

solianis

Multisensor Glucose Monitoring
System

February 2011



The Solianis CGM System does not have any regulatory clearance and is intended for demonstration and research purposes.

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1. This document

This document describes the operation of the Solianis Multisensor Glucose Monitoring System (MGMS). Images shown throughout the document might have been taken from earlier versions of the system. However they are compatible with the ones that appear in the current version the user works with.

The following naming conventions are applied throughout this document:

- User selection that requires a user action: *blue italics*
- Display information: *black italics*

Please read the entire document before the first use of the CGM System.

In case of questions please refer to the Solianis team:

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2. General

The MGMS is owned by Solianis Monitoring AG. It is under development and is not cleared by any regulatory agency, nor has it been subject to clinical validation.

3. System Overview

The MGMS comprises:

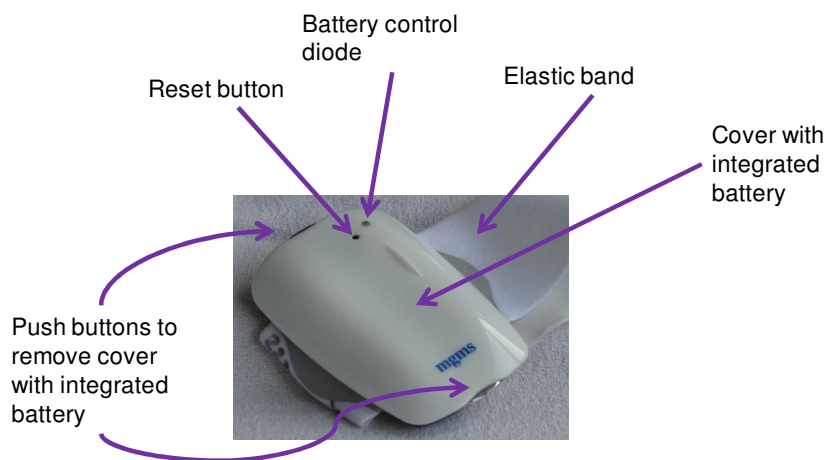
- One Multisensor with an exchangeable battery in the cover and an elastic band
- One Multisensor spare cover with an integrated battery
- One Multisensor battery Charger with a USB cable to be connected to the accompanying 5.0 V USB power supply
- PC / Laptop computer with the Solianis Toolsuite System installed

The system is delivered with cleaning tissues to clean the Multisensor.

The components of the system (Multisensor and Laptop) are paired to each other and can only be used within the dedicated MGMS.

3.1. Multisensor

The Multisensor is powered by an exchangeable and rechargeable battery. During a measurement run it is fixed to the (non dominant) upper arm with an elastic band. Measurement data are communicated from the Multisensor to the Laptop via Bluetooth.



3.1.1. General Handling and Maintenance

- Water:
 - The Multisensor is not waterproof. It may not be cleaned with water and needs to be taken off before showering, bathing or swimming.
- Cleaning:
 - The Multisensor has to be cleaned with the cleaning tissues provided by Solianis; other cleaning agents can harm the Multisensor. The bottom side with the sensors is cleaned by wiping gently over the surface for a few seconds. The upper side of the device can be cleaned in the same way if required.
 - The elastic band can be washed gently by hand with a soft soap and needs to be rinsed carefully.
- Reset:
 - On the upper side of the Multisensor next to the battery control diode is a small hole to reset the Multisensor. If a Reset of the Multisensor is needed, a stylus or a pin can be pressed into this hole. A short beep will confirm the successful reset of the Multisensor. A reset is recommended to be done only upon request of the Solianis team as stored data might be lost.



- Battery charging:
 - The rechargeable battery is integrated in the cover of the Multisensor.
 - The cover is removed from the Multisensor unit by pressing the two buttons at the upper and lower side of the Multisensor simultaneously.
 - To recharge the Multisensor battery, the cover is placed onto the Charger (~once per 12h of test runs).
 - The Charger is connected to a Laptop or to a 5.0 V USB charger via the USB cable for power supply.
 - The control light of the charger will be 'orange' during the charging procedure and switch to 'green' once the Multisensor battery is fully charged.



3.2. Laptop

The ToolSuit software for glucose monitoring and data transmission according to the Continua standards is preinstalled on the Asus Eee Laptop delivered with the MGMS. The Laptop operates under Windows XP Home Edition.

3.2.1. ToolSuite Software

The ToolSuite software is a tool, developed by the Solianis Monitoring AG to control and establish communication with the Multisensor. Each multisensor is paired with a specific laptop. Therefore, no additional actions are required on the Windows level.

3.2.1.1. Base System

The base system provides communication with the Multisensor.

To associate a communication port with the Multisensor, please press the *Devices* button on the left upper side.

Press *Add device*. Please select an appropriate communication port (e.g. Serial Port 3), which is associated with the Bluetooth unit of the Laptop (incoming port).

3.2.1.2. Monitoring Plug-in

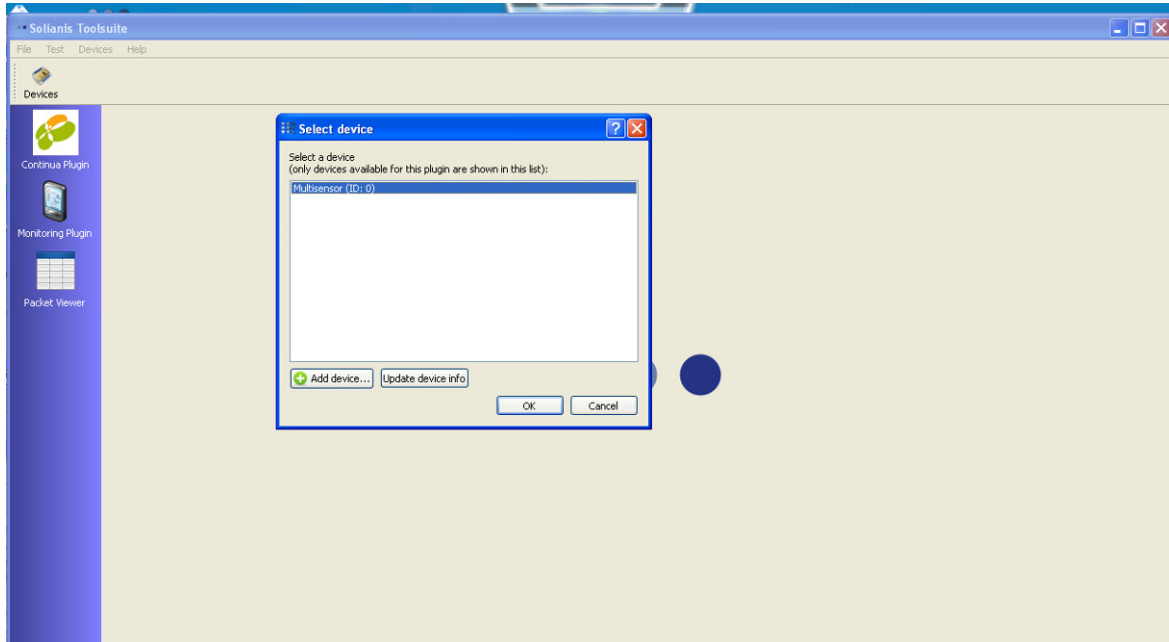
The Monitoring plug-in contains the tools for the correction of the raw data, estimating the glucose value, and displaying the results. It is the actual interface to the user.

Starting the plug-in

Press the *AHD symbol* on the left hand side of the main interface. You will be asked to select a device (multisensor) from a menu or add another device. If a device was already added in 3.2.1.1, just press *OK* (figures on the next page).

The interface of the Monitoring plug-in contains several fields for messages and one Monitoring application on the right hand side.

The text field shows messages and status of the glucose estimation.



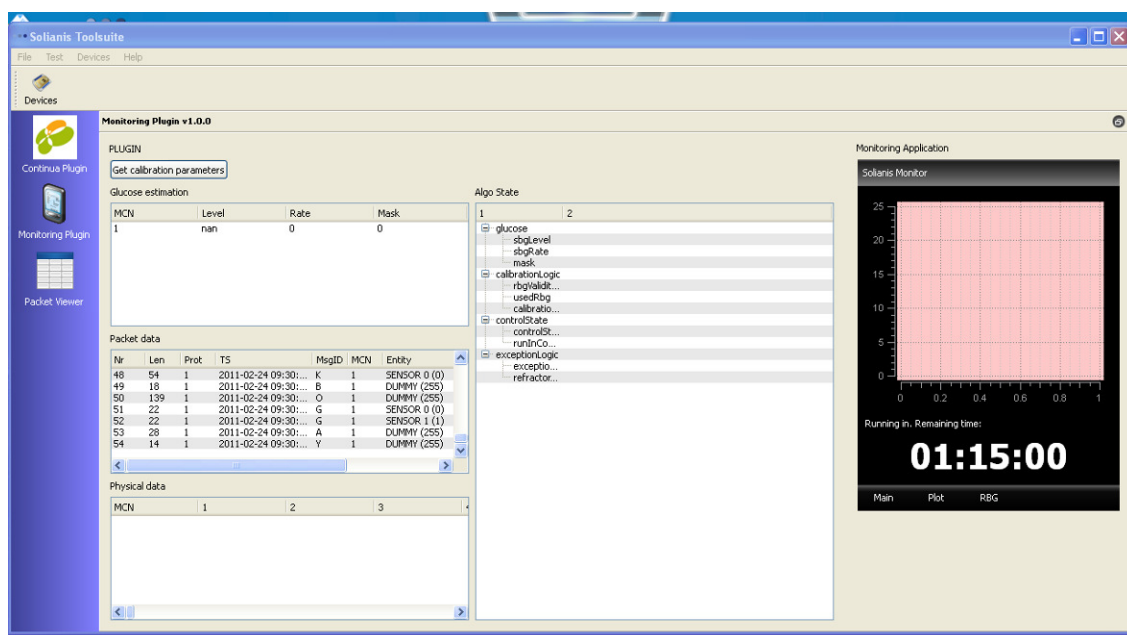
The Monitoring Application on the right-hand side has three modes, which can be changed by pressing the corresponding field on the bottom of the Monitoring Application:

1. *Main* mode. The mode is only active during glucose estimation. It is gray during run-in time and algorithm exceptions. When it is active, it shows colour and arrow-coded values of the current glucose estimation and arrow-coded glucose-change rate. Colour-coding is defined as follows
 - a. Green when glucose estimation between 5 and 6 mmol/l
 - b. Orange with an arrow up for the values from 6 to 7 mmol/l
 - c. Red with an arrow up for the values higher than 7 mmol/l
 - d. Red with an arrow down for the values lower than 5 mmol/l
2. *Plot* mode. This mode shows various information depending on the algorithm status:
 - a. During the run-in time (75 minutes), the application counts down the remaining time until a reference blood glucose is accepted. During that time the background of the plot is red
 - b. The curve of the estimated glucose values as a function of time during the running measurement. The background of the plot is green and the current estimated glucose is shown in mmol/l. The colour of the digits reflects the colour coding in the *Main* mode. The x-axis shows the number of measurements (3 per minute)

- c. During possible operation exceptions, the background of the plot is red, and the time until the next reference value is accepted is counted down.
3. *RBG (Reference Glucose Meter)* mode is intended to manually insert the reference glucose values measured by a conventional spot meter (BGM). Upon request of the Monitoring plug-in, the user enters a value and presses *Set RBG*. The plug-in confirms the value if it is acceptable for the algorithm

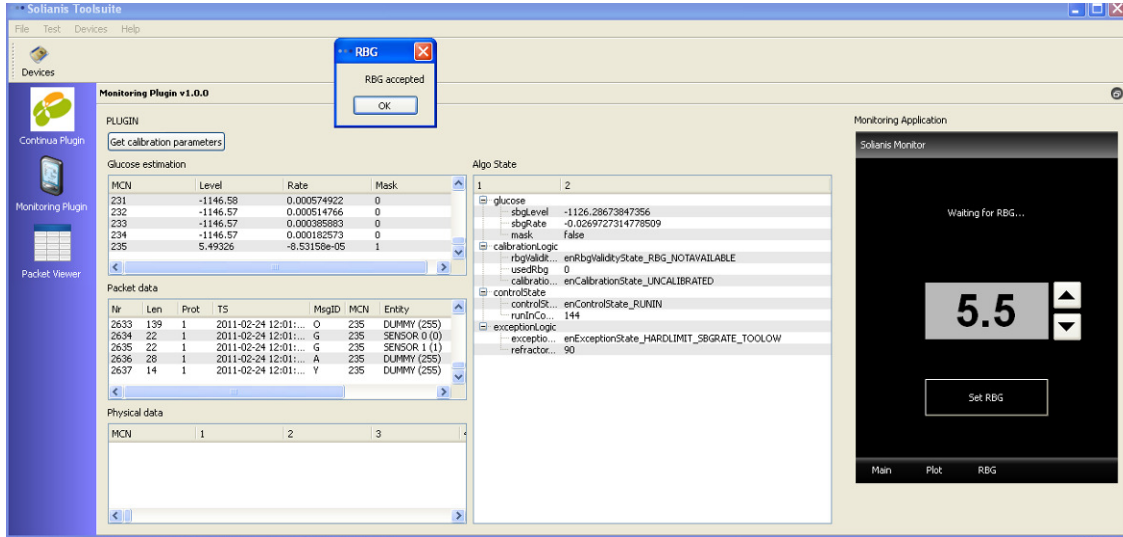
Initialization and Running-in time

The *Run-in* or Equilibration time is needed to allow the skin for the adaptation to the device. This time period has been arbitrarily set to 75 minutes. During this time, no glucose values are estimated. The Monitoring Application counts down the remaining time. The background in the *Plot* mode is red (see figure below)



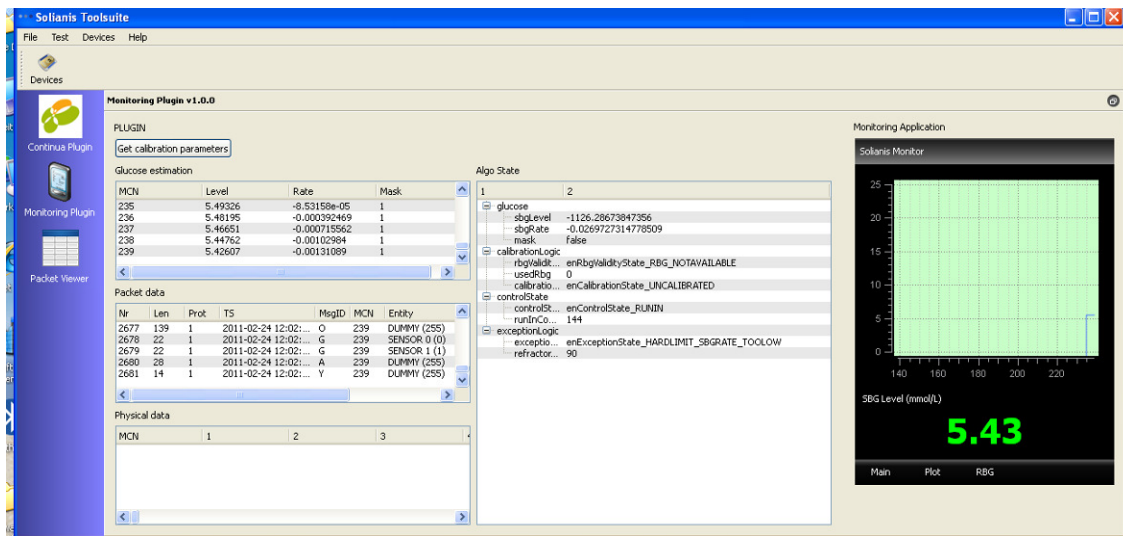
Insertion of the Reference BGM Values

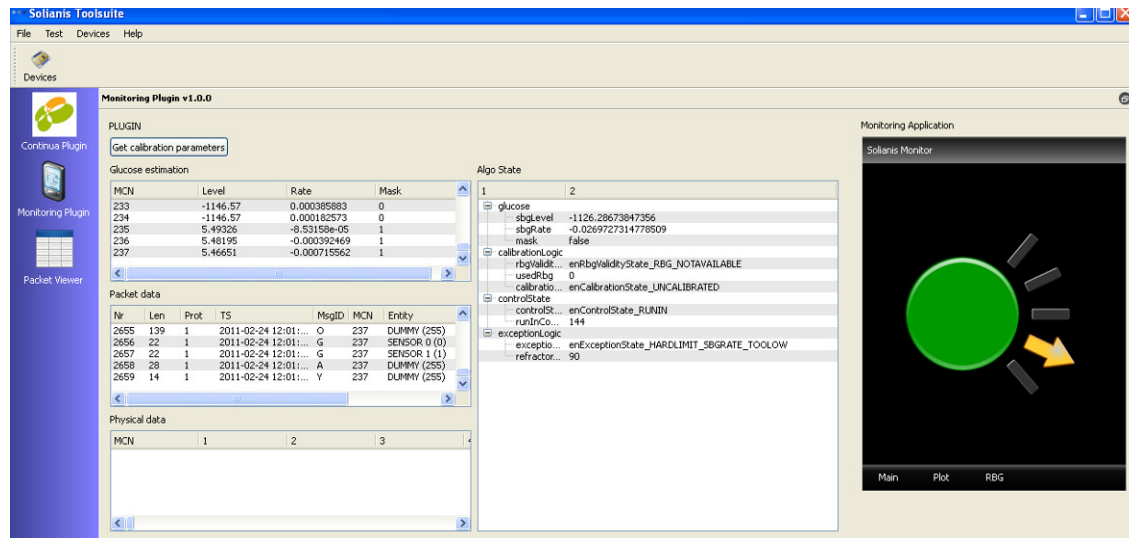
After 75 minutes of the run-in time, the system asks for a reference BGM (Blood Glucose Meter) value if the estimated change rate is not too high or too low. The user has to enter this value manually and confirm the selection. After some time (approx. 40 seconds), the ToolSuite confirms the selection if this value is acceptable for the algorithm.



Measurements and Estimation

This is the standard operation mode. The Monitoring Application displays the current status of the glucose either in colour/arrow code (*Main mode*) or as a number and plot (in the *Plot mode*)





Algorithm Exceptions

There might be situations during a measurement day when the estimation algorithm detects an exceptions. These exceptions can be caused by e.g. sensor detachment, too high or too low glucose estimation or change rate (non-physiological values), etc... In these cases, the algorithm stops display of the estimation for 30 minutes and asks for another reference BGM value after this time. The display in the Monitoring plug-in is similar to the case of the *Run-in time*.

Voltage of the Multisensor Battery

The Monitoring Application also shows the current status of the Multisensor battery. The values below 3.5V indicate a very low battery level. I.e. the Multisensor should be replaced. No warning will be given before the Multisensor switches off.

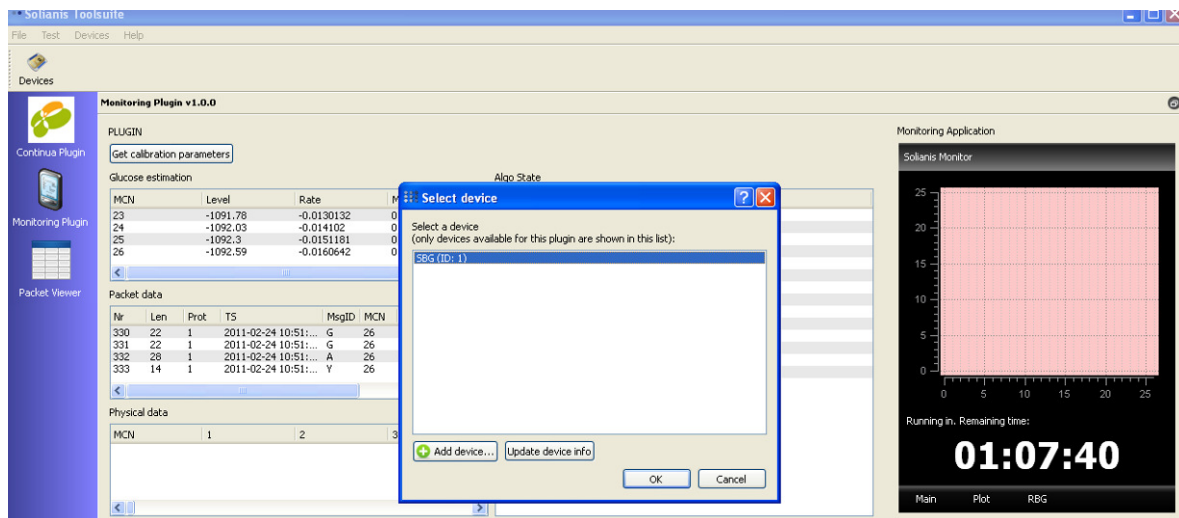
3.2.1.3. Continua Plug-in

The Continua plug-in receives the estimated values from the Monitoring plug-in and transmits them in real time to a Continua enabled manager. Only the TCP/IP connection via an Ethernet cable are supported at this time. Due to the fact that the IEEE 11073-10417 specialization is implemented, which does not allow for the transmission of CGM specific messages,

the Continua plug-in transmits a value of 0 (ZERO) during *Run-in time*, *Uncalibrated* and *Algorithm Exception* statuses.

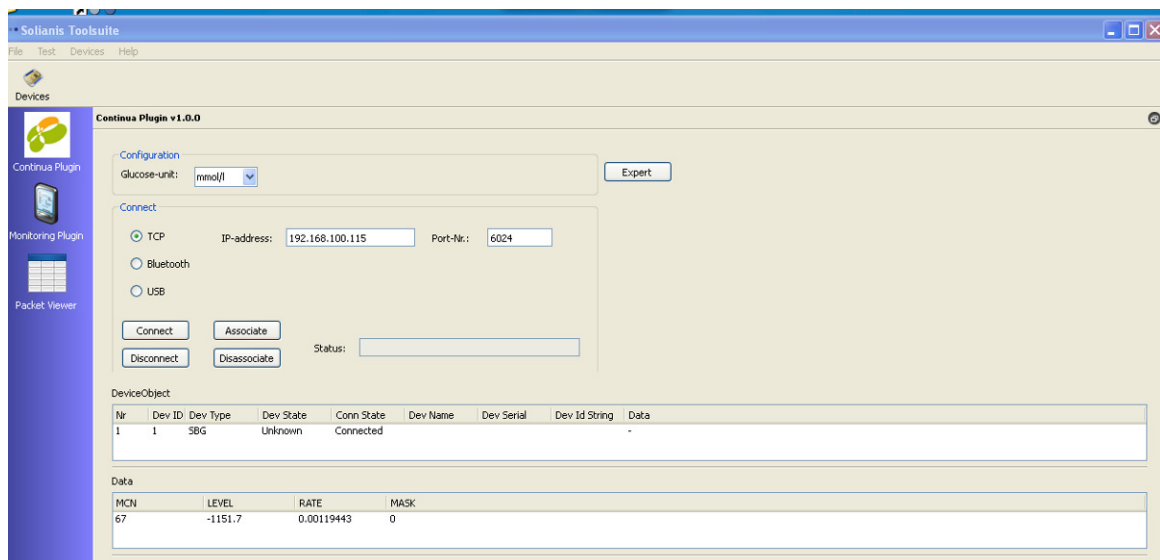
Starting

Press the *Continua logo* at the left-hand side. The system asks for the data source. Select the SBG.

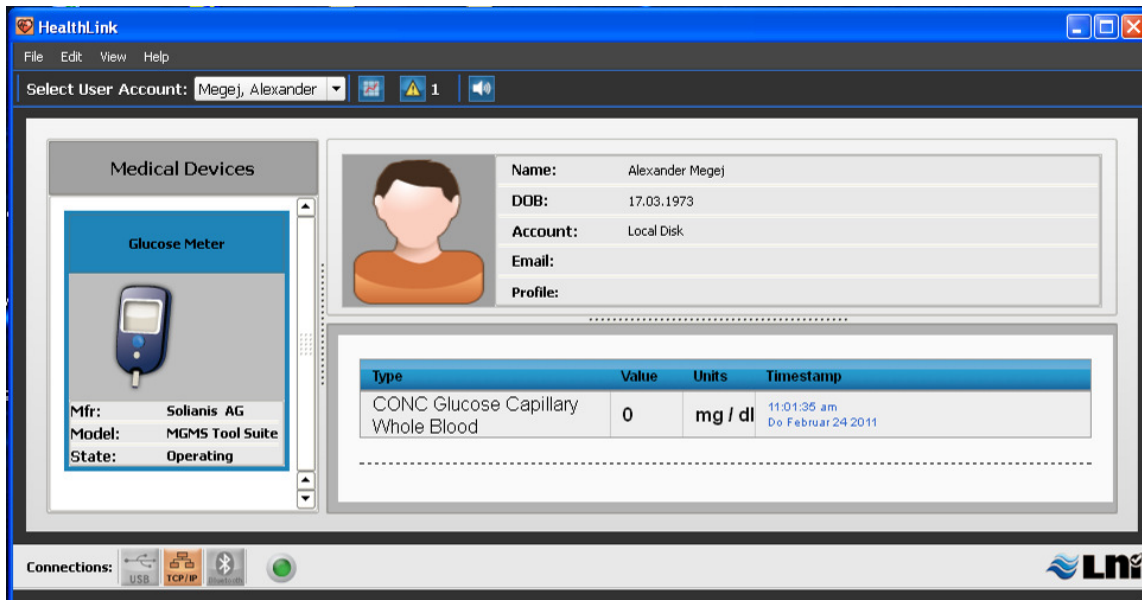
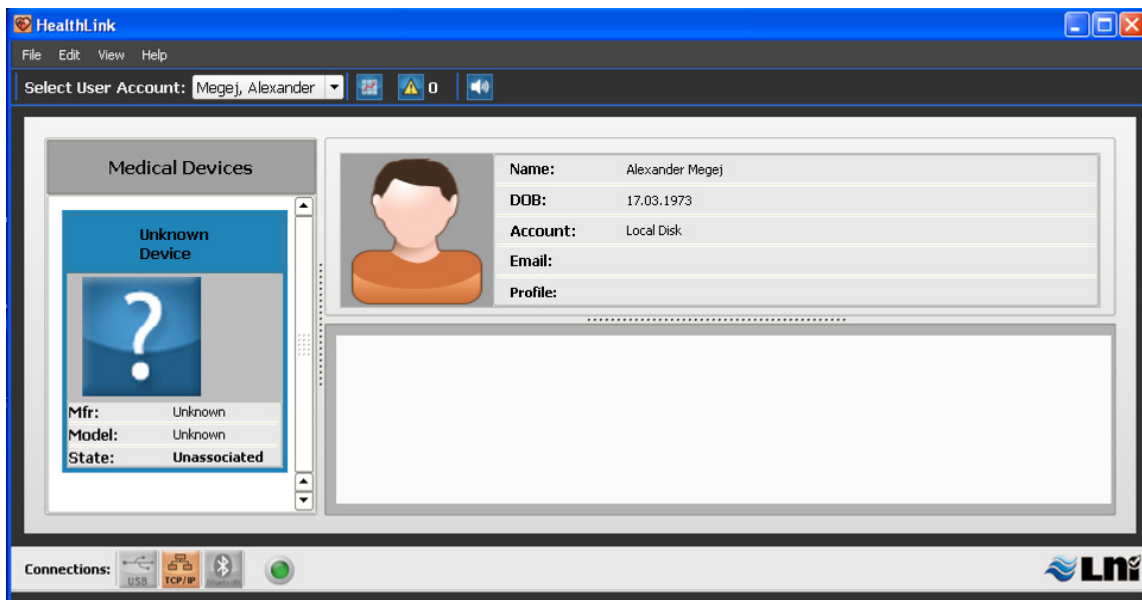


Connection to a Continua Manager

Place a tick on the *TCP* field. Please enter the IP of the host with the running Continua Manager (leave 0.0.0.0) for the local host.



Press *Connect* and *Associate* buttons subsequently. Figures below show the messages on the example of the LNI Continua Manager.



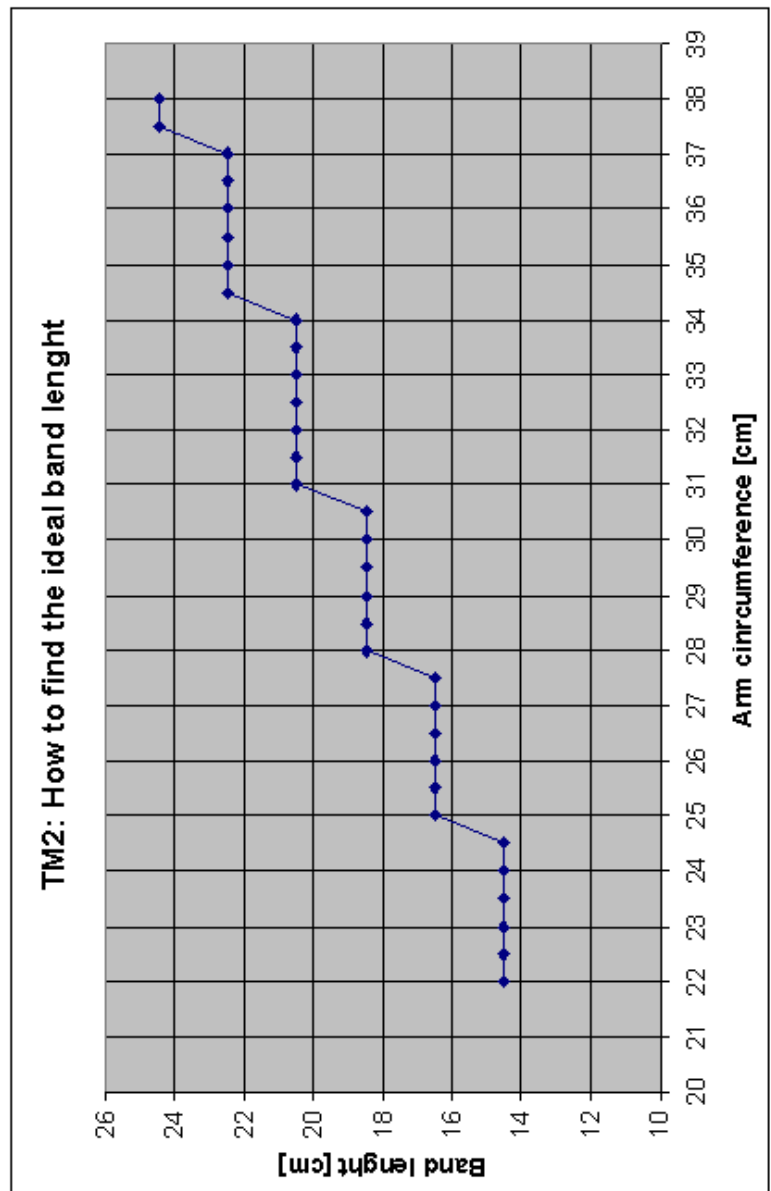
Expert Mode

The expert mode allows for the test of the connectivity and interaction with a Continua Manager. In this mode, the user can manually enter BGM values and send them to the Manager

3.3. Selecting the right band size

The maximum length of a band for a certain arm can be found like that: Arm circumference * 0.63. Choose the next smaller band available or even smaller if still comfortable to wear. Available band lengths are e.g. 14.5, 16.5, 18.5, 20.5, 22.5 and 24.5cm.

| Arm circumference | Ideal band length |
|-------------------|-------------------|
| 22 | 14.5 |
| 22.5 | 14.5 |
| 23 | 14.5 |
| 23.5 | 14.5 |
| 24 | 14.5 |
| 24.5 | 14.5 |
| 25 | 16.5 |
| 25.5 | 16.5 |
| 26 | 16.5 |
| 26.5 | 16.5 |
| 27 | 16.5 |
| 27.5 | 16.5 |
| 28 | 18.5 |
| 28.5 | 18.5 |
| 29 | 18.5 |
| 29.5 | 18.5 |
| 30 | 18.5 |
| 30.5 | 18.5 |
| 31 | 20.5 |
| 31.5 | 20.5 |
| 32 | 20.5 |
| 32.5 | 20.5 |
| 33 | 20.5 |
| 33.5 | 20.5 |
| 34 | 20.5 |
| 34.5 | 22.5 |
| 35 | 22.5 |
| 35.5 | 22.5 |
| 36 | 22.5 |
| 36.5 | 22.5 |
| 37 | 22.5 |
| 37.5 | 24.5 |
| 38 | 24.5 |



4. Measurement run

A measurement run of the MGMS should last between 2 and 12 hours. The first 75 min are taken for adaptation of the system and not used for glucose calculation i.e. in case the measurement run is 2 hours only the last 45 min will be used for glucose calculation.

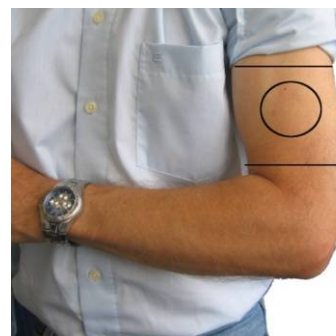
After each measurement run, the ToolSuite system has to be restarted. Only once data have been transmitted to the REACTION platform and the ToolSuite has been restarted, the system is ready for the next measurement run.

4.1. Reference Blood Glucose (RBG)

Users who have obtained regulatory and relevant national and international approvals to evaluate the CGM System in a clinical trial according to the Good Clinical Practice (GCP) might foresee some Reference Blood Glucose (RBG) measurements in their clinical protocol for comparison purposes. In this case, the first RBG relevant for the CGM System needs to be taken at the earliest 75 min after a measurement run has been started; it will be used for an initial calibration of the glucose calculation. The Monitoring plug-in will ask for a RBG when necessary. Additional RBG values might be taken during the measurement run for further reference and recalibration purposes. RBG values need to be recorded and entered in the ToolSuite manually (Section 4.1).

4.2. Preparing for a measurement run – the day before

- Multisensor placement area is on the non-dominant upper arm i.e. the left upper arm for right-handed people. The sensor will be placed in the circled area marked in the picture to the right.
- At least 8h before the test run, the hairs are preferably removed in the Multisensor placement area i.e. between the straight lines on the picture to the right. The hair removal can be performed by a depilation crème or by a shaver. Afterwards, the area needs to be cleaned gently from residual crème or shaving foam.
- No crème or body lotion should be applied to the placement area at least 10h prior to a test run.
- The battery of the Multisensor has to be charged and left connected to the power supply until the Multisensor is put on.



4.3. Attachment of the Multisensor

- Gently clean the Multisensor with a tissue delivered by Solianis.
- Check:
 - Multisensor placement area: There must not be any indication of the skin rash, redness or other skin irritations.
 - Laptop: Time and date on the Laptop has to be checked and manually updated if required.
 - RBG: If a RBG meter is used, the time of the RBG meter has to be checked as well and updated if needed.
- Put on the Multisensor:
 - Take the Multisensor without the cover.
 - Fix the elastic band to one side of the Multisensor.
 - Place the Multisensor onto the designated measurement area of the non-dominant upper arm (i.e. right-handed people measure on the left side). The slim side of the Multisensor needs to show towards the elbow.
 - Fix it with the elastic band by clicking the open side of the elastic band to the Multisensor.
 - Fix the Multisensor cover as shown on the right-hand side. An audible click confirms the correct fixation of the cover to the unit.
 - The Multisensor is in the right position if it is positioned 2-3 fingers wide above the elbow and faces to the front with 'MGMS' reading correctly.



- When moving the arm, the Multisensor position must not be affected and all four corners are to remain attached to the skin.



- The Multisensor confirms the attachment to the skin with a short beep (1 x short) after some 2 1/3 minutes.
- Connection to the Laptop via Bluetooth is confirmed with a series of three short beeps (3 x short).
- The Multisensor system is now ready to take measurements. The ToolSuite running on the Laptop shows the screen below. The message in the *Plot* modus should read *Run in period* with a time counter winding down.

Monitoring Plugin v1.0.0

PLUGIN
Get calibration parameters

Glucose estimation

| MCN | Level | Rate | Mask |
|-----|-------|------|------|
| 1 | nan | 0 | 0 |

Algo State

- 1 glucose
- 2 sbglLevel
- sbglRate
- mask
- calibrationLogic
- rbglValid...
- usedRbg
- calibratio...
- controlState
- controlSt...
- runInCo...
- exceptionLogic
- exceptio...
- refractor...

Packet data

| Nr | Len | Prot | TS | MsgID | MCN | Entity |
|----|-----|------|----------------------|-------|-----|--------------|
| 48 | 54 | 1 | 2011-02-24 09:30:... | K | 1 | SENSOR 0 (0) |
| 49 | 18 | 1 | 2011-02-24 09:30:... | B | 1 | DUMMY (255) |
| 50 | 139 | 1 | 2011-02-24 09:30:... | O | 1 | DUMMY (255) |
| 51 | 22 | 1 | 2011-02-24 09:30:... | G | 1 | SENSOR 0 (0) |
| 52 | 22 | 1 | 2011-02-24 09:30:... | G | 1 | SENSOR 1 (1) |
| 53 | 28 | 1 | 2011-02-24 09:30:... | A | 1 | DUMMY (255) |
| 54 | 14 | 1 | 2011-02-24 09:30:... | Y | 1 | DUMMY (255) |

Physical data

| MCN | 1 | 2 | 3 |
|-----|---|---|---|
| | | | |

Monitoring Application
Solianis Monitor

Running in. Remaining time:
01:15:00

Main Plot RBG

4.4. End a Measurement Run

Total duration of the Measurement run should be between 2 and 12 hours.

- Take off the Multisensor
 - Before taking off the Multisensor any potential sharps e.g. wrist watches, rings need to be taken off the arm the Multisensor is worn.
 - Take off the battery by pushing the both buttons on the short side of the cover
 - The Multisensor is taken off by moving it down the arm across the elbow and the wrist. Alternatively, one side of the band can be gently removed from its fixture.
- The skin under the Multisensor should be inspected for irritations. Slight redness or imprints due to the Multisensor or the band are normal and should disappear within a few hours.
- Measurement data need to be downloaded to the Laptop after each demonstrator run.

5. Glossary

Algo

Glucose estimation from measurement run data with initial calibration. This procedure is run in online during the measurement procedure.

Exception

Measurement run data that are not consistent.

Glucose estimation algorithm

Algorithm as defined by Solianis to calculate glucose information from Multisensor signals. A statistical model and logic to account for plausibility of the information that enters into the statistical model as well as of information that is calculated by the model is applied.

Measurement run

Glucose monitoring with the Solianis system for an uninterrupted period of up to 10 hours.

MGMS

Multisensor Glucose Monitoring System for non invasive continuous glucose monitoring.

RBG

Reference blood glucose value – typically taken with a commercially available Blood Glucose Meter.

ToolSuite program

Software installed on the laptop unit to collect, process, and send data of a measurement run.

Stable glucose

Glucose value in the range 3.8-16.6 mmol/L (70-300 mg/dl) and rate of change of glucose value in the range (-0.1)-(+0.1) mmol/L/min ((-2)-(+2) mg/dl/min).

6. Multisensor Signals

| Signal (acoustic) | Situation | What to do? |
|--|--|--|
| Short beep (1x) (after the Multisensor has been put on) | The Multisensor acknowledges its attachment to the skin and indicates that it starts to measure data. | Once the Multisensor was put on the user always has to wait for this signal, and then confirm on the PDA the Start of the measurement run by selecting <i>ok</i> . |
| long beep (3x) (during the measurement) | The Bluetooth-connection between Multisensor and the Laptop is interrupted. Laptop: Bluetooth icon in the dock is white | Make sure the Laptop is located close to the Multisensor. The SensorMonitor program background of display turns white and three short beeps (see below) of the Multisensor indicate that the Bluetooth connection has been reinstalled. If the connection cannot be restored, assure that the Bluetooth connection of the Laptop is switched on |
| short beep (3x) | The Bluetooth-connection between the Multisensor and the Laptop is active (again). | - |
| Sound sequence | The Multisensor was without Bluetooth connection for some 40 minutes | The user is requested to bring the Laptop and the Multisensor closer to each other. If the Bluetooth interrupt lasts for another 40 min the sound sequence is given again – data can no longer be stored on the Multisensor. |