sensor insertions
  - Eversense: 4 times per year
  - Current systems: 25–50 times per year
- Easy to wear and easily removed
  - For physical activities or discretion
- On-body vibration from transmitter provides extra safety measure

# The Goal: Increase Use of CGM

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- Improve glucose control
- Lower risk of hypoglycemia



# **Eversense<sup>®</sup> Continuous Glucose Monitoring (CGM) System**

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**March 29, 2018**

Senseonics, Inc.

Clinical Chemistry and Clinical Toxicology Device Panel