ISEsweat II®

Sweat Chloride Analyzer

User's manual

TECIL®

V00EVP012014

INDEX

1. INTRODUCTION

1.1 ISEsweat intended use

ISEsweat is intended for quantitative pilocarpine iontophoresis sweat chloride testing for the diagnosis of cystic fibrosis.

ISEsweat should only be used by Doctors, nurses and trained laboratory personnel. It is highly recommended that users gain prior experience before diagnosing Cystic Fibrosis.

The place for testing may be in laboratories, hospitals or clinics

In order to increase the possibility of collecting an adequate sweat sample, it is advisable to conduct the first chloride sweat determination tests on individuals older than 2 weeks and weighing above 2kg.

Sweat volumes are dependant on age, sex, corporal weight, race, skin condition and sampling system.

ISEsweat® is a Sweat Chloride Analyzer intended for Cystic Fibrosis Diagnosis.

CAUTION: ISEsweat® is intended only as a supplement in a patients' evaluation. It must be used in conjunction with other signs and symptoms. Don't take any clinical decision based only on the sweat test evaluations.

1.2 Operating principles

Cystic fibrosis is a multisystem disorder that causes formation and accumulation of dense mucus, that affects mainly lungs, intestines, pancreas, and liver. Cystic fibrosis is also characterized by the presence of a high chloride (Cl^-) concentration in sweat, which is the basisi of this diagnosis: (commonly known as the sweat test). This test QUANTIFIES the chloride levels excreted while sweating, and is indicative for CF diagnosis.

The ISEsweat® runs the sweat test in two different stages: IONTOPHORESIS or sweat stimulation and MEASUREMENT of the chloride concentration.

The first phase is called IONTOPHORESIS because sweat stimulation is done using this technique. Its purpose is to get a sweat stimulating drug, pilocarpine, through the skin, with the help of an electrical potential difference. Pilocarpine excites the sweat glands and stimulates sweat on the treated area. Once there is enough sweat, the second phase begins.

The amount of pilocarpine delivered varies directly in proportion to the current and time according to the Faraday equation below:

$$P = itMw/F$$

i	Intensity in mA
t	Iontophoresis time
Mw	Pilocarpine molecular weight
F	Faraday constant
P	mg of released pilocarpine

The second phase is called the MEASUREMENT phase. Chloride ion (Cl^-) concentration is measured in the sweat produced by iontophoresis. The analysis is made without any need to

manipulate the sample, using the microsensors on the Measurement side of the sensor card. There is no need to collect the sample, it is analyzed at once, thus avoiding evaporation or pollution problems.

Results obtained by the sensor card are transmitted by the remote module, and processed at the ISEsweat® base, to give the chloride ion concentration. ISEsweat® uses the direct potentiometry method, with a chloride ion selective electrode (commonly called ISE), responding only to the Cl ion in the sweat. The relation between the developed voltage and chloride ion concentration is logarithmic, and it is expressed by the Nernst equation:

$$E = E^{\circ}\frac{RT}{nF}\log(\gamma C)$$

E	Potential of electrode in contact with sample
E°	Potential of reference electrode
RT/nF	Temperature constant
N	Valency (chloride ion is 1)
Log	Logarithm base 10
γ	Chloride ion activity coefficient
C	Analyzed ion concentration

The analyzer measures the electrode potentials, and the data is processed by a microprocessor to calculate the chloride ion concentration.

1.3 How to use this manual

This user manual has been produced by Tecil in order to guarantee the correct use of the ISEsweat® equipment. Before putting the equipment to work, please read carefully all pages and, if you have any doubts, contact the relevant department. Only authorized Tecil agents can translate this manual.

Tecil, S.A.
Lope de Vega 99-101
08005 Barcelona (Spain)
Web: www.tecil.com
E-mail: calidad@tecil.com
Phone: + 34 902995746
Fax: + 34 933084871

Information in this manual can be changed without prior warning. This product is permanently being developed and perfected. The manufacturer keeps the right to make any modification on the design features without prior warning.

2. Device description

2.1 ISEsweat

ISEsweat® is intended for use by qualified personnel to measure chloride in sweat. The resulting concentration value of patient´s sweat is used for diagnosis of cystic fibrosis.
The current for iontophoresis was reduced to 0.4 mA, to minimize the risk of causing irritation to the patient. After 10 minute of iontophoresis, the stimulated area is washed with distilled water, and reverse face of sensor card is placed. After 15 minutes the concentration of chloride directly from the skin of the patient is measured. The data is then transferred to the base by radiofrequency (RF) and the value of chloride is displayed in mmol/l.
The analyzer consists of 2 separate parts:

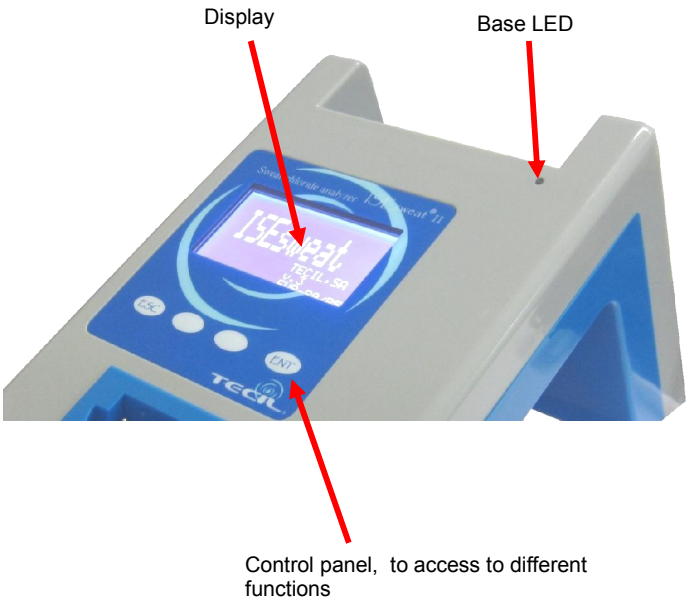
1. **Terminal or receiver base**, includes: an LCD screen where results of the analysis are displayed;

2. **Remote module**, has just one push button on the front. This remote module has the holder for the innovative disposable sensor card patented by Tecil which are involved with the stimulation, sweat collection and reading the chloride concentration obtained from the patient's sample.

ISEsweat® uses a detachable sensor card to run each sweat test. They consist of two different sides; each one performs a different process (IONTO side and MEASURE side).
Once the card package is opened, each sides have a different appearance, thus making it difficult to make a mistake when choosing the appropriate side. In the event of mistake, ISEsweat will alert you about wrong side placed !!

2.2 Terminal or receiver base

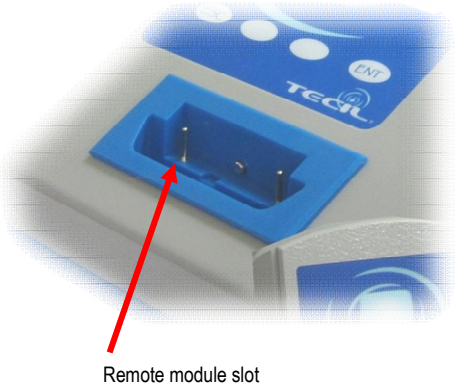
Receiver unit for the reception of data coming from the remote analyzer module, display and record in the internal data base memory



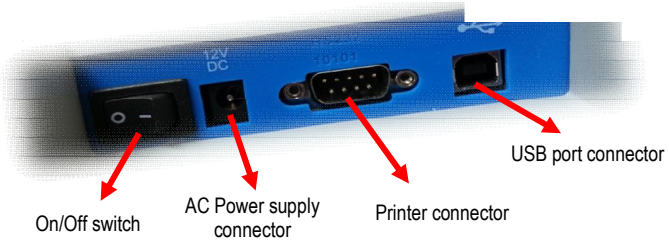
Display: Appears all the information about the test (phase, time remaning…)

Base LED: It turns orange or green at the same time as the charge led indicator on the remote. When it's orange is "**charging**" and when is "**green**" is charged.

Control panel: This four buttons helps the user to move around the interphase on the software's base. Their function could change, depending on which screen appears on the base.



Remote module slot: It's a connector to charge the remote battery, once the base of the remote It's plugged in on this slot.



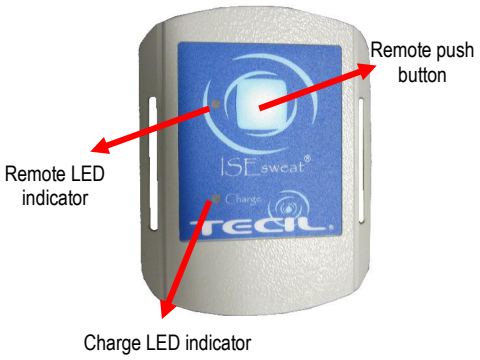
On/Off switch: Turns On or Off the base of the ISEsweat.

AC Power supply connector: Side where plug the power supply connector to the base of ISEsweat.

Printer connector: Port to connect a printer serial cable, to print the results.

USB port connector: Port to connect an USB cable to a PC.

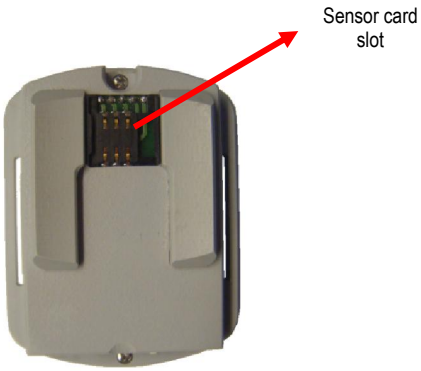
2.3 Remote module



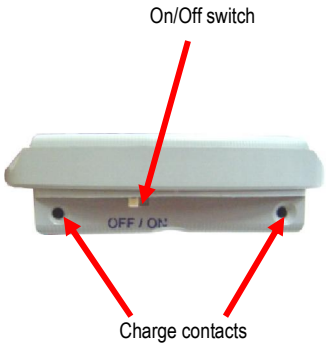
Remote LED indicator: Indicates the phase of sweat test, and if there's some problem, using a two colour LED.

Charge LED indicator: Indicates if it's charging (orange) or fully charged (green).

Remote push button: Pressing this button: starts, changes the phase and stop the remote.



Sensor card slot: Slot where the sensor cards are connected to run the iontophoresis, and the measurement phase.

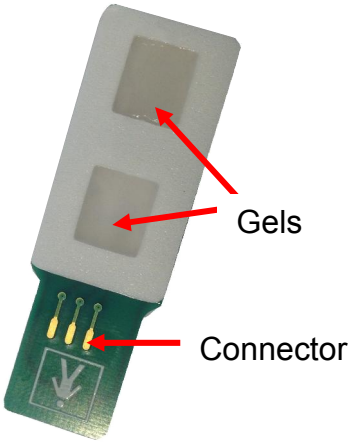


On/Off switch: Turns On/Off the Remote.

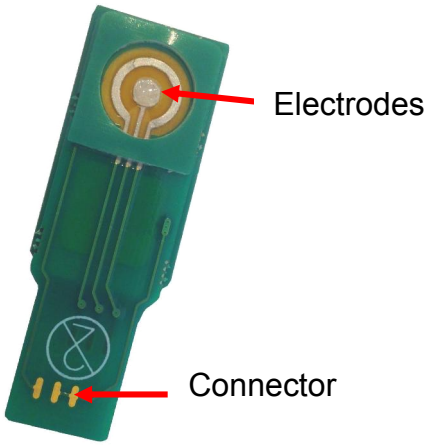
Charge contacts: Contacts where the remote it's plugged to the remote module slot

2.4 SENSOR CARDS

ISEsweat® uses a sensor card to run the analysis or sweat test. It consist of two different sides; each one performs a different process (IONTO side and MEASURE side). The name of each side alludes to its function.
Once the card package is opened, you can distinguish these two sides by the appearance, thus making it difficult to make a mistake when choosing the approriate side.



IONTO SIDE → this stimulates sweat on the patient through two square-shaped hydrogel iontophoresis pads containing a solution of 0.5% pilocarpine nitrate.



MEASURE SIDE → this measures the chloride concentration (sample or control) through the ISE technique. It consists of 2 concentric circular electrodes, covered by a transit gel that the user has to remove before using.

3. ISEsweat installation

3.1 Components

Use the list in the following table to check that you have received all needed components.
If any of the components are missing or damaged, please inform your distributor at once.
TECIL only takes responsibility for notifications received within 72 hours after product delivery. Once notified, you have 15 days from the receipt date to effect any return.
Use only the recommended accessories. If you have any doubts, please contact your distributor or the manufacturer.
It is recommended that you keep the packaging material in case it is needed for further transport.

Packing List

CODE	*DESCRIPTION*
T601	Complete ISEsweat®
T611	Receiver base
T620	Transmitter module (remote)
T700	Sensor cards
T800	Quality Control Kit
T900	DC 12v Power supply unit 1,5 A
T901	Printer Series Dock Cable – **OPTIONAL**
T902	USB cord - **OPTIONAL**
T903	Armband
TM-U220DS	Printer Series Dock - **OPTIONAL**
T908	Power Cord

3.2 Power source connection

WARNING: When you connect the ISEsweat, check that it works correctly before using it for clinical purposes. The accessories connected to the ISEsweat® data interface must comply with IEC EN 60950 regulations for data processing equipment certificate or IEC EN 60601-1 regulations for electrical medical equipment certificate. Any person that connects other equipment to the input/output ports (ISEsweat® data port connector) is configuring medical equipment, and as such is responsible for guaranteeing that the system follows the IEC EN 60601-1-1 and EN 60601-2 Regulations for electromagnetic compatibility. All accessories supplied by TECIL comply with all these regulations. Connect the equipment to a power supply with an earth connection.

WARNING: Use the equipment in dust free, mechanical vibration free and electrical interference free areas. Avoid the proximity of brush motors (in some centrifuges), heat sources or blinking fluorescent lights. Readings and signals could be affected.

CAUTION: DO NOT lift the ISEsweat® base by the power supply cable; it could become disconnected and damage the ISEsweat®.

CAUTION: DO NOT soak the equipment in water or put it in a very high humidity area.

CAUTION: In order to guarantee patient security and that the equipment remains in good condition, DO NOT place the ISEsweat® in any place from where it could easily fall.

CAUTION: DO NOT use the ISEsweat® in the presence of anesthetics or flammable gases to avoid risk of explsion.

Study the figure below and follow the instructions in order to make the power supply connection.

2 – Power supply On/Off switch
3 – AC power supply connector CA

1. Plug the power supply cord connector to the power supply connector (3).
2. Plug the power supply cord to a CA power network point with an earth connection (Shuko type).
3. Press the power On/Off switch (— / O) (2) to the ON position (— symbol) to start up.

When connecting the equipment to the power network, please ensure that it cannot become easily disconnected. After connecting and installing the ISEsweat®, press the power switch to the ON position (—), to initiate the program. ISEsweat® makes an acoustic signal (1 beep) and the base LED indicator will light (orange) and come on for a second. When the left hand switch is turned on, the following software load screen will appear on the ISEsweat® screen for 10 seconds.

1. Product brand
2. Company
3. Software version – Work mode
4. Work frequency – Base number / Linked remote number

1
2
3
4

3.3 Battery

The ISEsweat® transmitter module or remote includes a Lithium-ion (Li-ion) battery with a 650mAh capacity that allows it to work. When completely charged the battery will last for 6 hours and allow for 10 analyses.

It is highly recommended that the internal battery is replace every 2 or 3 years, depending on the use. Batteries capacity decreases with use (see *Battery replacement* section).

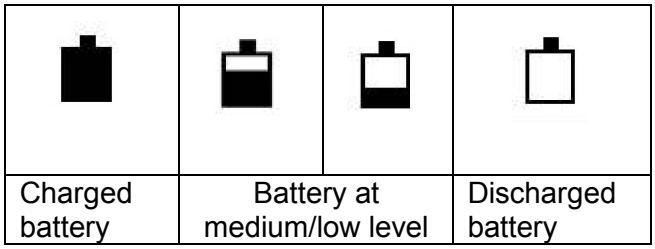
If the ISEsweat® is not going to be used for some time, it is recommended that you get in contact with the technical support service, and disconnect the remote using the switch on the front side.

Recharge the battery before using if it has been inactive for 3 months or more.

WARNING: ISEsweat® remote will not work if the battery is completely flat. Please, check the battery state before using the remote (see Battery Indicators).

Battery indicator

During use, you can check the battery charge state by referring to the symbol on the upper left hand corner of the base screen. The battery indicator appears once the analysis has begun.



Charged battery	Battery at medium/low level	Discharged battery

WARNING: Starting an analysis with a low battery level can influence the results. It is highly recommended that you recharge the battery level whenever it is low. Please, check that the remote has an adequate battery charge level before running the analysis; otherwise, the battery may discharge during the analysis. After running an analysis, plug the remote module into the base charger slot until next analysis, to avoid getting a flat battery.

Charging process

The Battery will only recharge if ISEsweat® is connected to a CA power supply (BASE ON and REMOTE OFF) . Therefore, it is recommended that the ISEsweat® base is always connected to the CA power supply, and that the remote is left in the charging slot, so the battery is fully charged for remote use at anytime.

NOTE: Distinction between connection and operation.
Operation refers to any part of the analysis (sweat test) or quality control phases, where the remote module is in use.

However, connection refers to the starting up/shutting down of the remote module using the switch at the lower side. If the remote is shut down it won't work; there is no power.

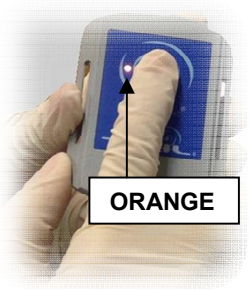
To start the charging process, please follow the instructions below:

1. *Interrupt the equipment operation*

In order to start the charging process, the remote must not be operating. The screen on the Base Unit should be showing the Start Screen or the Previous Phase, not any of the running mode screens, (measurement, ionto, wait, etc…)

To make sure the remote is not operating:

1. Press for 4-5 seconds the remote central button, until the remote LED turns orange.
2. Release the button when the LED color changes. The remote is now switched off and the remote LED indicator is should be off.



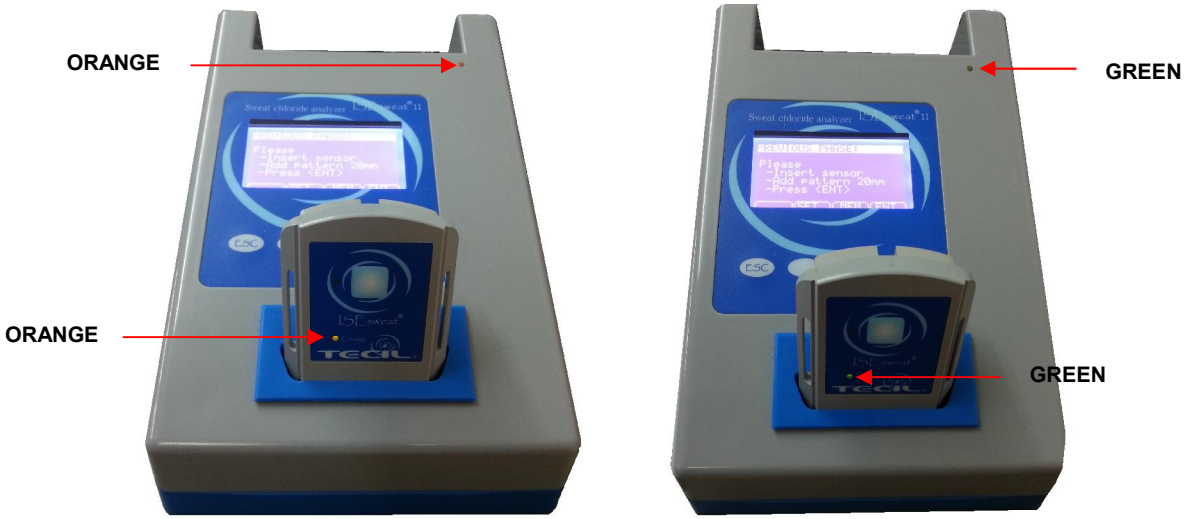
2. *Remote disconnection*

Once the remote is not operating and before starting the charging, please disconnect the remote completely by switching the side switch to **OFF.**

WARNING: During a test session you can continue to charge the equipment without disconnecting the remote but in this case, you will not be able to check that it is fully charged (green LED) because of the power the remote is consuming. After ending the test session, please disconnect the equipment and put the remote in the charging position, as described above, to achieve a full charge.

3. *Charging*

To charge the battery, put the remote in the charge slot on the ISEsweat® base unit, as shown in the following figure.,The estimated time to achieve a full battery charge is around 6 or 7 hours.
Once the remote is in the charging slot, the base and remote LED indicators (LED) will light up, and will give information on the charge state, changing from orange/red to green/green as shown,.



Charge light signals indicators:

Battery state	Remote LED	Base LED
Discharged	Orange*	Orange
Charged	Green	Green

*No more than 7 hours. In any other case, check *Problems* chapter.

Once the battery is fully charged, base and remote LEDs will glow GREEN, thus indicating the battery is at full charge.
The remote module can remain connected to the base indefinitely, without any problems for the equipment. LED indicator will remain GREEN at all times.

*WARNING: Make sure when using the remote again, to set the side switch to the **ON** position. In fact it won't connect to the Base Unit or work at all until you do this. If after charging for 7 hours, the remote LED is still showing Orange, there is the possibility that you have forgotten to disconnect the remote, because the remote's minimum power consumption prevents the remote from becoming fully charged (Green LED).*

WARNING: If you remove the remote from the charging slot with the green LED showing (charged battery) and replace the remote back in the slot the LED will glow red for a few moments even though the battery is fully charged,, because the remote needs some time to check the battery state.

Battery change

The advantages of the Lithium Ion batteries are, among other things, the lightness of their components, their high power capacity and their capacity to operate with a high number of regeneration cycles. However, the battery life will deteriorate over time. The number of battery charge/discharge cycles will determine its service life; with regular use, its useful life is estimated at between 2 and 3 years. It is highly recommended that the battery is left in the charging position when you don't expect to be using it for a long time. As said before, check the *Problems* chapter if you observe any charging anomaly.

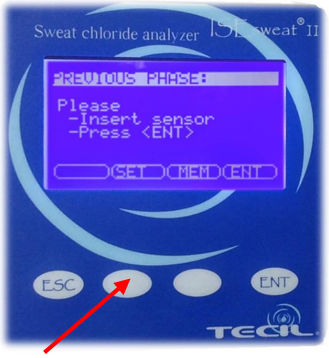
Remote indicator LED will emit a RED light if the battery state is not good, thus showing a problem in the battery.

CAUTION: Battery replacement can only be made by the TECIL Technical Support team or a TECIL authorized technical expert.

4. Sweat analysis

4.1 Settings

SETUP (SET).



Once the equipment is ON, and after the software has been loaded (you have to wait 10 seconds for this), the Start screen will appear. On the lower part of the screen, you will see <SET> This is the access portal to the Settings Menu (Setup). Using this menu, you can choose between different Work Modes.

ISEweat® is designed to run the Sweat Test and to establish the chloride concentration in a sweat sample.

To do so, ISEsweat® has 2 work modes:

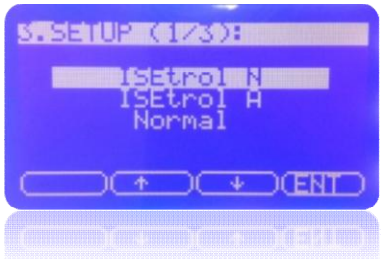
- **Normal Mode**, designed to run the analysis or sweat test.
- **Quality Control Mode (ISEtrol N or ISEtrol A),** designed to check the equipment. It is recommended to use TECIL controls or any other approved QC material for this.

Work Mode Selection

- Press **<SET>** at the Start Screen.

A menu will appear that allows you to choose between different programs or Work Modes:

QC (**ISEtrol N or ISEtrol A**) or **Normal (**Sweat Test)

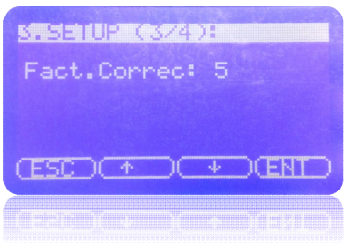


Use the scroll arrows to select a program from the control panel.

- Press **<ENT>** when you have selected the Work Mode you want to use.

You will see the Remote Linking menu screen, both in Quality Control and in Sweat Test modes

- The factory setting of the remote number is zero. Skip through this by pressing <ENT>



- Choose the correction factor that shows in the sensor card box, if there is not any specified on the box, choose 5. Skip through this by pressing <ENT>

An information screen on the linking between the base and the remote will appear automatically, and the device will proceed to the linking. To indicate this process, the base unit will emit a series of 3 beeps

- Press the remote module central button and keep it pressed during the process. Do not let it go until the base stops beeping.

During this 10 seconds (approximately) interval, while you keep .the remote module button pressed, the remote LED will indicate that the remote is correctly linked by the following color sequence

WARNING: Keep in mind that it is very important to keep the central button of the remote pressed all the time until the linking is done, otherwise the process will be interrupted, and you will have to initiate the process again until linking is successfully completed.

When linking is completed, the menu screen will change to the start screen menu, thus showing that correct linking between the base and the remote has occured.

CAUTION: In order to have good communication between the base and the remote, the distance between the two must not be over 10 meters. If you increase this distance, there is the possibility that the link between the remote and the base breaks which could lead to some errors.

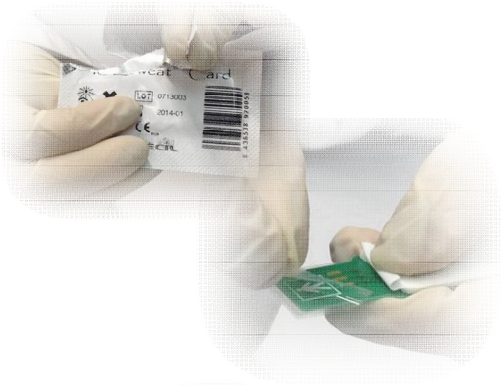
*NOTE: **Interruption of the analysis**. You can stop the test at any time by pressing the button on the remote unit until the LED remains orange (4 seconds) and release. Return to the Home screen.*

4.2 Sweat induction and analysis

PREVIOUS PHASE

Follow the instructions on the screen:

Insert sensor

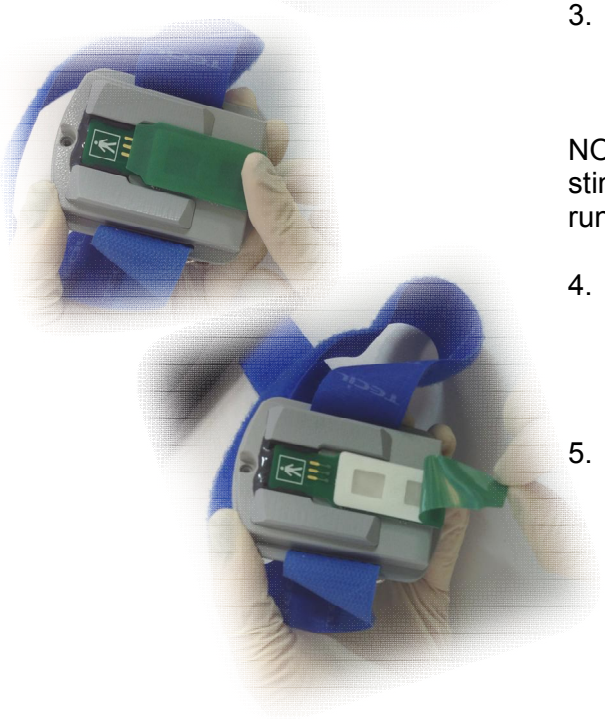


1. Select a card and take it out of the package

2. Remove the protective film plastic that protect the connectors. Dry any excess liquid from the connections zone with a tissue

3. Before starting the analysis, locate the IONTO side of the sensor card.

NOTE: The IONTO side of the card is designed for skin stimulation, in order to obtain a sweat sample prior to running the sweat test in the Normal Mode.



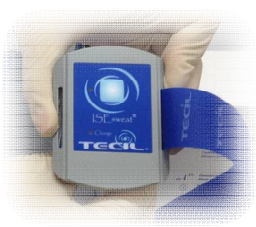
4. Place the sensor card with the IONTO side facing outwards in the remote connector slot, as shown in the image.

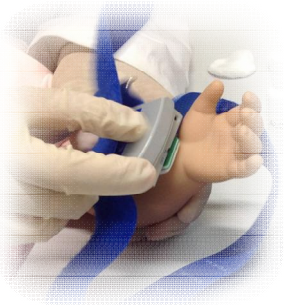
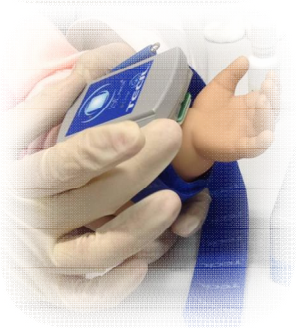
5. Remove the protective plastic protector strip on the IONTO side.

*CAUTION: Please, **do not touch** the hydrogels on the IONTO side; it could affect their composition. Pilocarpine found in the hydrogels can be toxic if inhaled or ingested. Please, clean carefully all contact zones after the analysis. In some cases, depending on the patients sensitivity, the gels can cause an allergic reaction such as red spots on the skin which may need to be treated with anti-inflammatory treatment. If the patient suffers any distress or pain, STOP the test immediately and cancel the analysis*

CAUTION: In case you introduce the card the wrong way round (opposite side of the one needed); the remote LED will remain red. Extract the card, turn it round and introduce it again, correctly. The LED will go out and you can continue the procedure.

CAUTION: Skin must be healthy, wholesome, with no cuts, eczemas or irritations. Whenever you clean the skin with alcohol, remember to moisturize it afterwards, to avoid skin dryness caused by alcohol



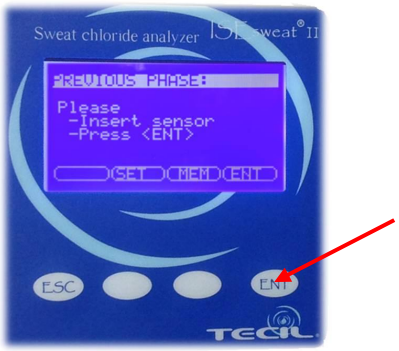
6. Place the card with the hydrogels on the skin pretreated with alcohol and destilled water, so there is contact between them and the patient's inside forearm.

7. Fix the card and the remote module to the patient's forearm using the armband. Adjust the armband as shown on the image, so the sensor card stays fixed on the patient's arm.

   a. Enter the rounded end of the armband into the slot with the cloth part on the inside.
   b. Without twisting, insert the end of the armband into the other slot.
   c. Adjust the size of the armband to fit the forearm so that the hook side attaches to the cloth side.

CAUTION: It is very important that the remote unit is fixed securely in place by the armband, in order to maintain good contact with the skin and to prevent sample evaporation and subsequent concentration of sample

Press <ENT>

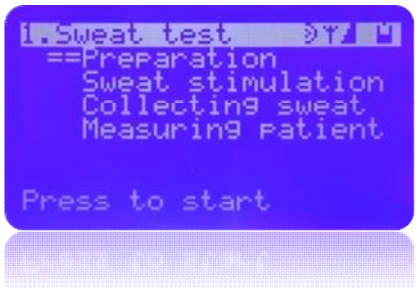


8. Once the card and the remote unit are fixed on the patient's forearm, press <ENT> on the receiver base unit.

NOTE: To avoid burns, the ISEsweat® is equipped with a current generator limited to 0,4 mA. Current is generated at the remote unit for 10 minutes, so the distance between remote and base units will not affect the analysis during this time.

Sweat Test

On pressing <ENT>, a new screen appears which allows the analysis to be monitored. The analysis consists of 4 phases:



Phase 1: Preparation

The ISEsweat® base unit will emit a repetitive sequence of 3 fast beeps, waiting for the user's confirmation.

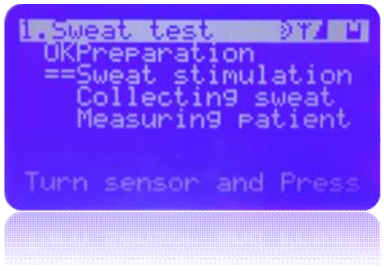
1. once the device is correctly placed on the patients's forearm, **press the remote button.**.
2. The Base unit beeps will stop and an **OK** will appear on the screen next to **Preparation**.
3. The process will continue to the next phase, Sweat stimulation, in which, sweat is stimulated from the patient's skin by means of the IONTO

Phase 2: Sweat stimulation

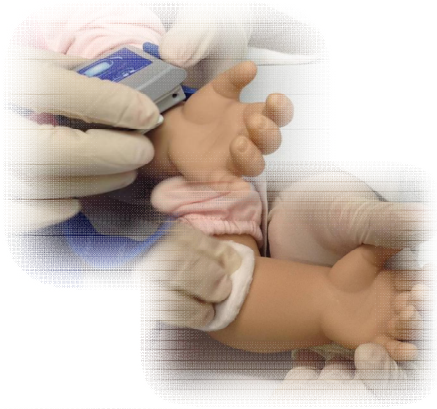
A flashing green light signal on the remote module shows that the sweat stimulation has started.

The screen shows that the sweat stimulation has start **==**

The sensor card stimulates sweat generation for 10 minutes through iontophoresis at the place it is lying on. During this 10 minute period, the remote unit will flash with **a green light**, to show the user which phase it is in.



4. Once 10 minutes has elapsed, the remote unit will stop delivering current and the acoustic signal will change to 3 consecutive beeps. The screen will display the words "Turn sensor and Press".
5. Loosen the armband and remove the remote unit from the patient's forearm.



6. Clean the stimulated zone with **deionized water** and then dry it.

CAUTION: DO NOT clean the stimulated zone with physiological saline or any other saline solution, since it can affect the test results.

7. Replace the protective plastic covering over the IONTO gels.

8. Then carefully remove the gel that covers the electrode on the measure side. Be careful you don't damage it. You can remove it with bare hands or with tweezers.

Do not use sensor cards in case that reference electrode is broken or in disrepair. (see image)

9. Clean the card surface to avoid leaving bits of gel on the electrode. Clean with plenty of distilled water, and dry with a gauze or blotting paper. The cleaning process is finished when the water drops are gone.

10. Fit the sensor card into the remote unit connector slot, with the MEASURE side upwards as seen at the image below.

11. Place the remote unit onto the patients skin with the electrodes aligned over the stimulated zone.

IMPORTANT: *Keep the remote unit in the same position and direction as it was before to ensure that the measure area is placed directly over the previously stimulated area.*

12. Fix the remote unit to the forearm with the armband again.

13. **Press the remote unit button**.. The "**Collecting sweat**" phase will start automatically and the bips stop.

The electrode position is very important. The measurement electrode must be in contact with the skin, directly over the previous stimulated zone (reddened zone). If it is anywhere else the sample of sweat generated may not be enough to give a result or the measurement electrode may not have a good contact with the sample, so you won't get a good result.

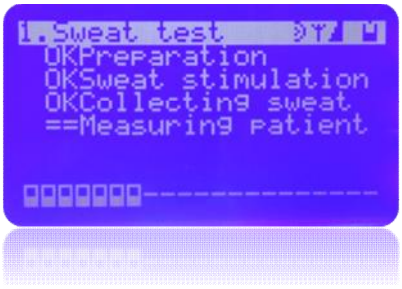
Phase 3: Collecting sweat

14. The screen shows:

The remote makes a repeated visual signal of **two green flashes**.

This process lasts for 10 minutes. During this phase, the remote unit needs to receive a sufficiently amount of sample to be able to analyze it (see *Technical specifications* chapter).

Phase 4: Measuring patient



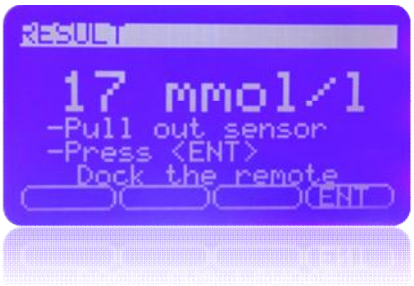
15. Once 10 minutes of the Collecting sweat phase is over, the equipment will automatically start the Measuring patient phase, where it will measure the chloride concentration of sweat, without further user involvement.

16. The screen shows:
== "Measuring patient"

17. The Measuring patient process takes 5 minutes; after this, the equipment sends the result from the remote unit to the base unit.

CAUTION: During measuring phase, ***it is important that the distance between the base and the remote is no greater than 10 meters****. If it's any greater it could lead to a break in the link and the test would have to be repeated.*

Results



Once the data has been transmitted, the base screen will show the value Chloride concentration in mmol/l.

The screen message has a reminder that, after ending the analysis, you have to:

1. Remove and discard the sensor card (see *Waste Management*).
2. Press **<ENT>** to go back to the Start Screen or Previous Phase screen. From there, you can run a new analysis.

After obtaining the concentration value in mmol/l, the equipment will automatically send the results to the printer, if conected.

4.3 Interpreting of sweat test results

Reference Values

- ***Negative value*** < 40 mmol/l*
- ***Intermediate value*** 40 ≤ X ≤ 60 mmol/l*
- ***Positive value*** > 60 mmol/l

* To newborn	< 30 mmol/l	Negative value
	30 ≤ X ≤ 60 mmol/l	Intermediate value

4.4 Calibration and control

The ISEsweat is factory-calibrated and does not requiere any calibration by the user.

Together with the device the control solutions with two levels are delivered, 20mmol/l and 80 mmol/l.

All quality control requirements and testing should be performed in conformance with local, state and/or federal regulations or requirements.
At least, once a month do the measures of both controls levels (See next section), if the results are out of range, please contact immediately to our technical service and put the device out of service.

4.5 Quality Control Mode (QC)-ISEtrol N and ISEtrol A

As has already been said in this manual, the usual working mode for the ISEsweat® is the NORMAL mode, to run sweat tests, but, to carry out Quality Control you need to change the Work Mode. To do this, please follow the instructions in the *Settings* chapter, and select Quality Control Mode (**QC**) **ISEtrol N** or **ISEtrol A** as the work mode.

To verify the correct operation of ISEsweat® it is recommended that you use ISETROL controls. The ISETROL controls are suitable for ISE (electrode ion selective) analysis of chloride, and are within the optimum working range of the device (see Technical *Specifications* section).

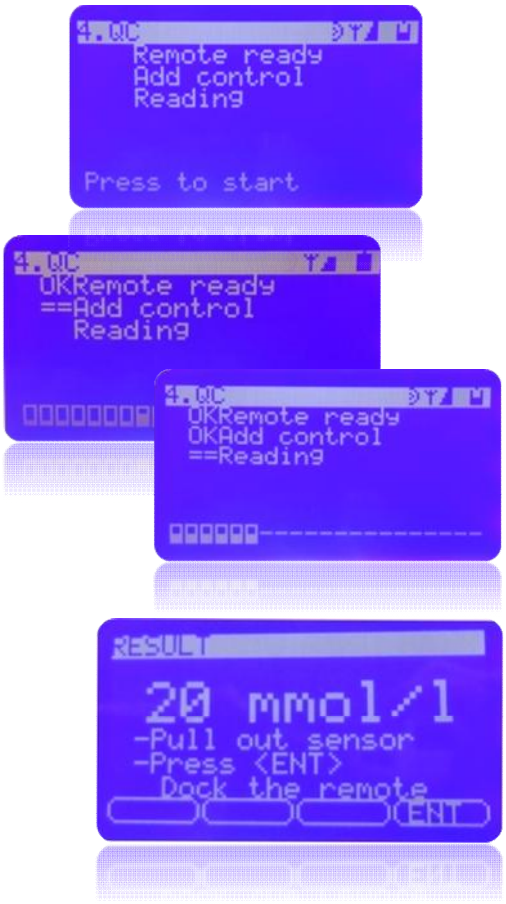
CAUTION: TECIL not responsible for any problems arising from the use of a control in poor condition or unsuitable for the technique or device. Therefore, before using a control, you should consult with TECIL as to its compatibility with the ISEsweat. Each hospital or laboratory should decide for itself the quality control steps to be taken but TECIL recommended to perform a quality control each day before the first test of your work list.

REMEMBER: To avoid confusion, please change back to Normal Mode once Quality Control has finished.

Select QC Work Mode , **ISEtrol N or ISEtrol A** (see *Work Mode* chapter 4.1)

The Start screen QC will appear

1. Take a sensor card out of the package
2. Then carefully remove the gel that covers the electrode on the measure side. You can remove it with bare hands or with tweezers Clean the card surface with plenty of deionized water and dry with a gauze or blotting paper.
3. Fit the sensor card into the remote unit connector slot, with the MEASURE side upwards as seen at the image.
4. Put the remote unit in a horizontal position, on an even and horizontal surface, with the electrode facing upwards. **Wait 1 min.**



5. Add a control solution drop directly onto the measurement electrode

6. Press <Ent> on the base to start the QC process. The base will emit three beeps repetitive to confirm that the user is ready to start. And appear the next screen

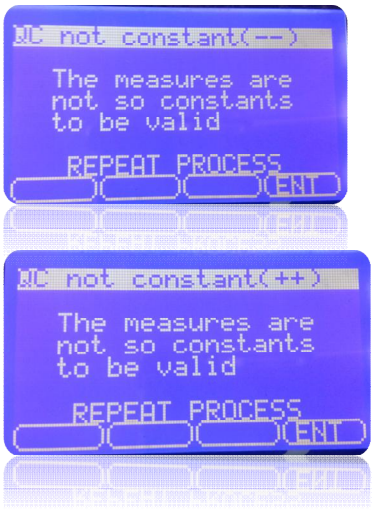
7. **Press the remote unit button**.

8. Next to each phase will be appearing OK to indicate that the phase has been realized

9. 4 minutes later the device will calculate the chloride value of the control

10. After obtaining the concentration value in mmol/l, the device will automatically send the result to the screen and the printer, if fitted.

** If Appears the screen **QC not constant (- -)**
Please clean the drop and place it in another position.
Press ENT on to the base.



** *If appears the screen **QC not constant (++)***

Please ENT on to the base until the QC re-start .

NOTE: The Manufacturer should provide an acceptance range as well as the certificate analysis for the standardized control. Take into account expiry dates.
Each laboratory will need to establish its own quality control procedures, but it is highly recommended to run a control before the beginning of a series of analysis and each time a new batch of sensor cards is used.

WARNING: Values that are out of range might indicate some anomalies. If after several tests, values continue to be out of the range suggested by the manufacturer, you must contact the manufacturer and stop using the device. Get in touch with TECIL for instructions on possibly changing the cards, or the control, or the device.

CAUTION: TECIL cannot take responsibility for any problem arising from the use of controls that are in bad condition, or controls that are not suitable for the device or technique. Thus, before purchasing a control, it is highly recommended that you check its compatibility with the device. Check with TECIL if you have any doubts.

5. Data port use

5.1 General summary

You can obtain patient data through the data ports at the back of the ISEsweat® if you connect it to a PC or to a printer in series such as Epson TM-U220DS M188D.
When you connect the ISEsweat® to the printer or the PC, you must check that it works correctly before using it in a clinic. Both the ISEsweat® printer or the PC must be connected to an AC power source with an earth connection.

WARNING: Epson Printer TM-U220DS is certificated according to EN 60601-1-1. The serial port is designed for this printer. Do not use any other printer. If you have any doubt, please check with TECIL Technical Support Service.

CAUTION: When connecting any peripheral equipment, either the printer or the PC, to the ISEsweat® base, all equipment must be disconnected (OFF). Do not connect or disconnect any cables or wires while the device is working.

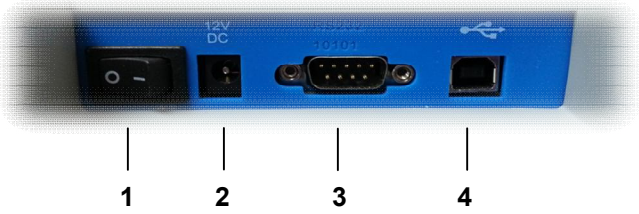
Any printer or PC connected to the ISEsweat® data port must be certified under the EN 60950 regulation. All equipment combinations must follow all the requirements of the EN 60601-1-1 regulations. Any person that connects a printer or a PC to the data port is configuring a medical device, and as such is responsible of guaranteeing that the system follows the EN 60601-1-1 and 60601-1-2 regulations on electromagnetical compatibility (EMC).

5.2 Data port connection

ISEsweat® data port can be connected to a printer via a Printer Series Dock Cable (code T900) or to a PC via a USB cord (code T902).

5.3 Print Data

The printer must be connected before the analysis starts. Data can be lost if it is not recorded, so it is highly recommended that you check first that the printer is connected and that it has enough paper.



1	Power supply On/Off switch (—/O)
2	AC Power supply connector
3	Data port connector
4	USB port connector

To print:

1. Connect the printer in

series to the ISEsweat® data port connector (4).
2. Turn on the printer.

At the end of each analysis, data is sent in real time and continuously to the data port at the back of ISEsweat®.

Each analysis results (both Sweat Test and QC) is seen on screen and is simultaneously transmitted to the communication outputs at the back of the device

As long as the printer is connected to the device, and working, results of each analysis will be sent to the printer at the same time that they appear on screen. The printing format is as shown in the following figure

The printing shows the chloride results expressed in mmol/l, and an identifier (ID) corresponding to the number of samples recorded on the internal meter.
Once printing is done, the user can write the laboratory identification number, as well as the patient's name, age, the analyst's name, the date and any other observation that may be needed.

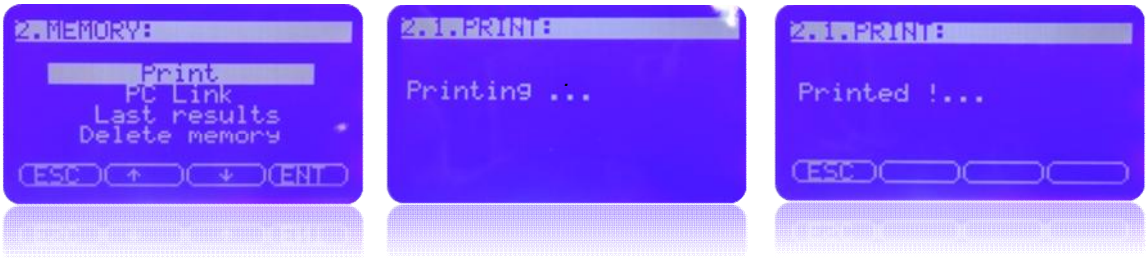
If the printer is not connected when the results appear, this value will be stored in the equipment memory.

5.4 Memory

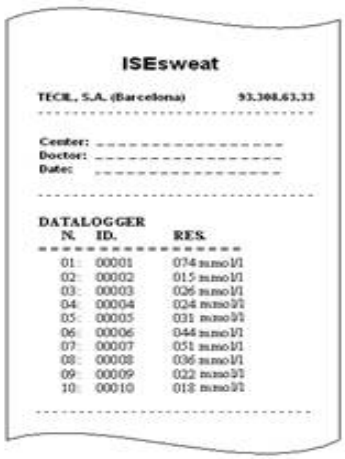
The ISEsweat® memory is capable of storing up to 50 results that can be printed out later or sent via the USB port to a computer connected to the base.

To open the MEMORY menu, press **<MEM>** at the buttons below the Start Screen.

- Choose **Print** and press <ENT> in order to print the stored results.



The printing format for the memory results is shown in figure. ISEsweat® will print the last 50 results, both QC results and Normal results.



- Choose **PC Link** using scroll arrows (↓↑) and press <ENT> in order to send the stored results via the USB port to a computer connected to the base.

- Choose **Delete memory** using scroll arrows (↓↑) and press <ENT> to delete all stored results. Once you have erased the memory, the identifier sequence number will be reset.

Press <ESC> to go back to the start screen.

- Choose **Last results** using scroll arrows (↓↑) and press <ENT>, the screnn shows the last 50 results

Press <ESC> to go back to the start screen

6. Maintenance

ISEsweat parts missing

Check the components

Remember:

- If you think any accessory is missing, please check carefully all the package contents. If you do not find the missing piece, please inform TECIL logistic department at once. TECIL can only take responsibility for missing items if notified within 15 days of receipt.
- If you receive any damaged items, please keep the packaging material for later inspection and inform the TECIL logistics department within 24 hours of receipt.

If you are returning goods to TECIL get in touch with TECIL Technical Support Service to get shipping instructions. Unless TECIL Technical Support Service says otherwise, you don't need to return sensor cards or any other accessories with the ISEsweat®.
Send ISEsweat® with the original package. If you don't have the original package, please use an appropriate box and adequate wrapping material to protect the ISEsweat® during shipment. If you have any doubt, please check with TECIL Technical Support Service before sending the device.

6.1 Technical service

The ISEsweat® does not need a routine technical service or calibration, but the battery needs to be changed every 24-36 months. Check the battery change process in the ISEsweat® user manual (*Battery change* chapter).

6.2 Periodic security check

It is recommended that you do the following every 24 months:
- Check the equipment for any mechanical or functional damage.
- Check the security and information labels to make sure they are still legible.

6.3 Cleaning

CAUTION: Do not spray, pour or spill any liquids on or near the ISEsweat® or its connectors and switches.

You can clean the ISEsweat® whenever you think it is appropriate, or in accordance with procedures laid down at your Hospital or Laboratory. Please bear in mind:
- ISEsweat® surfaces can be cleaned with a cloth slightly moistened with a commercial non-abrasive cleaning product or alcohol, but don't rub too hard.
- Make sure the data port connectors on the base unit are dust free with a dry cloth. Connectors on the remote unit will accumulate grease because they are in contact with the skin. Clean them with alcohol.

6.4 Waste management

International concern on environmental pollution, due to improper disposal of products and materials after use, has increased the legislation control on the methods and procedures of waste management for electric and electronical devices. Although in some countries the regulations have increased to the point that they are part of the official laws, in other regions this process is still ongoing. The result is a tighter control over product waste disposal and over recycling components once they are out of use. Check WEE Directive (waste of electrical and electronical equipment) 2002/96/EC for more information.

Regulations on instrument and accessory disposal may change according to where you are, so TECIL suggests the following guidelines to help determine the available options when taking the decision to replace or discard items:

• Contact TECIL or any authorized representative to gather information on the national and local regulations about product disposal and recycling in your area. In some cases, the provider may be legally obliged to take the product back and arrange for its correct disposal. Alternatively, the provider should be able to give specific instructions regarding correct product disposal.

• Contact your local government department responsable for waste collection and disposal. They can help you determine the current procedures and restrictions which apply, in order to ensure proper disposal. They can also inform you of suitable places to dispose of items .

• Contact TECIL Support Service:

Technical service
e-mail : sat@tecil.com
Phone: + 34 902995746
Fax: +34 933084871

TECIL staff will give you local contact details for product disposal, or instructions to ship the product back to TECIL.

CAUTION: The ISEsweat® uses single-use sensor cards. Once used, they must be discarded. ***Do not throw them in the waste bin****. Like any other material subject to possible biological contamination they should be discarded in a container designated for biological waste.*

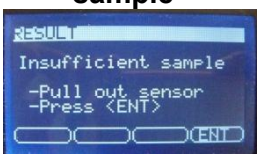
ANNEX A: Troubleshooting Table

Error/Action codes

There is a possibility that the remote module cannot link correctly with the receiver base due to background interferences. The signal symbol blinks when there is a linking error.**Make sure the base and the remote are never more than 10 meters apart.**

If the device suffers electronic failure or the remote light signals do not go on after charging the battery, please contact the technical support service of TECIL or your local distributor.

If there are any of the problems listed in Table 4, follow the instructions given.

Alarm	Problem	Cause	Solution
Remote link lost:please bring the remote closer to the base	No communication between remot and base	Interference	Repeat the linking
"Insufficient sample" 	There is no sample, the pattient does not sweat	Patient with sweating problems.	Sweating is related to skin state and other factors that cannot be completely controlled.
	No signal	Interferences or distance between the base and the remote is greater than 10 m.	Do not run the analysis in environments with electromagnetic emissions or put the remote closer to the base.
"  "	Low battery	Lack of charge	Charge battery
< 5 mmol/l or >150 mmol/l	Chloride value is over 150mM or under 5mM (out of scale;)	Sample problems due to concentration or evaporation.	Repeat the test

ANNEX B Product Specifications

Technical specifications

CAUTION: *DEVICE ADJUSTMENTS ARE NOT ALLOWED. This device does not require any kind of internal calibration.*

Output

Minimum sample volume	*10 microliters*
Precision	*±3 mmol/l*
Limit of Detection	*3 mmol/l*
Range	*5 to 150 mmol/l*
Repeatability (CV)	*CV < 7% (10 to 50 mM)* *CV < 4% (50 to 130 mM)*
Accuracy (SD)	*SD < 2 for 10 to 50 mM concentrations,* *SD < 4 for 51 a 130 mM concentrations*
Reference values	*< 40 mmol/l → Negative level.* *>40 ≤ X ≤ 60 mmol/l → Doubt level* *> 60 mmol/l → Positive level.*

NOTE: The sweat test requires human manipulation and the collection of very small samples of sweat. This can give rise to measurement errors, however, if results are lower than 10mM or greater than 150mM they will not be of any diagnostic significance.

Electrical specifications

Reading	*LCD screen with graphic capability*
Power ***Base*** ***Remote module***	*100V – 240VAC, 50/60Hz, 0.8 A* *12 V, 2.5 A, 30 W max* *24 VDC; 0.4mA; 10mW max.*
RF Communication	*833 Mhz Europe / 902.15 ~902.25 Mhz USA*
Firmware	*CIIPLUS*
Remote battery life	*10 samples without recharging battery*
Equipment classification 	*Protection class: Class I* *Applied part type: BF* *Work: Continuous*

Background conditions

Storage conditions	*Device: keep between 18ºC and 35ºC* *Cards: keep between 2ºC and 8ºC*
Environmental use conditions	*18ºC – 35ºC, Humidity 50 – 80%*

Physical features

Dimensions	
Base	Width: 150 mm, Long: 195 mm. High: 60 mm
Remote module	Width: 556 mm, Long: 75 mm, High: 22 mm
Receiver base weight	553 gr.
Remote module weight	65 r.

ANNEX C Possible interference

Recommendations to realize the sweat test to a patient:

1. To carry out the sweat test without any problem the patient should not be having administered intravenous fluids in a shorter period of 24h

2. The patient should not have been treated with any medicines that contain corticosteroids in a period less of 24h.

3. It must take into account the patient's fluid imbalance because dehydration problems could give a high result.

The analgesic ointment AMETOP could give positive results in the test, so is recommended not perform the sweat test in sites where Ametop has been applied within the previous 24 hours.

ANNEX D Recommendations for the results interpretation

Causes for repeating the sweat chloride determination (Sweat Test)

- All positive results of chloride in sweat must be repeated and confirmed with the mutation determination. CF diagnosis should not be based in only one positive test.
- All doubtful results about the chloride results obtained from the sweat test (with a chloride concentration between 40 and 60 mmol/L) should be repeated. If results are still in the intermediate level, some additional tests will be useful.
- Collection and determination of chloride in sweat must be repeated in CF confirmed patients who do not follow the expected clinical pattern. In order to monitor the patient's course, clinical, laboratory and thorax X-ray results must be coherent with CF diagnosis. It is particularly important to evaluate patients again whose initial diagnosis was made based on the delayed growth or on a positive familiar history; or whose clinical symptoms prior to the initial sweat test disappear, or there features are in keeping with asthma, with no suppurative lung illness, or where there is a normal growth pattern, without evidence of Hippocratic fingers, Pseudomonas colonization or any changes in thorax x-rays.
- The sweat collection can be repeated at any time after the first test, but it is advisable to do it when the patient is clinically stable and hydrated, with no accute intercurrent illness and is not taking mineralocorticoids.

Illnesses or disorders associated with a high electrolytes sweat concentration, not related to Cystic Fibrosis:

Anorexia nerviosa	Klinefelter's syndrome
Atopic dermatitis	E1 Prostaglandin long term infussion
Autonomic dysfunction	Mauriac's síndrome (malnutrition)
Ectodermal dysplasia	Mucopolysaccharidosis type I
Environmental deprivation	Nephrogenic diabetes insipidus
Familiar cholestasis (Byler's disease)	Nephrosis
Fucosidosis	Protein-calorie malnutrition
Problema de adaptación psicosocial	Pseudohypoaldosteronism
Hypogammaglobulinemia	Untreatable suprarrenal failure
Glucose-6-phosphate dehydrogenase deficiency	Untreatable hypothyroidism
Glycogen type 1 storage disordr	

- **Sweat test indicators: (*)**

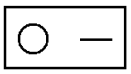
Pulmonary and upper respiratory tract	Gastrointestinal	Metabolic and others
Chronic cough Recurring or chronic pneumonia Wheezing Hyperinflation Tachypnea Retraction Atelectasis (particulary at the right upper lobe) Bronchiectasis Hemoptiysis Mucoid infection by pseudomonas Nasal polyps Pansinusitis Hippocratic fingers	Meconium ileus Meconium plug syndrome Prolonged neonatal jaundice Steatorrhea Rectal prolapse Mucoid impacted appendix Late intestinal obstructoin Recurring intussusception Cirrhosis Portal hypertension Recurring pancreatitis	Positive family history Growing delay Salted skin taste Salt crystals on the skin Salt-depletion syndrome Metabolic alkalosis Hypoprothrombinemia A Vitamin deficiency (Fontanelle bulging is a key sign) Azoospermia Missing vas deferens Scrotal calcification Hypoproteinemia Edema

(*) Taken from CLSI C34-A3 protocol

ANNEX E Symbol Definitions

General symbols


Electrostatic discharge


On/ Off


USB Dock


Selective refuse collection. Do not throw to regular trash.

RS232


Applied part: Type BF

Packaging symbols


Keep away from sunlight


Read carefully instructions of use.


Irritant


Expiration date
Ex: 2010 – 06
(Year– Month)

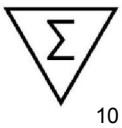
Batch Code


Manufacturer

Temperature limitation

Serial number


Do not reuse



Contents for 10 analysis

Catalogue number


Caution/Warning


Avoid water contact


Do not use if packaging is broken


Note

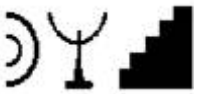
CE 0120 This product complies with European regulations, certified by a Notified body.

Symbols on the ISEsweat® screen (top right)

Battery:

			
Charged battery	Battery at medium/low level		Flat battery

Radio Coverage:

			
Correct coverage	Coverage at medium/low level		No coverage

ANNEX F Regulations

This product has been designed and manufactured in accordance with U.S. and European regulatory requirements as out-lined below. Modifications made to this product that are not expressly approved in writing by the manufacturer will void the user's authority to operate this product, previously issued factory approvals, and the user's rights under the warranty.

All quality control requirements and testing should be performed in conformance with local, state and/or federal regulations or requirements.

Regulation	Description
EN 60601	General Requirements for electrical medical equipments in relation to Electromagnetical compatibility and Electrical security.
ISO 7000	Graphic symbols for equipment use.
ISO 1258	Guidelines for electrical medical equipment development and instructions use.
ISO 1000	Units
EN 980	Symbols + EN 20780
ISO 8601	Date representation
ISO 639-1	Language representation codes
ISO 15225	Nomenclature
ENTR 15133	General terminology
EN 1041	Information supplied by the manufacturer of Medical Devices
EN 2860	Date format
EN 2078	Packages and graphic symbols on manipulation.
21CFR820	Quality system regulation
CLSI C34-A3	CLSI Guideline Sweat Testing

Federal Communications Commission (FCC) Statement

15.21
You are cautioned that changes or modifications not expressly approved by the part responsible for compliance could void the user's authority to operate the equipment.

15.105(b)
This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to part 15 of the FCC rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one or more of the following measures:

-Reorient or relocate the receiving antenna.
-Increase the separation between the equipment and receiver.
-Connect the equipment into an outlet on a circuit different from that to which the receiver is connected.
-Consult the dealer or an experienced radio/TV technician for help.

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

1) this device may not cause harmful interference and
2) this device must accept any interference received, including interference that may cause undesired operation of the device.

ANNEX G Manufacturer declaration

This product complies with the EN/IEC 60601-1-2:2008 regulation.

CAUTION: Use of accessories, sensor cards and cables that are not specific for ISEsweat® can lead to increased electromagnetic emissions and greater susceptiblility to interference. This can also cause inexact readings.
The Power supply included with the device is medical grade. If the user changes the power supply, you must make sure that the new one is also of medical grade.

Wires and cords comply with these regulations:

• RF emissions, EN 55011, Class B/Group 1
• EN 60601-1-2; 2008

Table 10: Wire and cords regulations

The ISEsweat® is designed for use in the electromagnetic environment described below. The user must ensure that it is used in such an environment.

- Electromagnetical emissions.

Emission test	Performance	Electromagnetical environment - guideline
RF Emissions CISPR 11 (IEC 55011 and IEC 55022)	Group 1	The ISEsweat® only uses radiofrequency power for communication within a room. Its RF emissions are very low and there is little probability of them causing interference with other nearby electronic equipment.
RF Emissions CISPR 11 (IEC 55011 and IEC 55022)	B Class	The ISEsweat® can be used in public places, including diagnostic establishments and places with direct access to the public and in buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	A Class	
Tension fluctuation /blinking emissions IEC 61000-3-3	Pass	

Table 11: Electromagnetical emissions

- Electromagnetical immunity.

WARNING: The back of the equipment base unit, where the connections are made, must not be touched when the equipment is ON.

WARNING: The remote card connector due its extreme sensitivity could occasionally stop the measurement or cause a reset while the remote unit is being positioned. If this happens, reset the base and remote units and start the analysis again.

NOTE: U Var % is the network CA tension before applying the test level (230 V / 50 Hz).

Susceptability test	IEC Test level 60601	Performance level	Electromagnetical environment - Guideline
Electrostatic discharge (ESD) IEC 61000-4-2	Direct contact of ±6 kV Airborne of ±8 kV	Pass	Floor must be made of wood, concrete or wooden tiles. If it is covered by any synthetic material, relative humidity must be 30% minimum.
Transitional Fast/Burst IEC 61000-4-4	Power lines of ±2 kV	Pass	Power network supply must be the usual one in a hospital or commercial environment.
Surge IEC 61000-4-5	Differential mode (symmetrical application) of ±2 kV Ordinary mode (asymmetrical application) of ±1 kV	Pass	Power network supply must be the usual one in a hospital or commercial environment.
Voltage drops, micro interruptions and inline voltage variations IEC 61000-4-11	>95 U Var. % for 10 milliseconds	Pass	Power network supply must be the usual one in a hospital or commercial environment. ISEsweat® must run the program again after interruption
	60 U Var. % for 100 milliseconds	Pass	
	70 U VAr. % for 500 milliseconds	Pass	
	>95 U Var. % for 5000 milliseconds	Pass	
	>95 U Var. % for 20 milliseconds	Pass	
Magnetic field associated with the supply frequency (50/60 Hz) IEC 61000-4-8	3 A/m	Pass	Magnetic fields associated with the supply frequency must have similar features to a usual hospital or commercial environment.
Conductive RF IEC 61000-4-6	3 V rms 150 kHZ to 80 MHz	3 V rms	Portable and radiofrequency communication equipment must not be used near the ISE Sweat and its cables. For the test, the distance between the RF source and the instrument being tested must not be less than 3m.
Radiated RF IEC 61000-4-3	3 V/m 80 MHz to 2,5 GHz	3 V/m	

Table 12: Electromagnetical susceptability

ANNEX H Warranty

TECIL,S.A. guarantees to repair or replace free of charge parts and pieces with working failures due to manufacturing causes for 24 months after delivery, as well as providing all labour needed to repair them.

All parts that have been replaced when repairing the unit will automatically become property of TECIL,S.A.

Damage caused by improper use or by non-compliance with the operating instructions will result in the invalidation of the warranty.

Interventions from persons other than TECIL,S.A. authorized specialists may lead to invalidity of warranty.

ANNEX I History Sweat Test

Although several techniques have been created for the collection and measurement of sweat electrolytes, the most reliable test is based on the pilocarpine iontophoresis technique described by Gibson & Cooke in 1959, which is still considered to be the gold standard for CF diagnosis specially in babies.

However, this is a complex combination of techniques that requires weigh sweat using an analytical scale, elution and undergo biochemical analysis of electrolytes. According to this method, it is necessary to collect at least 70 mg of sweat.

In order to make the test simpler, many labs have been using alternative methods. One of these methods includes the use of the device Macroduct® – a sweat collection system, through which sweat is collected into a plastic coil after stimulation by pilocarpine iontophoresis. Weighting is thus eliminated. The sweat can be taken from the coil and its ionic composition can be later analyzed using the usual biochemical techniques, or it may be immediately placed in the conductivity analyzer – Sweat- Chek – Wescor, which will quickly provide the equivalent values of sweat sodium chloride (NaCl) in mmol/L.

Because of methodological problems , confirmation or rejection of the diagnosis of CF should only be based on the results of quantitative pilocarpine iontophoresis sweat chloride described in the specific guidelines. Those guidelines consider not acceptable for CF diagnostic the direct reading in situ test using Orion ISE or older electrical conductivity measurements, or measurements or osmolality or sodium. Conductivity instruments designed specifically for use with microbore tubing collector was approved by CFF as screening method but only for use outside accredited Cystic Fibrosis Care Centers.

In 2010 Tecil introduced ISEsweat®, a new method for direct sweat Chloride measurement who eliminates all intrinsic sources of error associated to collection methods and with microISE specifically designed for microsamples. ISEsweat gives the concentration of sweat chloride independently of the sample quantity, that's why there is no need to measure the amount of sweat collected.

A multicentrical clinical trial made in 113 subjects and presented at the European Cystic Fibrosis Society concluded that ISEsweat is a valid and safety new device for sweat chloride concentration measurement. The results of this first clinical assay are very encouraging and warrant further research with larger samples of patients, to confirm that the ISEsweat can become a useful tool for the diagnosis of CF and even prove to be a reliable and more convenient alternative method compared to the reference sweat test as approved by current guidelines.

ANNEX J Reference

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