Manual 39
Continuous Glucose Monitoring Procedures
ARIC Visit 11

Version 1.6
November 5, 2024

Continuous Glucose Monitoring (CGM)
Manual of Procedures
Table of Contents

OVERVIEW

0. MANUAL REVISIONS

Version Number	Date	Author	Section(s)	Description of Update
0.1	Sept 01, 2023	Liz Selvin, Arielle Valint	All	Initial Draft for Visit 11 CGM Manual. For review.
1.0	Dec 18, 2023	Liz Selvin, Arielle Valint	All	Updated based on comments from pre-pilot feedback.
1.1	Jan 31, 2024	Arielle Valint	2.5 Sensor Removal and Return Instructions; 2.6 CGM Post-Return Field Center Instructions	Added details to include SN QR code on biospecimen bag. Include "R" on shipping log and ARIC ID label if this is a replacement sensor for the ARIC participant.
1.2	March 18, 2024	Kelley Reeves, Arielle Valint	2.2 Procedures for CGM Application; 2.3 Procedures for starting the CGM Sensor	Added clarification regarding initializing the Freestyle Libre 3 device. The FSL3 reader and patch have reduced NFC range and the reader should be touching the sensor during the initialization process.
1.3	May 17, 2024	Arielle Valint	5.1 Freesyle Libre 3 Blinded Reader	Added manual check of reader date/time after each charge and after daylight savings time changes.
1.4	August 22, 2024	Mirela Scott	1.4.1 Exclusions	Added battery-operated to the description of the medical devices; added defibrillator as example of excluded medical devices.
1.5	September 3, 2024	Amelia Wallace	5.1 Freesyle Libre 3 Blinded Reader	Added instructions to record time display on reader and clock time in updated CGMR form. Instructed not to reset time on readers.
1.6	November 5, 2024	Sonia Guarda	1.4.2 Contraindications	Removed exclusions related to imaging and travel per new FDA guidance.

1. STUDY OVERVIEW

1.1 Study Aims

1) To characterize glucose patterns detected by continuous glucose monitoring (CGM) technology (measures of glycemic variability, hyperglycemia, and hypoglycemia) and assess concurrent symptoms in adults aged 80+ with and without diabetes.

2) To quantify the cross-sectional associations of CGM-detected glucose patterns with health conditions in older adults. We will evaluate the associations of CGM parameters (measures of glycemic variability, hyperglycemia, and hypoglycemia) with frailty and poor physical and cognitive function.

3) To evaluate the prospective associations of CGM-detected glucose patterns with clinical outcomes and determine if these associations are independent of traditional risk factors and biomarkers of hyperglycemia during 4 years of follow-up in old age. We will evaluate outcomes after high glycemic variability and glucose excursions (low and high), including the development or progression of subclinical and major clinical disease. We will assess whether CGM captures prognostic information above and beyond traditional short- and long-term hyperglycemic biomarkers (i.e., HbA1c, fructosamine, glycated albumin, 1,5-anhydroglucitol).

To achieve these aims, we will conduct 2-week CGM in all participants at ARIC Visit 11 to evaluate glucose patterns during the 2-week wear period.

1.2 Background and Rationale

Older adults are less able to maintain homeostasis or maintain physiological constancy and, although diabetes is common in old age, glucose instability is an underappreciated concern. Diabetes exists along a continuum and there is no clear glycemic threshold above which complications occur. Indeed, approaches to diagnosis and thresholds have changed substantially over time as our understanding of diabetes and its treatments have evolved. We contend that disordered glucose patterns among very old adults (80+) may be present even in the absence of overt diabetes and may be related to concurrent health status and future clinical outcomes.

Continuous glucose monitoring (CGM) technology is the recommended approach to the assessment of glycemic variability and hypoglycemia and is being increasingly used in diabetes care. The burden of disordered glucose homeostasis and its link to clinical outcomes in very old adults (80+) with diabetes is uncharacterized and no prior studies have included older adults without diabetes. Indeed, the evidence-base for understanding CGM-detected hypoglycemia and glycemic variability in older non-diabetic adults is practically non-existent.

Wearable CGM technology is an opportunity to rigorously characterize glucose patterns in older adults across the glycemic spectrum (from no diabetes, to prediabetes, to

diabetes) and evaluate associations with concurrent and prospective health outcomes. We contend that glucose patterns detected by CGM, especially episodes of hypoglycemia and measures of glycemic variability, will add prognostic information above and beyond our typical laboratory biomarkers of average glycemic control such as HbA1c, fructosamine, and glycated albumin.

The data generated by this project will provide the first-ever information on 'normal' glucose patterns in old age and possible associations of disordered glucose patterns (e.g. high variability, episodes of low glucose) with symptoms in persons with and without diabetes. In persons with diabetes, our results will assist clinicians in formulating more specific recommendations regarding diabetes treatment goals and the health consequences of disordered glucose homeostasis in old age. The lack of information on normal glucose patterns in older adults and uncertainty regarding clinical utility of CGM in type 2 diabetes are motivations for this project.

1.3 Key Measures

- Up to 14 days of continuous glucose monitoring (CGM) data (glucose measured every 5 minutes using Libre 3 in blinded mode)

1.4 Study Participants

The continuous glucose monitoring (CGM) protocol will be offered to all consenting participants returning for the Visit 11 examination. ARIC staff may also apply the CGM sensor during home visits. If the participant is scheduled for ARIC imaging within 14 days, the CGM protocol should be offered at a later date.

1.4.1 Exclusions

If any of the following exclusions apply to a study participant, the CGM protocol will not be offered:

- The participant has a history of allergic skin reaction to adhesive tape
- The participant cannot mail the device back to the field center or deliver the device back to the Field Center.
- If the participant has a battery-operated, implantable medical device such as a pacemaker or defibrillator. The performance of the Abbott system has not been evaluated when used with implanted medical devices. The Abbott system has been tested and found to be safe with one brand of implantable pacemaker devices but has not been extensively tested with other brands of pacemakers. This exclusion is made out of an abundance of caution.
- Examples of devices that DO NOT need to be considered for exclusion: cochlear implants, mitral valve clips, other stents or heart valve replacements, Watchman or other battery-less cardiac implants, heart monitor recorders (including LINQ or loop implantable recorders), optical implants, radiation therapy ports.

If the study participant is excluded from the CGM protocol at the time of their Visit 11 appointment, but still eligible for the study (i.e. the participant is interested in the study and does not have an allergic skin reaction to adhesive tape), the protocol should be offered to the participant at the closest time point when monitoring is possible.

Note: Participants will **not** be excluded if they already use a continuous glucose monitoring device. They can wear both devices simultaneously. The sensor being used in this protocol is blinded (participants cannot obtain real-time information on glucose from the sensor). If participants have diabetes, they should be advised to continue to take their medications and continue their normal routine for self-monitoring of their glucose levels.

1.4.2 Contraindications

The Libre 3 sensor must be removed prior to high-frequency electrical heat (diathermy) treatment. The effect of diathermy on the performance of the System has not been evaluated. The exposure may damage the Sensor and may impact proper function.

Some individuals may be sensitive to the adhesive that keeps the sensor attached to the skin. If a participant notices significant skin irritation around or under their sensor, they should remove the sensor.

1.4.3 Participant Reimbursement

Participants will be reimbursed $25 when the sensor is returned to the clinic.

1.5 Equipment, Materials, and Supplies

- 1 Abbott FreeStyle Libre 3 System
    - 1 blinded reader
    - 1 sensor pack (single use only)
- Alcohol wipe
- Skin Tac adhesive
- 1 participant mailer kit
    - 1 padded cardboard mailer with paid postage
    - 1 biohazard bag
    - Printed participant mailing instructions

1.5.1 Forms

- Continuous Glucose Monitoring – Device Initialization and Tracking Form (CGMR)
- Continuous Glucose Monitoring Results Form (CGX)

1.6 Consent Process

The CGM Consent Process has been moved out of MOP39 and is stored in a separate attachment to this document.

1.7 Overview of Study Procedures

Participants returning for the Visit 11 will be invited to participate in the protocol. Staff will place a small CGM sensor on the underside of the upper arm and secure the sensor using a liquid adhesive (to prevent it from being accidentally dislodged during the wear-period). Participants will wear the sensor for up to 14 days. On day 3, staff will call participants to answer any questions and to encourage participants to wear the device for the full 14-day period. On day 14, staff will call participants to remind them remove the device, provide instructions regarding removal if needed.

Participants who cannot come to the Visit 11 exam will be offered home visits and the CGM sensor will also be applied to participants during the home visits using the same protocol.

The estimated time for placing the CGM sensor during the ARIC Visit is 5 to 15 minutes, mostly involving time for consent and explaining the study. The total dedicated time for the participant once they leave the clinic is approximately 15 minutes: 5 minutes for each follow up phone call (on day 3 and day 14) and an extra 5 minutes to remove, package, and return the sensor via mail.

1.8 Overview of the Continuous Glucose Monitoring Device

We have selected the Abbott Libre 3 Continuous Glucose Monitoring (CGM) System for this protocol because of its ease of use and acceptability to participants. The Abbott Libre 3 CGM sensor is small (the size of two pennies stacked on top of one another) and is worn on the arm for 14 days and is factory calibrated (no fingerstick is required). The blinded Libre 3 system we are using in ARIC records interstitial glucose once every 5 minutes and stores the 14 days of data. Participants do not interact with the device, and they are masked to the glucose readings. The sensor is small, discrete, and designed to be worn while going about one's daily life. After 14 days, the sensor will be returned by participants in a pre-paid mailer.

The sensors will be mailed in batches by the ARIC field centers to Abbott for data download.

The Abbott Libre 3 system is an FDA cleared device. The Libre 3 is a CGM device indicated for detecting trends and tracking patterns in persons with diabetes. Outside of the research setting, the system is intended for use by health care professionals and requires a prescription.

1.9 CGM Timeline Schematic

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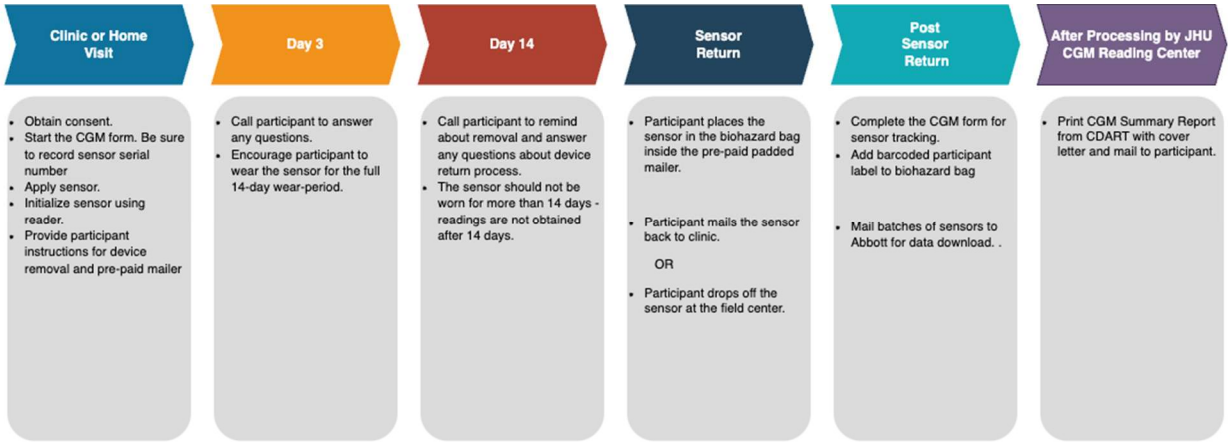


2. DETAILED STUDY PROCEDURES

2.1 Overview of the Abbott FreeStyle Libre 3 System

Libre 3 Glucose Monitoring System involves a handheld Reader (we are using a blinded version provided by Abbott specifically for this study) and a disposable CGM sensor. The CGM sensors are single-use only. The readers are used to initiate the sensors on multiple participants.
Note: Sites will be supplied with 3 or more readers. Please label them: #1, #2, #3, etc. with a permanent marker on the back side of the device to identify the readers.

Diagrams of each component can be found below.

Figure 1. Description of the reader kit.

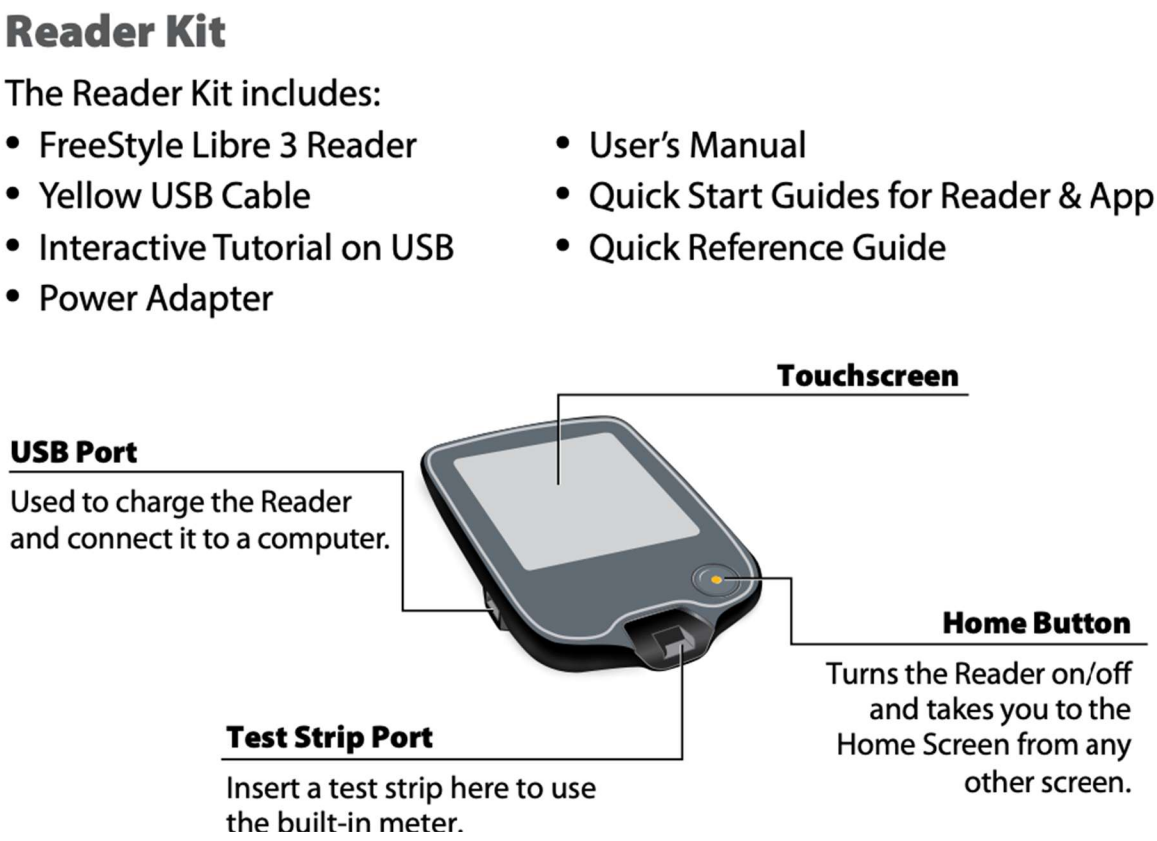


Figure 2. Description of the sensor kit.

Sensor Kit

The FreeStyle Libre 3 Sensor Kit includes:

- Sensor Applicator
- Product insert

Sensor Applicator
Applies the Sensor to your body.

The sensor measures and stores glucose readings when worn on the body. By following the instructions, prepare and apply the sensor to the underside of the back of the participant's upper arm. The sensor has a small, flexible tip that is inserted under the skin. The sensor can be worn for up to 14 days. The back of the arm is where the sensor has been shown to be most accurate.

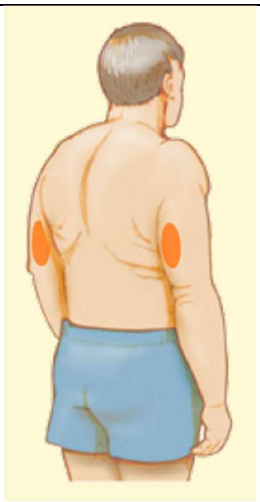
Figure 3. Left: the sensor applicator; Right: the sensor from three angles

Figure 4. Examples of Proper placement of the sensor

Figure 4 shows proper placement of the sensor. Staff at each field center have some flexibility regarding placement of the sensor, as long it is located somewhere on the back of the arm. Note that the sensor has a small hole in the center which allows air to circulate and escape from under the skin. This reduces moisture accumulation and helps with adhesion.

Note: some of the images above are of the larger, Libre Pro sensor; placement location for the Libre Pro and Libre 3 is the same.

2.2 Procedures for CGM Sensor Application

0.	The CGM Sensor is placed on the back of the upper arm using the disposable applicator. Only apply the Sensor on the back of the upper arm. The optimal area for placement can be determined by having the participant place their arm like they are going to flex their bicep and then place the sensor under the arm. The ideal location is where the sensor will not be exposed but also so it doesn't touch the inner torso. Avoid areas with scars, moles, stretch marks or lumps. Select an area of skin that generally stays flat during normal daily activities (no bending or folding). If relevant, choose a site that is at least 1 inch (2.5 cm) away from any insulin injection site. 
1.	Clean hands and put on protective gloves prior to sensor handling/insertion to help prevent infection.
2.	Clean the application site using an **alcohol wipe** and ensure that it is dry prior to sensor insertion. This helps the Sensor stay attached to the body. If the participant's arm is abundantly hairy, shaving the application site may also be helpful to aid in sensor application. Note: The area MUST be clean and completely dry, or the sensor may not stick to the site. Adhesion of the sensor to the skin for the full 14-day wear period is very important. If the sensor falls off, data will no longer be collected. If the sensor is loose, bad data may be collected. To help with adhesion, wipe the placement site with a **Skin Tac wipe** (single use). Skin Tac is a liquid adhesive that will help keep the sensor in place during the wear-period. The Skin Tac is packaged and used like an alcohol wipe but it is sticky and will help the sensor stay on the skin for the 14-day period. The Skin Tac should be applied over the entire sensor placement area on the participant's arm. There is no wait period between applying the Skin Tac and completing the sensor application. Additionally, a Tegederm-style cover or Kinesio tape may be placed over the CGM to help keep the CGMs secure for the full 14 day period. Do not cover the hole in the middle of the sensor when adding additional adhesive. The hole in the middle of the sensor allows airflow to the skin under the sensor during the wear period.

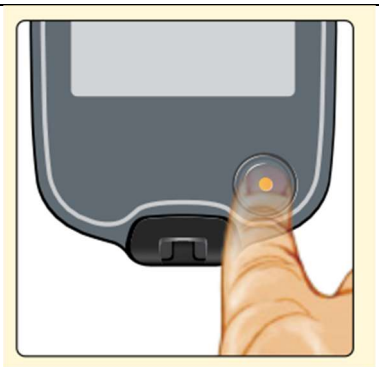
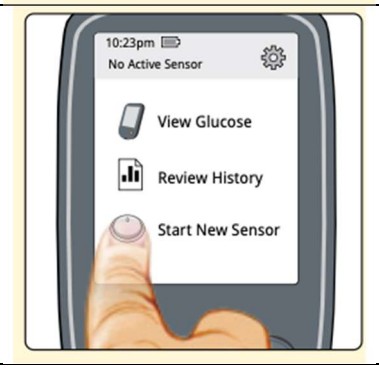
	
3.	Place the Sensor Applicator over the prepared site and push down firmly to apply the Sensor to the body. **CAUTION:** Do NOT push down on the Sensor Applicator until placed over prepared site to prevent unintended results or injury.
4.	Gently pull the Sensor Applicator away from the body. The Sensor should now be attached to the skin. **Note:** Applying the Sensor may cause bruising or bleeding. If there is bleeding that does not stop, remove the Sensor, and apply a new one at a different site.
5.	Make sure the Sensor is secure after application. Put the cap back on the Sensor Applicator. Discard the used Sensor Applicator according to your facility's procedures.

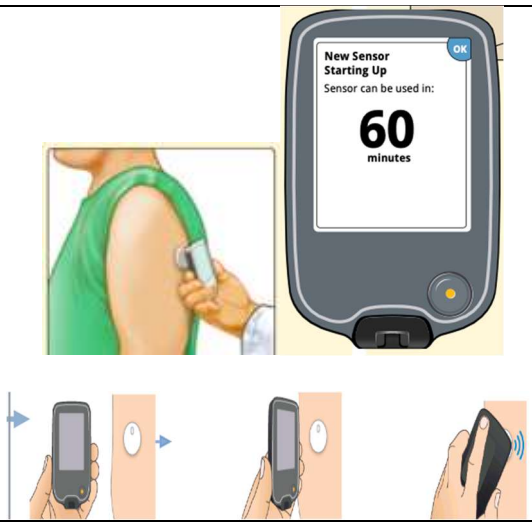
After assembling and applying the Sensor to the participant, use the Reader to start the Sensor and confirm it is working.

NOTE: For our study, the optimal location for the sensor is **under the back part of the arm** (NOT on the outer arm as might be seen in various other images of people wearing the Abbott Libre 3 sensor). There is some discretion of where the sensor can be placed on the back of the arm. Field Center staff can have the participants hold their arms loosely down at their sides to help determine most comfortable location for placement of the sensor, i.e., where it will not rub against the torso.

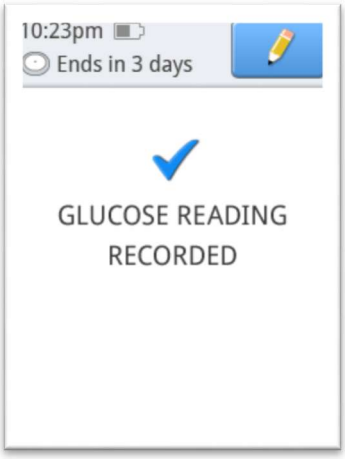
Figure 5. The blue arrow indicates proper location for placement of the sensor.

2.3 Procedures for starting the CGM Sensor

1. Press the home button to turn on the Reader.	
2. Touch **Start New Sensor**.	

3.	Hold the Reader so the screen touches the Sensor to start it. If sounds are turned on, the Reader beeps when the Sensor has been started. **Note:** If communication is not established within 15 seconds, the Reader displays a prompt to try again. Touch **OK** to return to the Home Screen and touch **Start New Sensor** to start the Sensor.	
4.	Clean the Reader between participants.	

The Libre 3 system we are using in the ARIC Study stores glucose readings every 5 minutes for up to 14 days. The first reading is stored 1 hour after the sensor is successfully started. That is, there is a 1 hour warm up period, but the initial check (beep when starting new sensor) should identify most connectivity problems such that it should not be needed to wait 1 hour to check that the sensor is working in most participants. If staff would like to check that the sensor is working, they can scan the sensor after 1 hour to determine that glucose readings are being stored. The sensor is blinded so no glucose value will be displayed. The blinded reader for the Libre 3 system will show the following message if scanned after the 1-hour warm-up period:



2.4 Procedures for Reapplication of CGM Sensor

For some participants, the CGM sensor may fall off before the 14-day wear period is completed. If this happens, participants should be instructed not to attempt to reapply the sensor and to instead call their field center. If the sensor was worn for fewer than

10 days and the participant is willing, field center staff should set up an appointment as soon as possible to replace the dislodged sensor and restart the 14-day wear period. When the participant returns to the center, they should bring their dislodged sensor and mailer kit with them. If the sensor falls off a second time or the sensor was worn for 10 or more days, the participant should be instructed to use the mailer kit to return the sensor to the field center and the sensor will not be replaced. In the case where the participant does not want the sensor to be replaced, they may mail the sensor back to the field center using the prepaid mailer kit.

Multiple occurrences are allowed for data entry on the CGMR form. Staff should record each sensor initialization in a separate occurrence in the CGMR form.

2.5 Sensor Removal and Return Instructions

Before leaving the clinic (or at the end of the home visit), participants will be provided with 1) information about the sensor and instructions for removal of the sensor after 14 days of continuous wear; 2) “Tac-Away” adhesive remover wipe to help with removal of the device (if needed); and 3) a prepaid mailer kit for returning the sensor, prelabeled with the participant’s ARIC ID and sensor serial number. To label the sensor serial number, the site may cut the bottom flap of the sensor packaging containing the sensor QR code and tape this to the biohazard bag. Before taping the sensor packaging to the biohazard bag, the flap should be copied and stored with the participant’s file to ensure that the serial number is not lost if the participant loses the shipping kit. For sites where participants are blinded to their ARIC ID, the ARIC ID label can be omitted from the mailer kit in favor of alternative identification to ensure the sensor is linked to the correct participant.

Figure 6. Cut the bottom flap off the CGM sensor box. Copy the flap using a scanner and save a copy with the participant’s file. Then, tape the flap to the biohazard bag to assist with sensor identification upon return to the clinic.

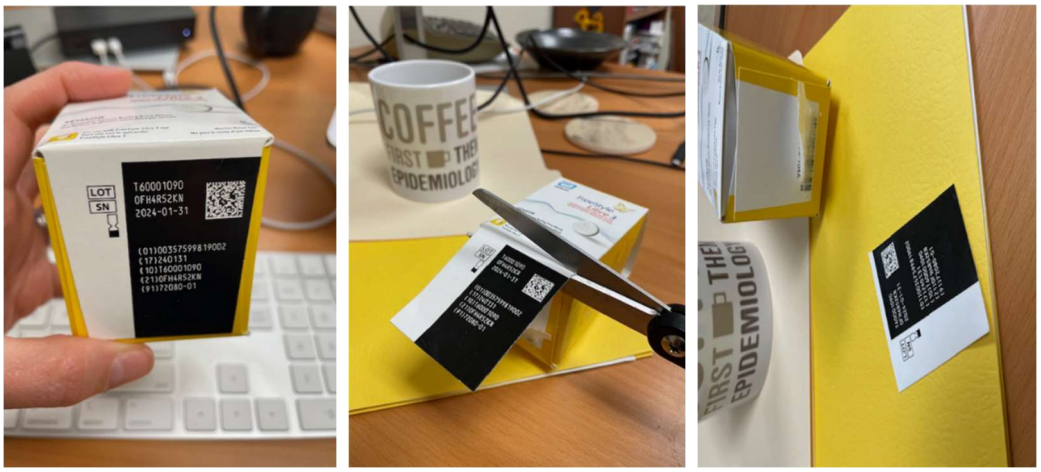
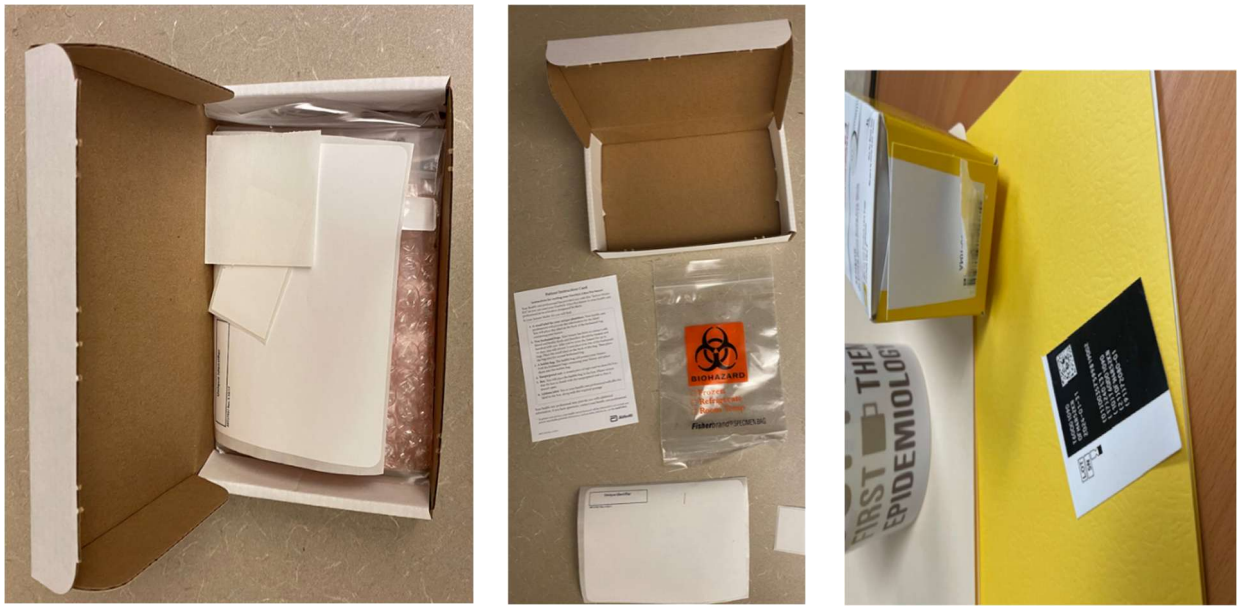


Figure 7. TacAway is used to remove adhesive residue to remove the CGM sensor.

Participants will be given the option of returning to the clinic to have the sensor removed. They can also call the clinic for help in removing the sensor if desired.

Participants will be provided with a kit and instructions for mailing the CGM sensor back to the ARIC clinic. The mailer kit will contain a padded cardboard mailer and biohazard bag for the sensor.

Figure 8. On the left: a sensor packaged and prepared for shipment back to the field center. In the middle: contents of the padded cardboard mailer include a cardboard box, bubble wrap, biohazard bags, instructions, and postage. On the right: the bottom flap of the CGM sensor packaging to be taped to the biohazard bag for sensor identification.



Each ARIC site will need to arrange for US postal service postage prior to providing the mailer kit to participants.

2.6 CGM Post-Return Field Center instructions

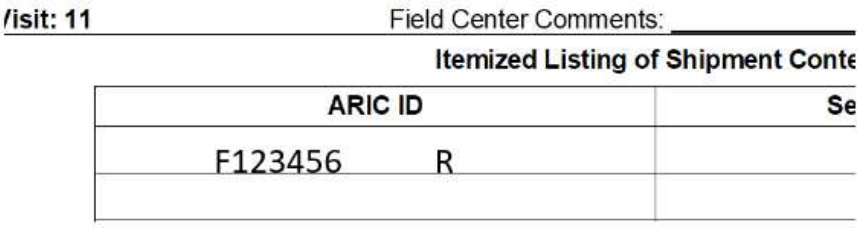
Upon receipt of the used sensor via mail, field center staff will apply a barcoded ARIC participant ID label to the biohazard return bag. The Coordinating Center will provide sites a pdf of barcoded participant labels. Please use Avery Address labels (1" x 2-5/8") ex. Avery 5960 and print locally on any laser or inkjet printer.
Weekly, all sensors received from participants in the previous week will be gathered by the Field Center Staff and mailed to Abbott Diabetes Care for data download and processing.

The used sensor should remain in a biohazard bag and placed in the mailer kit box with the ARIC ID marked on the box. All biohazard bags and mailer kit boxes should be labeled with ARIC ID to facilitate tracking. For sites where participants are blinded to their ARIC ID, sites must add the appropriate barcoded participant ID to the biohazard bags and mailer kits before shipment to Abbott. All mailer kit boxes should be put in a larger box with a CGM Shipping and Receiving form and FedEx label for shipment to Abbott.

If shipping the second/replacement sensor for a participant, then sites should handwrite the letter "R" on whitespace of the ID label of the biohazard bag to ensure that the data is processed as a replacement for the participant. Sites should also include an "R" on

the ID line of the shipping log. Both the replacement and original sensor should be shipped to Abbott for processing when possible.

Figure 9. Example of replacement sensor line item recorded on CGM shipping log.


/isit: 11 Field Center Comments: _____

Itemized Listing of Shipment Conte

ARIC ID	Se
F123456 R	

All tracking information should be shared with Abbott Diabetes Care in advance and Abbott will acknowledge that sensors were received.

FedEx shipments to Abbott should happen every Tuesday.

Shipping information:

Attention: Annette Peinado
1360 South Loop Road
Alameda CA 94502

Data downloads (at Abbott Diabetes Care) will be supervised by Annette Peinado and performed by Robbie Scott and Nelson Rosa

Annette Peinado
External Scientific Research Manager
Clinical and Computational Research
Abbott Diabetes Care
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annette.peinado@abbott.com

Nelson Rosa
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Mobile: 925-963-0290
robbie.scott@abbott.com

3. DATA AND RESULTS REPORTING

3.1 CGM Sensor Tracking

Field Center staff will need to associate the ARIC participant ID with the serial number (containing 9 alphanumeric characters) of each Libre 3 sensor in the CGMR form at the time of the clinic visit. There is a matching unique serial number on the box of the device and the applicator. The biohazard bags in the mailers should also be labeled with the participant's ARIC ID and sensor serial number to facilitate tracking. When the sensor is returned to the clinic, the CGM serial number should be verified against the serial number that was entered at initialization in the CGMR form. In the case of a mismatch, the serial number should be reconciled with the serial number recorded in the CGMR form and the Coordinating Center should be notified with any discrepancies.

Figure 10. The sensor serial number is the alphanumeric 9-character string found next to the "SN" box on the CGM sensor pack.

3.2 Results Reporting

There are no alerts as the data are not available in real-time and the data collected are not clinically actionable at the time of the data download. Hemoglobin A1C, a measure of diabetes and glucose control, is already reported to participants as part of the parent ARIC NCS protocol.

JHU CGM Data Processing Center will receive all CGM data from Abbott and produce a 1-page auto-generated CGM Summary Report, which is a summary of the 14-day glucose data (graph of glucose values with information on the normal range). These reports will be uploaded to CDART. Field Center staff will retrieve the CGM Summary Reports from CDART and send with a cover letter to participants and/or their health care provider with permission.

Once the JHU CGM Data Processing Center posts the CGM Summary Report to CDART, field centers will be notified of results availability for each participant using the CDART Results Status Report. Field center staff will print the CGM cover letter from the ARIC website and the CGM Summary Report directly from the CGX form under the participant's ARIC ID.

If the sensor wear period was fewer than 14 days, the participant may still be provided with the data summary. However, in cases where the wear-period was fewer than 10 days, this summary may not be completely representative of the participant's glucose profile. If the participant had the sensor replaced, they should be provided with only the summary of results for the sensor that was worn for the longest time. See **Appendix 5.2** for more detailed instructions on handling multiple sensors.

3.3 Rationale for Reporting

CGM technology is often used in the care of adults with type 1 diabetes. It is not standard of care for adults with type 2 diabetes and it is not commonly used in this population. In adults with type 2 diabetes not on insulin therapy, CGM is currently considered to be of little clinical benefit.

The CGM device being used in this protocol does not provide real-time information on glucose readings (participants are masked to any glucose readings). The device is designed to be worn for 14 days and, at the end of the wear period, the sensor will be returned via mail and the data are downloaded at the ARIC clinic. Thus, participants will not be aware of their glucose measures collected during the 14-day period. Even if subsequent analysis of the CGM data reveals clinically relevant information (e.g. very low or very high glucose values), this information is not directly clinically actionable at the later date.

Participants, especially those participants with diabetes, may be interested in seeing a summary of their glucose patterns. We will return a cover letter and one-page summary if requested by a participant.

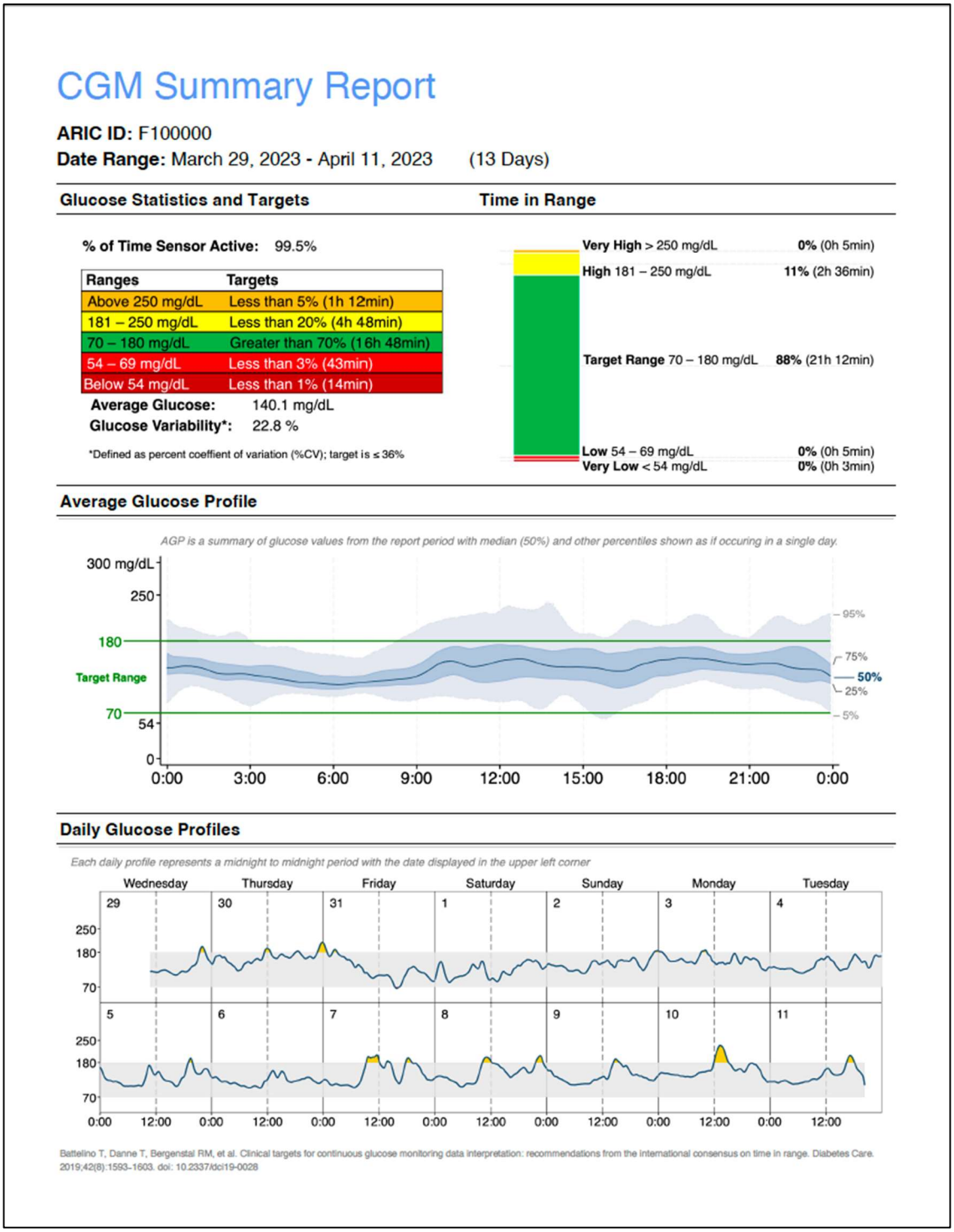
Interpretation of results (information for Field Center staff)

The data from the Abbott Libre 3 device is not intended for the diagnosis or screening of diabetes. In persons with a diagnosis of diabetes, the Abbott Libre 3 system is sometimes used to guide and adjust diabetes treatment, typically in persons who are using insulin to manage their diabetes. The data we are collecting in this study are for research purposes only. For participants with a diagnosis of diabetes, the 1-page report

provided by JHU may be of particular interest and they may wish to review it with their doctor. It is helpful if the data from the Libre 3 device is reviewed and interpreted with the assistance of a medical professional.

We will provide training to Field Center staff on the interpretation of the Abbott Libre 3 system results to ensure that Field Center staff are comfortable answering any questions participants may have about results that are reported to them.

Figure 11. Continuous Glucose Monitoring Report Sample



CGM Summary Report

ARIC ID: F100000
Date Range: March 29, 2023 - April 11, 2023 (13 Days)

Glucose Statistics and Targets

% of Time Sensor Active: 99.5%

Ranges	Targets
Above 250 mg/dL	Less than 5% (1h 12min)
181 – 250 mg/dL	Less than 20% (4h 48min)
70 – 180 mg/dL	Greater than 70% (16h 48min)
54 – 69 mg/dL	Less than 3% (43min)
Below 54 mg/dL	Less than 1% (14min)

Average Glucose: 140.1 mg/dL
Glucose Variability*: 22.8 %

*Defined as percent coeffient of variation (%CV); target is ≤ 36%

Time in Range

Average Glucose Profile

AGP is a summary of glucose values from the report period with median (50%) and other percentiles shown as if occuring in a single day.

Daily Glucose Profiles

Each daily profile represents a midnight to midnight period with the date displayed in the upper left corner

Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. Diabetes Care. 2019;42(8):1593–1603. doi: 10.2337/dci19-0028

4. TRAINING AND CERTIFICATION

All ARIC Field Center Staff involved in the CGM protocol will participate in a central web-based training. This training will cover application and initialization of the CGM device and data entry and processing in CDART. During a portion of the training, a representative from Abbott Diabetes Care, the maker of the CGM sensor, will be available for questions. The complete training will be recorded for future reference in case any questions arise. In addition to this centralized training, ARIC Field Center Staff should review Manual 2 for Field Center Procedures as well as Manual 39 which details the CGM protocol.

4.1 Certification Checklist:

1. Procedure is explained to participant including length of wear, what to do about bathing/showering, who to call with questions, etc.

2. Technician uses proper technique for site preparation including: removal of clothing covering installation site, selecting an area free of blemishes, scars, etc., sensor placement site is prepped using the correct technique using alcohol wipe, Skin Tac liquid adhesive wipe is applied appropriately, technician washes hands prior to installation, and technician wears gloves.

3. Technician uses proper technique for sensor placement: preparing participant with instructions for discomfort, technician applies the sensor placement tool against skin, technician places sensor cover correctly, technician asks participant about any final questions, technician cleans area of debris and disposes of any potentially biohazardous waste appropriately.

4. Technician initializes the sensor, correctly records sensor serial number, sensor application date and time, the time on the reader at sensor application, and reader # used within CDART, and labels biohazard bag with participant ID# and sensor serial number.

Any staff member who successfully completes the CGM training and successfully places 2-3 CGM sensors (observed by a coordinator or senior staff member) is considered certified for the CGM protocol. The placed sensors do not need to be worn, just placed.

5. APPENDIX

5.1 FreeStyle Libre 3 Blinded Reader

Blinded/Masked Mode for FreeStyle Libre 3 - Overview
- While the reader is in masked mode, the sensor glucose values are not displayed
- System alarms (low battery, etc) are displayed as normal
- Signal loss alarms (after 1-hour warm up period, reader will try to connect to sensor to download glucose and will alarm when not in range) cannot be turned off. Staff should ignore these alarms.

Generic instructions/images for use of the blinded reader from Abbott are provided below. Please note that these blinded readers will only be used to initialize the sensors in ARIC participants. ARIC staff will not be using the readers to obtain CGM data. ARIC staff should ignore instructions or use of logbook, notes, or other activities related to reader use during the CGM wear period.

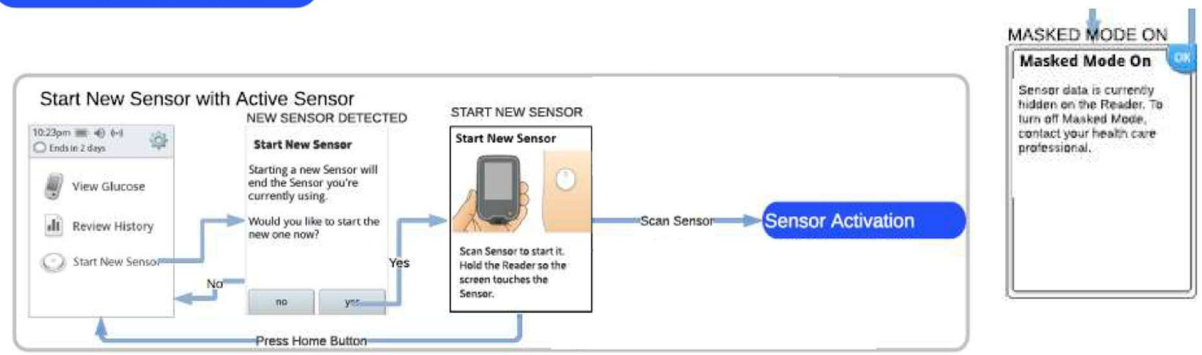
These readers are designed to connect with the CGM sensors and download data in a blinded fashion in real-time during the 2-week wear period. In the ARIC Study, we will NOT be using the readers for this purpose. We will only be using the blinded readers to initialize the sensors. Thus, staff will need to ignore various signal loss alarms (described below). (All CGM data downloads will be conducted by Abbott Diabetes Care).

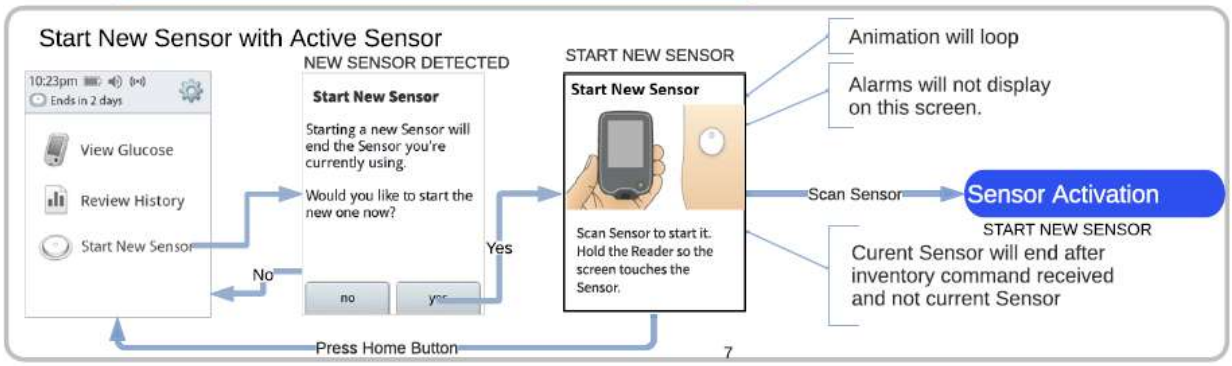
If there is concern whether the sensor is working correctly, the initialized sensor on the participant can be scanned with the blinded reader after 1 hour after initialization to check that it is recording glucose values (this assumes that the reader has not been used to subsequently start a different sensor). Once a reader has been used to start a new sensor, the 1-hour check cannot be performed on any previously initiated sensor.

Staff should note that once a sensor has been initialized and >1 hour has passed, the reader will try to connect and download data from that sensor. I.e., if the initialized sensor and the reader are ‘separated’ (>30 feet), a “signal loss” alarm will occur. Staff will need to ignore all signal loss warnings. These signal loss alarms, unfortunately, cannot be turned off.

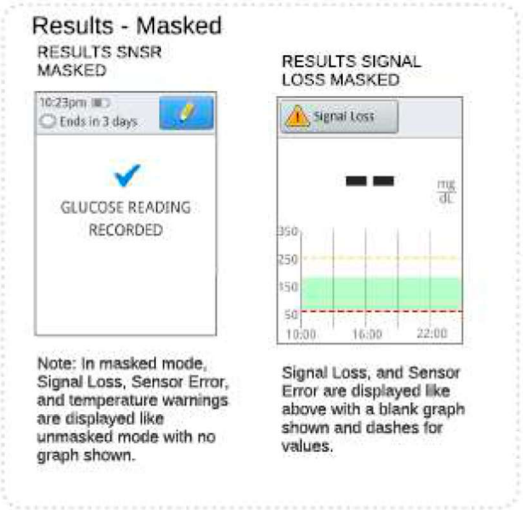
Once one sensor has been initialized, staff will use the same reader(s) to initialize subsequent sensors. Make sure to record the reader # used for each sensor. Staff will need to ignore warnings about initializing a new sensor (i.e., ignore the error message, “Starting a new sensor will end the sensor you are currently using”).

Sensor Activation

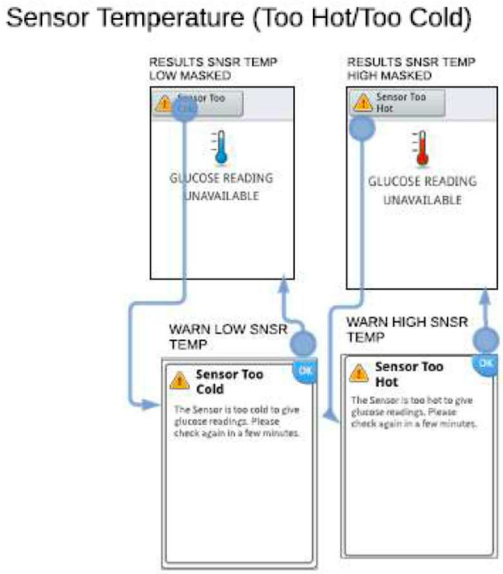




Sensor Results - I



Sensor Results II



NOTE: You will have 3 or more readers. Please use a permanent marker to label them #1, #2, #3, etc. to uniquely identify each reader. The readers must remain charged at all times. If a reader completely looses charge (goes ‘dead’) the clock inside the reader will be disrupted. Even if the reader is subsequently recharged, it should NOT be used to initialize new sensors. It will need to be returned to Abbott to be re-set.

Theoretically, the readers should last a week on each charge but staff should monitor the three battery bars and make sure the reader gets charged up before it gets down to one bar.

Do not change the time on reader display. Make sure to record the time on the clock as well as the time on the reader display in the CGMR form at time of sensor application (Q5a and 5b). It is very important to record times exactly and not round to the nearest 5 minute. Clock times should be recorded using a computer time or a clock that automatically syncs to Coordinated Universal Time (UTC), e.g. cell-phone that is connected to the internet. Also record the # on the reader in CGMR form (Q5c).

5.2 CGM Recruitment and Wear Outcomes and Form Actions

Outcome	Actions
The participant has the CGM sensor successfully placed. The participant wears the sensor for 10 or more days. **This is the most common scenario.**	1. Answer all prompts in the CGMR form as needed to initialize the sensor. 2. The participant returns the sensor, complete the remaining items in the CGMR form. Mail the sensor to Abbott Diabetes Care. 3. Once notified results are available in the results status report, print and mail the PDF results and cover letter to the participant.
The participant declines participation in the CGM study.	1. Open the CGMR form and answer the prompts in the Administrative Information section of the form indicating the reason why the participant declined participation then save and close the form.
The participant meets the additional exclusion criteria in the CGMR form and does not agree to future participation in the CGM study.	1. Answer all eligibility prompts in the CGMR form then save and close the form. Do not assign a sensor to the participant.
The participant meets the additional exclusion criteria in the CGMR form and agrees to future participation in the CGM study.	1. Answer all eligibility prompts in the CGMR form then save and close the form. Do not assign a sensor to the participant. 2. Wait at least 2 weeks before attempting further recruitment for the CGM study. 3. With each subsequent recruitment attempt, the same CGMR form occurrence should be used and updated to reflect the most recent attempt. 4. Continue recruitment attempts until the participant can have the sensor placed OR the participant does not agree to future participation in the CGM study. If participant does not agree, record this response in the CGMR form.
The participant has the CGM sensor successfully placed. The sensor is removed on or before day 9 of the 14-day wear period. The participant agrees to have the sensor replaced.	1. Initialize the sensor following instructions in the CGMR form. To replace the original sensor, schedule a clinic or home visit as soon as possible to replace the sensor. 2. To initialize the replacement sensor, **a second occurrence of the CGMR form** is completed in CDART. Answer each prompt in the CGMR form (including the exclusion criteria questions) before assigning the sensor. 3. Send both sensors to Abbott Diabetes Care for processing. When results are returned, send one results pdf to the participant corresponding with the sensor that was worn for the longest amount of time.
The participant has the CGM sensor successfully placed. The sensor is removed on or before day 9 of the 14-day wear period is complete. The participant does not agree to have the sensor replaced	1. Initialize the sensor following instructions in the CGMR form. 2. When the sensor is removed, ask the participant to return the CGM sensor by mail. 3. Once the participant returns the sensor, complete the remaining items in the CGMR form. Mail the sensor to Abbott Diabetes Care. 4. Once notified results are available in the results status report, print and mail the PDF results and cover letter to the participant.