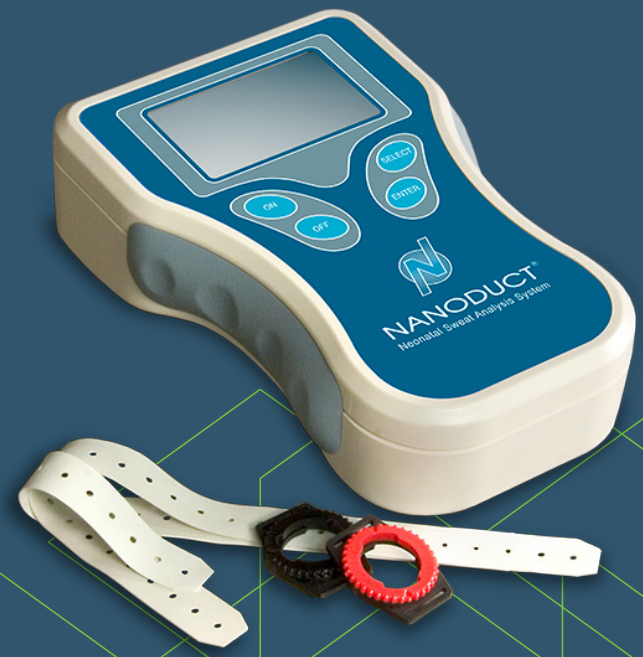
NANODUCT®

Neonatal Sweat Analysis System
MODEL 1030

USER'S MANUAL



ELITechGroup
EMPOWERING IVD

NANODUCT®

NEONATAL SWEAT ANALYSIS SYSTEM

MODEL 1030

USER'S MANUAL

57-0008-02B

(Last update 8/24/2021)

Manufactured in the United States of America by:

ELITechGroup Inc.
370 West 1700 South
Logan, Utah 84321-8212 USA

CE

2797

The Notified Body number above signifies that British Standards Institute BSI has certified the Production Quality Assurance System of ELITechGroup Inc., according to Annex V of the Medical Device Directive 93/42/EEC (MDD). The scope of that certificate, CE 59518, is:

The manufacture of sweat analysis systems for cystic fibrosis; and sweat inducers (to obtain samples for use in the subsequent laboratory diagnosis of cystic fibrosis).

This covers the Class IIa devices Macroduct Advanced Model 3710, Macroduct Model 3700, and Nanoduct Model 1030. Together with the Declaration of Conformity issued by the manufacturer according to Annex VII, this allows the CE marking of these devices. There are no accessories to which the CE certificate or the BSI Notified Body Number 2797 applies.

Table of Contents

Section 1: Introduction

1.1 Overview

This manual describes the complete procedure for the laboratory diagnosis of cystic fibrosis, particularly in the early neonatal period, through examination of sweat electrolyte concentration using measurement of electrical conductivity. The first section gives a brief description of the system, its components, and how to set up the system. The second section describes the procedure for stimulating and analyzing sweat. The third section gives needed information on the analysis of sweat. In addition, instructions for troubleshooting and maintenance of the system are provided in the fourth section. A detailed description of the development of the Nanoduct System is presented later in the manual, along with additional useful information.

Intended Use

The Nanoduct Neonatal Sweat Analysis System is intended for laboratory use by qualified personnel to provide laboratory diagnosis of cystic fibrosis.

Application

Anyone operating a Nanoduct Neonatal Sweat Analysis System must be thoroughly familiar with the procedures and cautionary information detailed in this manual before attempting a sweat test. Abbreviated instructions printed elsewhere are provided for reference only. Do not use them as a substitute for the complete information contained in this manual.

The Pilogel Discs for Nanoduct are designed to be used with this instrument and should be used wherever they are legally available. In areas where they are not available, users should check with ELITechGroup for the availability of fiber pilocarpine reservoirs of the same size as Pilogel discs, for use with pilocarpine solutions supplied by the user. Unless otherwise indicated, any mention of Pilogel discs in this manual applies equally to the fiber pilocarpine discs.

Safety Regulations (Nanoduct Model 1030)

Classification

This equipment is classified as Type BF Medical Equipment, Internally Powered.

This device has been built and tested in accordance with safety regulations under EN 60601-1. In order to maintain this condition and ensure safe operation, the operator must observe all the instructions and warnings contained in this manual. For current information about applicable standards, please refer to the CE Declaration of Conformity included with the documents shipped with this device.

NOTE: This equipment complies with the following emission and immunity requirements: IEC/EN 60601-1-2 and FCC CFR 47 Part 15 Class B/ICES-003 Class B (using IEC CISPR 22 / EN55022).

Specification of Safe Use

Using this equipment in a manner not specified by ELITechGroup may impair safety protection and may lead to injury. Do not use where flammable anesthetic is present or in any oxygen-enriched environment. Do not connect the serial port or USB port to external sources while the Nanoduct is connected to a patient.

⚠ WARNING!

Do not use this equipment if it is not functioning properly.

Statement of Environmental Limits

This equipment is designed to be safely operated at 15 to 30 °C, with maximum relative humidity less than 85%, and atmospheric pressure ≥ 79.5 kPa.

Understanding Warnings

This manual uses three warning levels to alert the operator to important information as shown in the following examples.

⚠ WARNING!

A Warning alerts to the possibility of personal injury, death, or other serious adverse reactions stemming from the use or misuse of this device or its components.

⚠ CAUTION:

A Caution alerts to possible problems with the device associated with its use or misuse. Such problems include device malfunction, failure, damage, damage to the sample, or damage to other property. Where applicable, a Caution may include precautions to be taken to avoid the hazard.

NOTE: *A Note reinforces or supplies additional information about a topic.*

Specific Warnings

Pay particular attention to the following safety precautions. If these safety precautions are ignored, personal injury or damage to the device may occur. Each individual precaution is important.

⚠ WARNING!

Due to the possibility of an explosion, never attempt iontophoresis on a patient receiving oxygen-enriched respiratory therapy in an enclosed space, such as an oxygen tent (nasal cannula is acceptable). With medical approval, remove the patient from that environment during iontophoresis.

⚠ WARNING!

Do not stimulate or collect sweat from the following sites:

- **Head, including forehead (possible burns).**
- **Trunk (current crossing heart).**
- **Any area of inflammation (e.g. eczema or rash); serous or bloody discharge (contamination).**

⚠ WARNING!

Do not use over areas with metal plates/pins.

⚠ WARNING!

Never attempt to reuse single use components/accessories.

⚠ WARNING!

Do not use electrodes or Pilogel discs that have been altered or appear damaged.

⚠ WARNING!

Consult a physician before performing a test on patients with clinically diagnosed cancer.

Section 1: Introduction

⚠ WARNING!

Consult a physician before performing a test on patients who have had previous adverse reactions to electrotherapy.

⚠ WARNING!

The lithium coin cell backup battery used to power the clock is not accessible to the user and should only be replaced by qualified service personnel.

⚠ CAUTION:

A Nanoduct sweat analysis test should be carried out at a time when the patient is clinically stable, well-hydrated, free of acute illness, and not receiving mineralocorticoids.

⚠ CAUTION:

Consult a physician before performing multiple tests on a patient within a 24-hour period.

⚠ CAUTION:

Pilogel discs should be refrigerated at 2 °C to 10 °C. DO NOT FREEZE. Never use discs that have been frozen or that are cracked.

⚠ CAUTION:

This equipment has been designed and tested to EN 55011/CISPR 11 Group 1 Class B and FCC CFR 47 Part 15 Class B. In a domestic environment it may cause radio interference, in which case, the operator may need to take measures to mitigate the interference.

⚠ CAUTION:

Only spare parts and accessories supplied or specified by ELITechGroup should be used with this device. Using non-approved parts may affect the performance and safety features of the device. If the device is used in a manner not specified by ELITechGroup, the protection provided by the device may be impaired. If in doubt, contact an ELITechGroup representative.

⚠ CAUTION:

The USB connection on the device is intended to be used by authorized personnel. For security purposes, it is recommended to execute a virus/malware scan on any computers prior to making connection. Do not connect to a line powered computer when the instrument is attached to a patient.

Contraindications

- Patients with an implanted device, such as a defibrillator, neurostimulator, pacemaker, or ECG monitor.
- Patients with a history of epilepsy or seizures.
- Patients who are pregnant.
- Patients that have a known sensitivity or allergy to any ingredient.
- Over damaged, denuded skin or other recent scar tissue.
- Patients with cardiac conditions or with suspected heart problems.

EXPLANATION OF SYMBOLS

SYMBOL	EXPLANATION
	Classification of degree of protection against electric shock (BF)
	Authorized Representative in the European Community
	Batch Code
	Biological Hazards (Biological Risks)
	Catalog Number (Model Number)
	Serial Number
	Consult Instructions For Use
	General Warning, Caution, Risk of Danger
	Caution, Consult Accompanying Documents (Attention, see instructions for use)
	CE Mark, product meets the essential requirements designated in Annex V of the Medical Device Directive 93/42/EC (MDD).
	Do Not Reuse
	Do not use if package is damaged
	Manufacturer
	General Symbol for Recovery, Recyclable
	Waste of Electrical and Electronic Equipment (WEEE) Symbol. Under Directive 2012/19/EU, this equipment cannot be disposed of in a normal landfill.
	Environment Friendly Use Period

SYMBOL	EXPLANATION
	Use By
	Temperature Limitation – indicates high and low limits
	Warning, Biological Hazard
	Harmful / Irritant
	Environment Hazard
	Toxic

1.2 Customer Service

ELITechGroup is dedicated to assisting in every aspect of sweat testing theory and practice. ELITechGroup is the acknowledged world leader in the development of innovative systems for cystic fibrosis diagnosis by sweat testing.

This manual contains basic maintenance, troubleshooting, and service information. ELITechGroup is prepared to help you resolve any difficulty with the operation or performance of your Nanoduct Neonatal Sweat Analysis System. If a problem cannot be solved using the procedures described in this manual, please contact ELITechGroup's Service Department to help resolve any questions about the operation or performance of your Nanoduct system.

Customers should contact ELITechGroup by telephone, fax, or e-mail. Outside the U.S., many of our authorized dealers offer customer service and support.

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1.3 System Description

Nanoduct is a complete, integrated system for inducing and analyzing sweat for cystic fibrosis (CF) diagnosis—all while attached to the patient. This reduces the possibility of intrinsic error and enables pristine samples to be obtained from neonates and analyzed in situ.

Nanoduct incorporates the classic method of inducing sweat by pilocarpine iontophoresis. The pilocarpine is introduced into the skin of the patient using controlled DC electrical current from the Nanoduct induction/analysis module. This is followed by continuous-flow analysis using the unique sensor.

Results appear quickly on the display. During the process the operator installs and then removes the various components that fit in the holders described later.

A description of the various components of the Nanoduct system follows.

Holders

Two plastic holders are attached to the patient with comfortable but secure non-latex elastic straps. These holders accept the electrodes and later the sensor, holding them securely against the patient's skin. Holders are color-coded, one red to accept the (positive) anode and subsequently the red sensor; the other black to accept the (negative) cathode. Strap retainers are pushed through the holes in the strap to maintain the correct tension.

Iontophoretic Electrodes

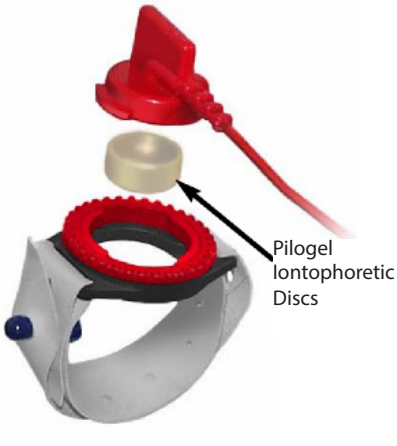
Two color-coded electrodes, one red for the anode (positive) and the other black for the cathode (negative), are otherwise identical, both having a small stainless-steel disc as the electrode plate.

These electrodes are part of the electrode cable assembly (see below) that also includes the sensor cell connector to attach the separate sensor cell. Both electrodes have projecting flanges, for securing the electrodes in the holder rings. Electrodes provide current from the module through Pilogel discs during iontophoresis. The black cathode electrode also serves as an electrical reference to detect sweat flow to the sensor cell during the analysis phase.

Electrode Cable Assembly

This dual-purpose 1.8 m long cable assembly includes the red anode and black cathode iontophoretic electrodes and the red sensor cell connector. The cable connects to the Induction/Analysis Module at the electrode connection socket on the top of the instrument.

Inspect lead wires periodically for breaks or cracks in the insulation. Replace the electrode set if any cracks or breaks are apparent in the electrode wires, insulation or plastic housing.



Pilogel Iontophoretic Discs

Pilogel discs are small (surface area 2.5 cm^2) iontophoretic discs that are inserted into the electrode assemblies before iontophoresis. Designed especially for neonates, these discs have a pilocarpine concentration of 1.5% for optimum stimulation of the sweat gland, which also reduces the iontophoresis time to approximately 2.5 minutes.

Pilogel discs contain sufficient glycerol to provide substantial protection of gels against damage from accidental freezing. Cracked discs due to freezing can contribute to burns. Refer to the appendix for more information.

Pilogel discs contain trisodium citrate, an excellent buffer in the acid range of pH. This reduces anodic acidification of the gel during iontophoresis by 90%. At the cathode, the increased pilocarpine, a good buffer at moderately alkaline pH, also reduces iontophoretic accumulation of alkali. This buffering prevents skin burns due to pH change in the gel. Each of these features contributes to the safety of the procedure. Refer to Appendix H for important information about pilocarpine iontophoresis.

In areas where Pilogel discs are not available, users should check with ELITechGroup for the availability of fiber pilocarpine reservoirs of the same size as Pilogel discs, for use with pilocarpine solutions supplied by the user.

⚠ **WARNING!**

Pilogel discs should be refrigerated at 2 to 10 °C. DO NOT FREEZE. Never use discs that have been frozen or that are cracked. This does NOT apply to fiber pilocarpine reservoirs.

⚠ **WARNING!**

Pilogel is considered toxic, as is pilocarpine nitrate in other forms. Do not ingest. See Appendix D, E, or the SDS.

Sensor Cell

Color-coded red, the sensor has two external flanges (as with the electrodes) for latching to the red holder. The base of the sensor is a shallow concavity leading at its center to an entry port, and from there to a fine internal channel passing by two analyzer micro-electrodes, forming a micro conductivity cell.

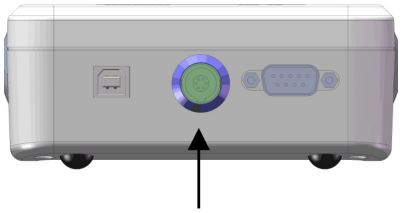
The sensors pass through stringent quality controls before shipment to the customer. To be accepted, sensors must be highly consistent throughout each batch.

Induction/Analysis Module

The battery-operated electronic induction/analysis module controls the Nanoduct system. The module performs six separate functions:

1. Provides a timed and controlled current for iontophoretic sweat stimulation.
2. Measures electrical conductivity of the excreted sweat during the analysis phase.
3. Automatically averages the conductivity reading over a defined 5-minute period.
4. Automatically computes the initial sweat rate.
5. Displays the above information on the LCD readout and reports sweat test and calibration results to the serial port.
6. Provides a time and date display for calibration and test results.

1.4 Controls and Connections



Electrode Socket

Electrode Socket

The electrode socket on the top of the enclosure connects the electrode/sensor cable assembly to provide electrical current for sweat stimulation and to receive sensor signals to the induction/analysis module during the analysis phase.

Keypad Keys

ON

The ON key turns the instrument on when pressed. The ON key is also used in conjunction with the SELECT key to access the Setup Menu.

OFF

The OFF key powers the instrument off. Pressing the OFF key cancels all operations and turns power to the module off.

NOTE: *To preserve battery power, leave power off except while performing a test. During idle periods the instrument shuts down automatically after 10 minutes and must be turned on again to complete testing or retrieve a result.*

SELECT

The SELECT key scrolls through menu selections and increments parameter settings. Use the SELECT key in conjunction with the ON key when accessing the SETUP MENU.

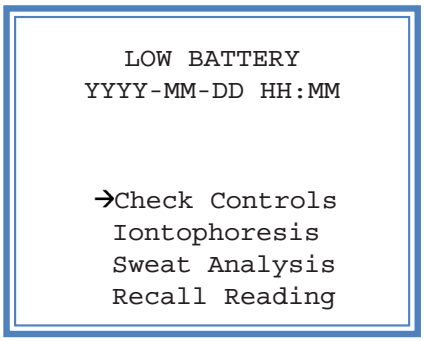
ENTER

The ENTER key selects menu selections, advances through menu screens, and starts the iontophoresis and analysis phases of the sweat test. A warning tone sounds if a fault condition occurs–such as an open electrode or circuit fault. The fault condition is displayed and reset by pressing ENTER.

Display

The LCD alphanumeric read-out displays all functions and results as they occur, including iontophoresis status and analysis results, plus the time and date of the last procedure. The user responds to prompts on the display to activate various functions. The instrument emits a short beep tone at the start and end of each operation.

The instrument displays conductivity measurements in mmol/L (equivalent NaCl) during analysis. If desired, display readings can be suppressed so readings are not visible, but can be recalled later.

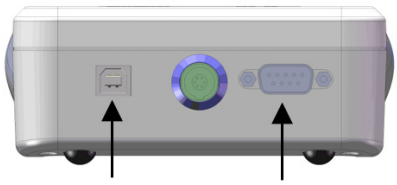


Low Battery Indicator

If the battery voltage drops below a preset level at power-up, a “Low Battery” message appears on the display. When this indicator first appears, it is possible to complete a small number of tests before replacing the batteries. If battery power is too low to complete a test, the module automatically shuts off and iontophoresis cannot be started. The batteries must be replaced to continue. Refer to Section 2.1 to replace the batteries.

NOTE: *Use only four standard alkaline AA cells to power the Nanoduct. Using other types of AA cells may cause low battery indicator inaccuracy.*

Serial Data Ports



RS-232 Port

The Nanoduct RS-232 port uses a DB9 connector located on the top of the instrument. This port is for asynchronous serial communication with a printer or computer. The RS-232 port can be used to print out results of sweat tests (with a time and date stamp). Data output is in ASCII characters. Refer to Appendix C for additional information.

WARNING!

Electrical shock hazard. Never connect to a line powered printer or computer when the instrument is attached to a patient.

USB Port

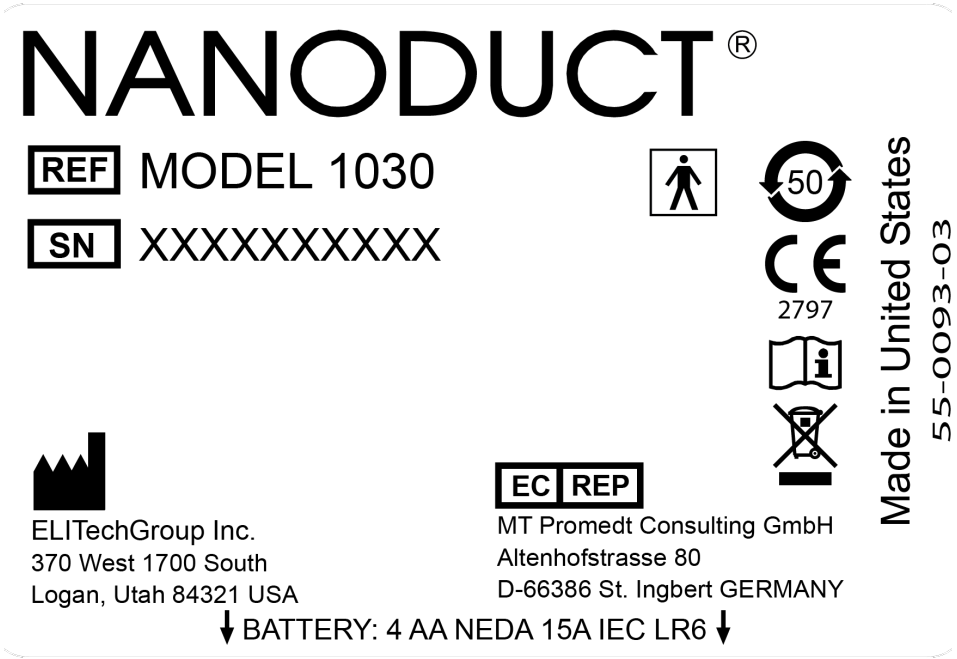
The Nanoduct Universal Serial Bus (USB) port uses a standard USB type-B receptacle. The port is configured as a USB device (not a host). Data output is in ASCII characters. The USB port allows the updating of firmware in the field and allows a reading to be transferred to the Nanoduct Lab Report application. The port cannot be used with a USB printer. Refer to Appendix C for additional information.

WARNING!

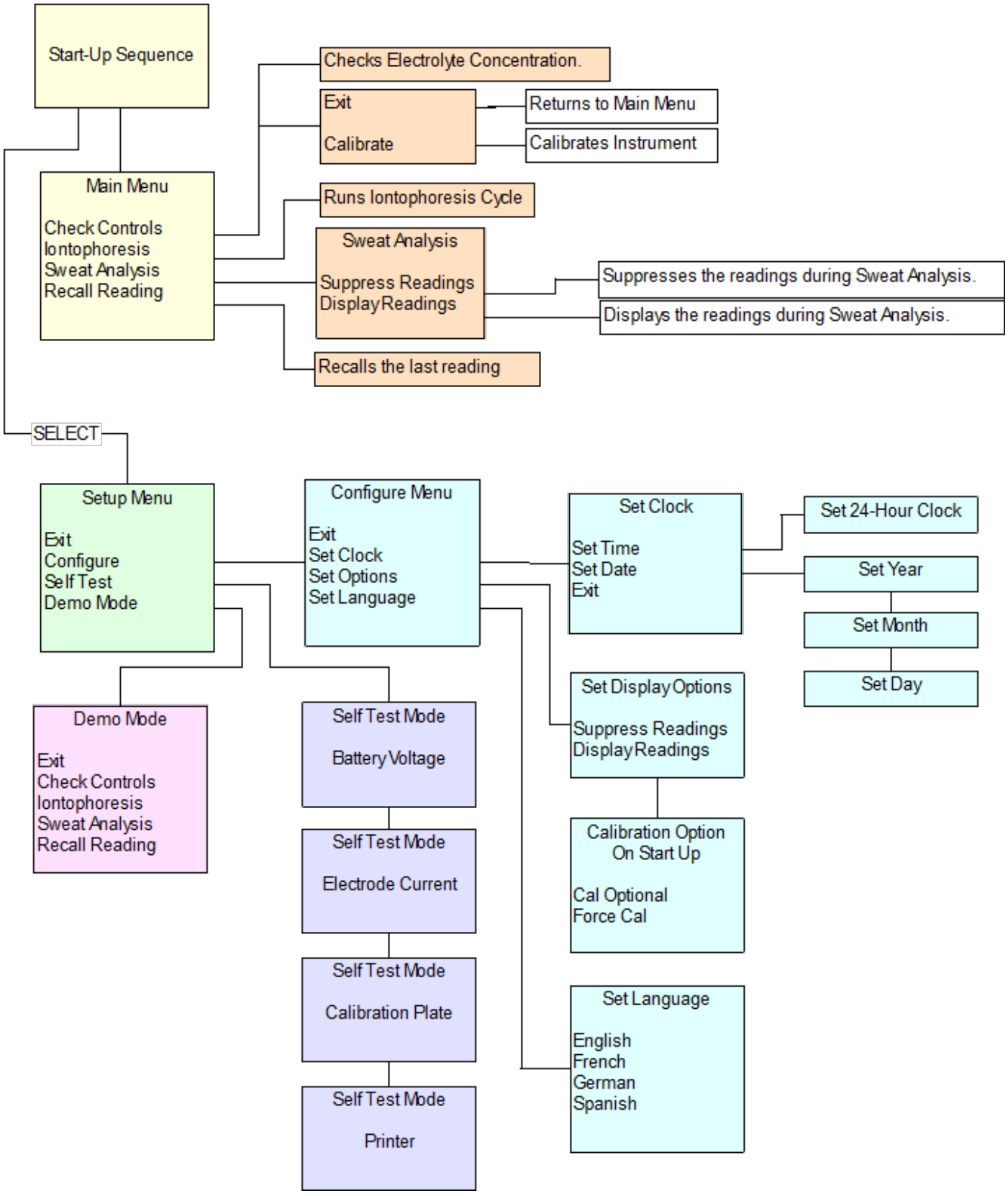
Electrical shock hazard. Never connect to a line powered printer or computer while the instrument is attached to a patient.

Model/Serial Number Identification Label

The following label is located on the back of the instrument.



User Interface Block Diagram



Section 2: Initial System Setup

2.1 Installing or Replacing the Batteries

1. The battery compartment is on the back of the instrument. Turn the instrument so that the back is facing up. Using a Phillips screwdriver, remove the two screws that are holding the battery door in place. Remove the battery door.
2. Insert four fresh alkaline AA batteries (ANSI/NEDA 15A, IEC LR6) making sure that each battery is inserted with the correct orientation as shown. There are markings within the battery holder that show proper orientation of the batteries.
3. Reposition the battery door and insert the screws. Using a Phillips screwdriver, tighten the two screws that hold the door in place.
4. Dispose of the spent batteries according to battery manufacturer's instructions and local regulations.

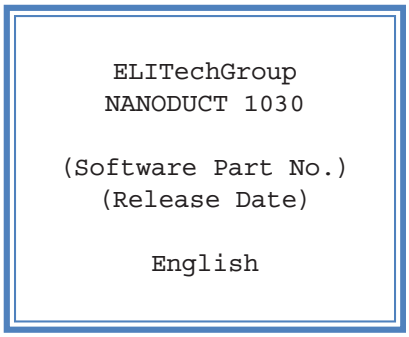
NOTE: *Batteries are installed in the instrument at the time of shipment. Unless the Low Battery message displays, the batteries do not need to be replaced. If you are not using the instrument for an extended period of time, remove the batteries. Batteries can leak and damage terminals if left unused for extended periods.*

⚠WARNING!

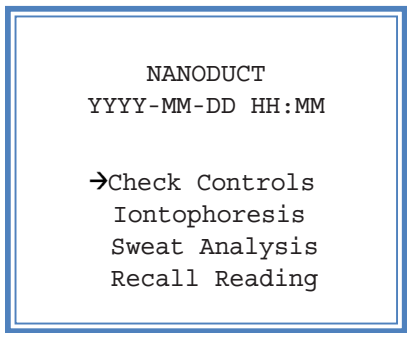
Do not install batteries backwards, charge, put in fire or mix with other battery types. Batteries may explode or leak causing injury. Replace all batteries at the same time.

2.2 Menu Basics

Startup Menu



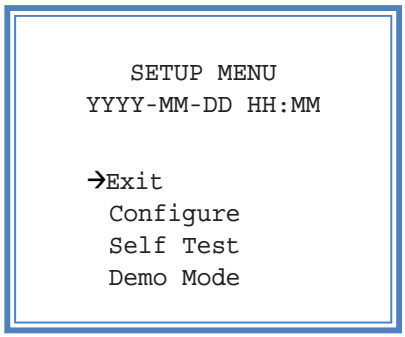
When the Nanoduct is first powered on (by pressing the ON key), a sign-on screen appears for a few seconds, similar to the one at the left. The sign-on screen includes ELITechGroup's name, the Nanoduct product name, the software part number, the release date, and the display language. The Nanoduct then performs a system check with a "Checking Operation" message displaying briefly.



After the sign-on screen, the display advances to the main menu. The menu selections are covered later in the manual.

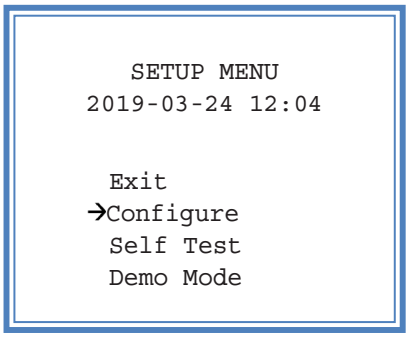
Accessing the Setup Menu

The SETUP MENU allows the instrument to be customized for individualized use, to run an instrument self test, or to operate the instrument in a demonstration mode.



1. Make sure the Nanoduct is OFF. While pressing and holding down the SELECT key, press the ON key. Keep the SELECT key pressed until the SETUP MENU displays on the screen. (When the Nanoduct first turns on, a sign-on screen appears for a few seconds. The Nanoduct then performs a system check and a "Checking Operation" message displays, followed by the SETUP MENU.)
   Scroll down through the menu by pressing SELECT. When the pointer reaches the last item in the menu, pressing SELECT returns the pointer to the top of the menu.
   Make selections by pressing ENTER when the pointer is next to the desired menu item.
   Select "Exit" and press ENTER to return to the main operation menu.

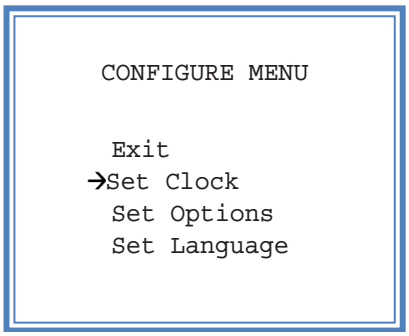
Using the Configure Menu



Use the Configure Menu to set the clock, display language, for suppressing or displaying test results, and forcing a Calibration Check when the instrument is turned on.

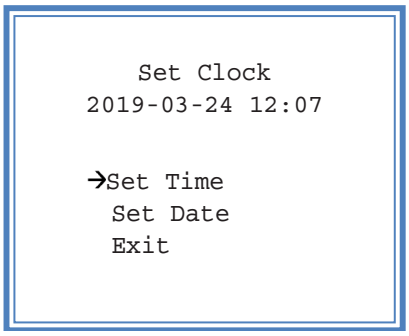
1. Select “Configure” from the SETUP MENU and press ENTER.

Setting the Time and Date



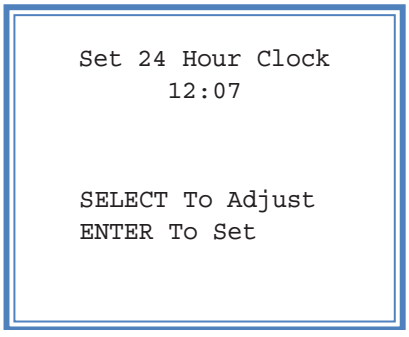
Setting Time

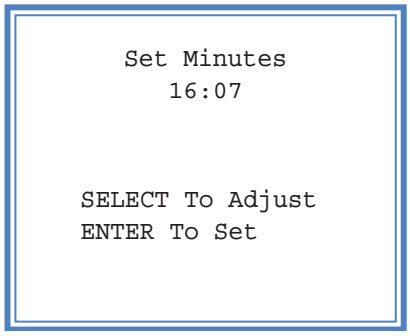
1. To set or adjust the clock, from the CONFIGURE MENU select “Set Clock” and press ENTER.



2. Select “Set Time” and press ENTER. The display shows the “Set 24 Hour Clock” screen with the hour digits flashing. Pressing the SELECT key increments the hours one hour at a time. Pressing and keeping the SELECT key held down increments through the hours at a slightly faster rate. After reaching 23, the hour returns to 00.

   With the desired hour displayed, press ENTER to set the hours. The screen then displays “Set Minutes” with the minutes digits flashing.

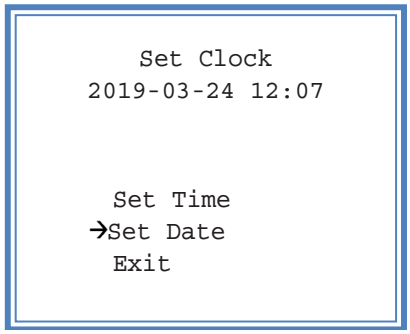




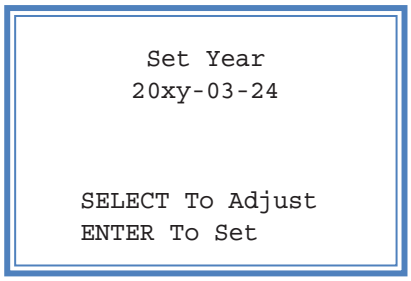
3. With the minutes digits flashing, press SELECT to adjust the minutes. Pressing the SELECT key increments the minutes one minute at a time. After reaching 59, the minute returns to 00.

   With the desired minutes displayed, press ENTER to set the minutes. Control returns to the Set Clock menu.

Setting Year, Month and Day

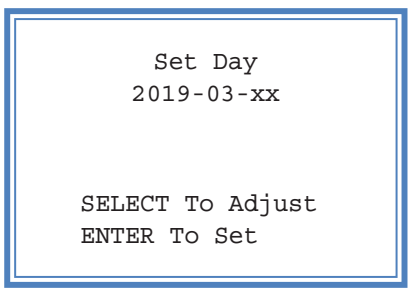


1. Select “Set Date” and press ENTER. The display shows the “Set Year” screen with the last two digits of the year flashing.



2. When setting the year, there are two digits to set. With the “x” digit flashing, press SELECT to adjust the ”x” digit (decade).
   Press ENTER to set. Automatically advances to the “y” digit.
   With the “y” digit flashing, press SELECT to adjust the “y” digit.
   Press ENTER to set the year.
   The screen advances to the Set Month screen with the months digits flashing.

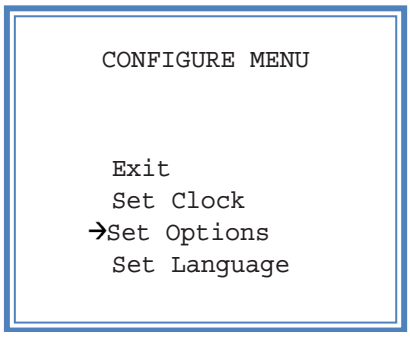
3. While the month digits are flashing, press SELECT to adjust the month. Press ENTER to set the month. The screen advances to the “Set Day” screen with the day digits flashing.



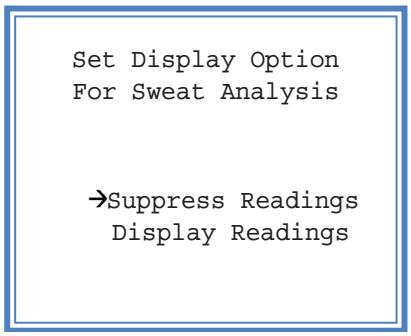
4. While the day digits are flashing, press SELECT to adjust the day. Press ENTER to set the day. Control returns to the Set Clock menu.

5. From the Set Clock menu, select “Exit” and press ENTER to return to the CONFIGURE MENU.

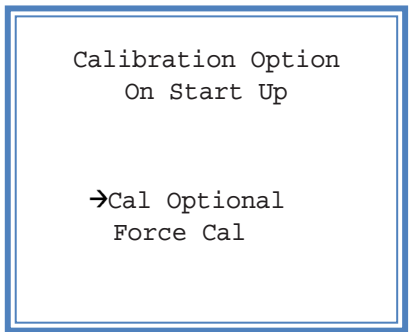
Setting Options



1. From the CONFIGURE MENU, select “Set Options” and press ENTER.



2. To display or suppress the results of the sweat test, select either “Suppress Readings” or “Display Readings” and press ENTER.



3. The Calibration Option menu allows the instrument to automatically go to the Check Controls menu or the main menu on power-up. Select “Force Cal” to automatically go to the Check Controls on power-up. Select “Cal Optional” to calibrate only under user control and to automatically go to the main menu on power-up. Press ENTER when the desired selection has been made. The default setting is “Cal Optional.”

Setting Language

```
CONFIGURE MENU


  Exit
  Set Clock
  Set Options
→Set Language
```

1. The display language is set from the CONFIGURE MENU. Select “Set Language” and press ENTER. Language selections include English, French, German, and Spanish.

```
Set Language


→English
  French
  German
  Spanish
```

2. Select the desired language and press ENTER. Control returns to the CONFIGURE MENU with the selected language displayed. Select “Exit” and press ENTER to return to the SETUP MENU.

Self Test Mode

The Self Test allows testing of current output, conductivity, and battery voltage.

```
SETUP MENU
2019-01-31 12:03


  Exit
  Configure
→Self Test
  Demo Mode
```

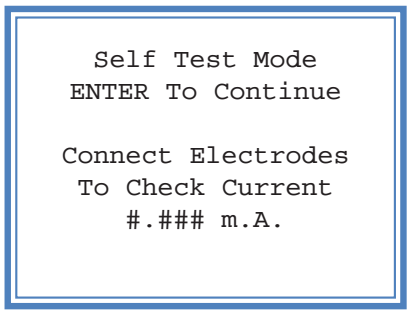
1. From the SETUP MENU, select “Self Test” and press ENTER.

⚠**WARNING!**

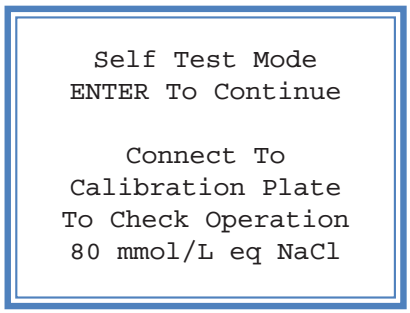
Do not run the Self Test while the module is connected to a patient.

```
Self Test Mode
ENTER To Continue


Battery Volt: x.xx
```

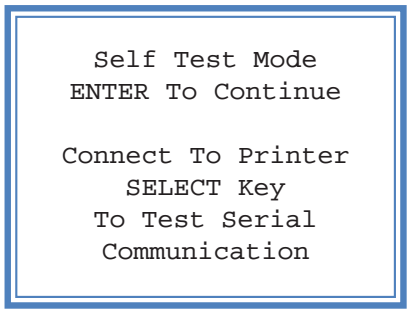
2. Self Test Mode begins by displaying the battery voltage. A good battery voltage reading should be greater than approximately 5.2 volts. Fresh batteries should read approximately 6.4 volts.



3. Connect the electrodes by placing a Pilogel disc in each holder and then holding the two discs together between two fingers to check the current. The current should read approximately 0.5 mA. The instrument continues to read and display the electrode current reading. Current that continually decreases is an indication of low or weak batteries. Press ENTER to continue with the Self Test.



4. Connect to the calibration plate to check for proper operation. The display should read the value of the calibration point that the cable is connected to. For example, if connected to the 80 mmol/L calibration point, then the reading on the display should be 80 mmol/L.



5. Connect to the printer to test the serial communication. Press SELECT to send data out the serial port. The date and time are sent out the port along with the message “PRINT TEST” each time SELECT is pressed.

```
2019-04-21 15:24
PRINT TEST
```

Press ENTER to return to the SETUP MENU.

Demo Mode

The Demo Mode is used to simulate typical displays that are seen during normal operation. This can be useful for demonstrating instrument function or to familiarize the user with the instrument. No actual iontophoresis or sweat analysis occurs in this mode and only simulated results display.

In Demo Mode, the instrument functions much like it would when running on an actual patient. The display screens and menus appear as they would during an actual test, with the exception that Demo Mode appears near the top of the display. While running in this mode, the ENTER key acts as a shortcut key and advances the instrument through the phases of the operation, allowing the next display to be seen without waiting for the full instrument countdown.

The Check Controls option in Demo Mode works as it does under normal operation. It is possible to check the readings using the calibration plate and to also calibrate the instrument. When exiting Check Controls, the instrument returns to the Demo Mode main menu.

```
SETUP MENU
2019-01-31 12:03

  Exit
  Configure
  Self Test
→Demo Mode
```

```
DEMO MODE
2019-01-31 12:03
  Exit
→Check Controls
  Iontophoresis
  Sweat Analysis
  Recall Reading
```

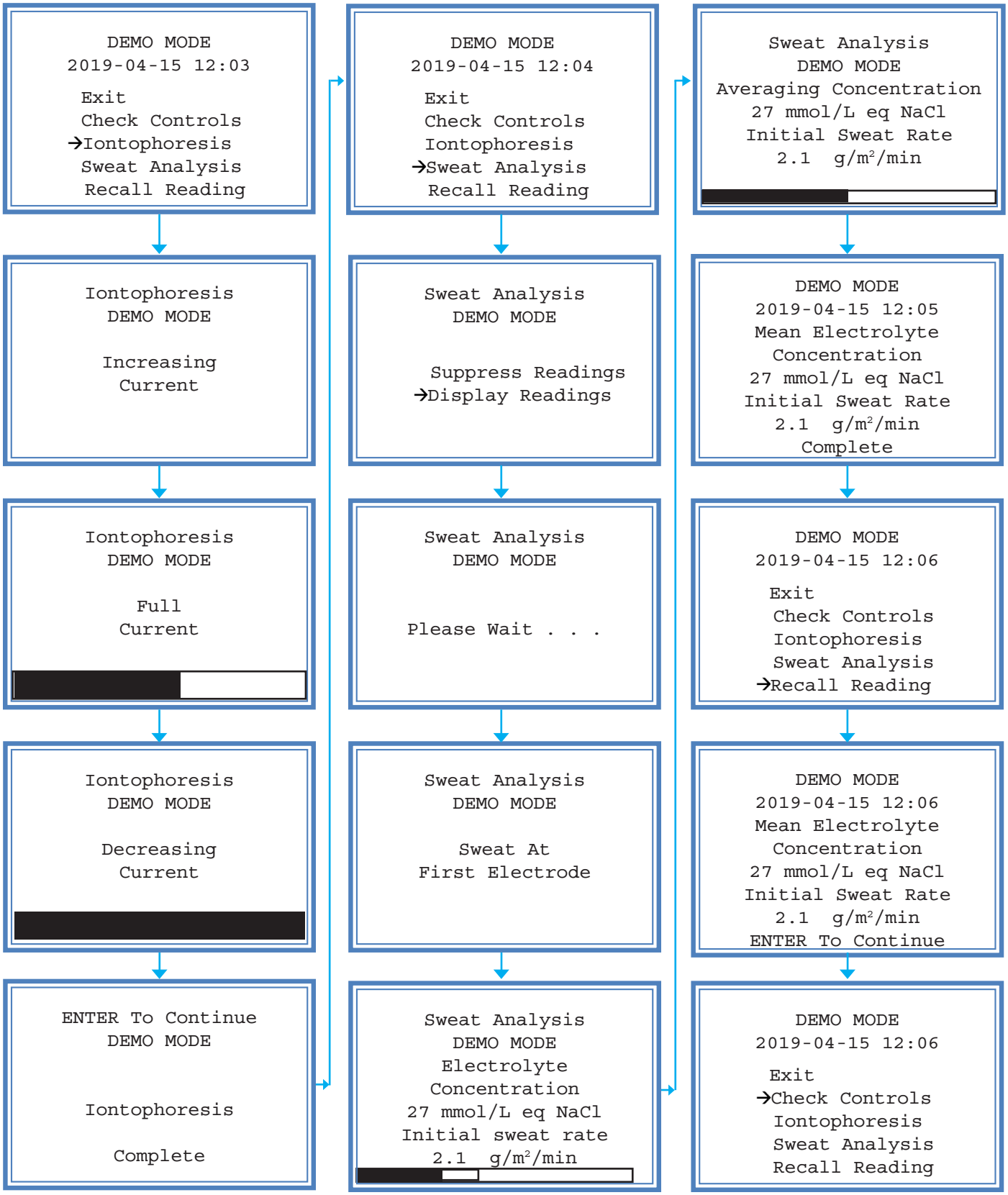
```
Check Controls

  Electrolyte
 Concentration
80 mmol/L eq NaCl

  Exit
→Calibrate
```

```
Calibrating
Please Wait. . .
```

```
Calibration
 Complete
2019-03-24 9:34
```

Section 2 : Initial System Setup

The following is a sequence of displays when working in Demo Mode. From the Demo Mode main menu, select Iontophoresis and press ENTER. To advance to the next screen, press ENTER or wait for the test to complete.



Section 3: Sweat Induction and Analysis

3.1 Performing the Sweat Test

⚠ WARNING!

Due to the remote possibility of ignition, never attempt iontophoresis on a patient receiving oxygen-enriched respiratory therapy in an enclosed space. With medical approval, remove the patient from that environment during iontophoresis.

1 Assemble Equipment and Supplies

Make certain everything is on hand for the complete procedure:

- Nanoduct 1030
- Two holders
- Two holder straps with strap retainer posts
- Two Pilogel discs
- One sensor
- Electrode cable for connecting the iontophoretic electrodes or the sensor to the induction/analysis module

A supply of deionized water, alcohol, cotton balls or gauze pads, cotton swabs, powder-free gloves, and a roll of 1-inch wide plastic surgical tape (3M Transpore™ recommended) is needed.

Make sure that the battery for the instrument is not dead, and that the gel discs are rubbery, translucent and not cracked or otherwise damaged.

NOTE: *The operator should wear powder-free gloves throughout the iontophoresis and sweat analysis processes (graphics on the following pages do not show the operator with gloves on; however, gloves should be worn as stated.)*

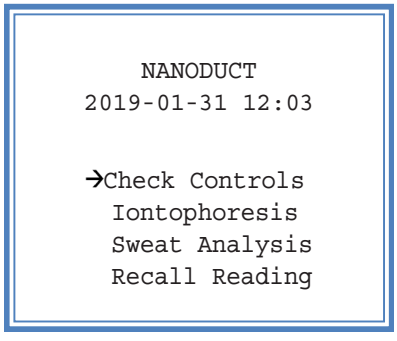
2 Inspect Electrodes, Leads, and Cables

Clean the electrodes if necessary. Check the lead wires and insulation for damage.

⚠ WARNING!

Replace the electrode cable assembly if wires, insulation or plastic housing are cracked or frayed.

Connect the electrode cable assembly to the electrode socket.



3 Calibrate and Check Control Values

Turn the power on. Check for a low battery condition on the display. The arrow on the display should indicate Check Controls on the menu. We recommend checking control values (using the calibration plate mounted in the carrying case) before each session. Refer to Section 4.3 to perform a calibration.

NOTE: *In the SETUP Menu, selecting the Force Cal. option brings up the Check Controls operation whenever the instrument is turned on.*

4 Clean Selected Skin Areas

Select the anodic (positive) skin site for the greatest density of sweat glands. The site must be well-removed from the wrist where movement of tendons or ligaments could possibly affect the stability of the attached units. In neonates, the optimum site is the flexor aspect of the forearm, approximately halfway between wrist and elbow. The cathodic (negative) electrode site is not as critical, place it an inch or two from the anode in the direction of the elbow.

⚠ **WARNING!**

Never place electrodes across the chest or on opposite limbs. Even though the DC iontophoretic current is extremely low, there is a very remote risk of interference with cardiac rhythms.

Inspect the selected sites. The skin should be free of breaks, fissures, and any structural abnormality. The area should be wrinkle free and as hairless as possible. There should be no inflammation or signs of eczema. Apart from exacerbating the complaint, there is always the possibility of contamination of the sweat by serous exudates.

To minimize the electrical impedance (resistance) of the skin, remove as much dead epithelial material, dirt and fatty substances as possible by swabbing the area vigorously with surgical alcohol, followed by plenty of distilled or deionized water. Then totally remove the excess water.

5 Attach the Holders

NOTE: *ELITechGroup provides perforated non-latex elastic straps of different lengths to fit infants, older children and adults.*

⚠ **WARNING!**

Watch for any signs of interference with blood circulation in the limb, such as cyanosis, swelling, or unusual pallor, and discontinue the test on that limb if any of those conditions should occur.

To save time, pre-arrange strap holder assemblies to fit varying sizes of patients. Select the red holder and attach a rubber strap of appropriate size as follows:

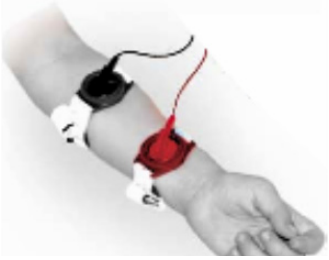
A. Attach the strap to one side of the holder by inserting it, **from below**, through the holder slit, and down to form a small loop. Align two perforations in this loop and push a strap retainer post through the aligned holes such that the post points away from the patient's arm. (In use, the flat retainer base should rest against the skin of the patient.)

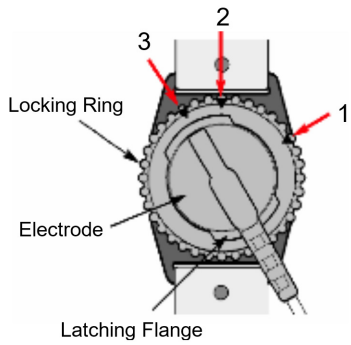
B. Run the free end of the strap through the opposite slit **from below**. Hold this loop open as you run the arm of the patient up through the loop.

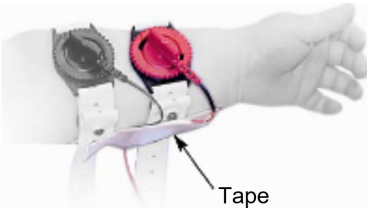
C. Place the holder precisely over the cleaned skin site selected for sweat stimulation and hold it down while drawing the free end of the strap down and around the arm. Pull the strap to tighten, stretching slightly and affix it to the retainer post.

D. Grip the holder and lift it briefly above the skin to equalize strap tension on each side of the holder, then replace it on the skin surface. Adjust strap tension as needed to ensure correct contact.

NOTE: *Attach the strap firmly, but avoid excessive tightness. Correctly applied, the holder should grip the skin firmly enough to resist moderately forceful attempts to change its position. The surrounding skin areas should move with the holder when it is moved.*







E. Draw the skin back around the holder to remove any underlying wrinkles.

F. Position the negative (black) holder (on the same limb) in the same manner.

6 Insert Pilogels Into the Iontophoretic Electrodes

Insert a gel into each electrode assembly. Press lightly and rotate to ensure an air-free and moist interface between electrode plate and gel.

⚠ WARNING!

Pilogel discs should be refrigerated at 2 to 10 °C. DO NOT FREEZE. Never use discs that have been frozen or that are cracked. This does NOT apply to the fiber pilocarpine reservoirs.

7 Insert Each Electrode Into Its Holder

Fit the red (positive) anode into the holder with the red locking ring and fit the black (negative) cathode into the holder with the black locking ring as follows:

A. Rotate the holder locking ring to align cutouts with those of the underlying holder. The arrow indicator should be at Position 1 (shown at left). Match the latching flanges of the electrode with the cut-outs and insert the gel-fitted electrode into the holder.

B. Lightly press the electrode down against the skin and maintain pressure while rotating the locking ring counter-clockwise until the arrow indicator is in line with the holder strap holes (Position 2 at left). Release pressure on the electrode and continue to slowly rotate the locking ring counter-clockwise until the electrode clicks into the detent (Position 3 at left).

***NOTE:** Electrode wires should be securely taped to the patient's arm to prevent disturbing the gel-to-skin contact during iontophoresis. Use 1-inch surgical tape to secure wires firmly to the skin about 2 inches from each strain relief. Leave slack between taped area and electrodes to prevent strain to the electrode assembly.*

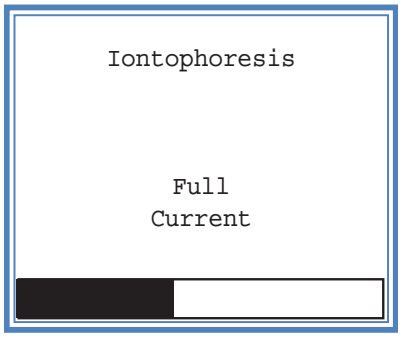
8 Activate Iontophoresis

A. After completing Check Controls, the arrow on the display points to Iontophoresis on the menu.
Press ENTER to start iontophoresis.

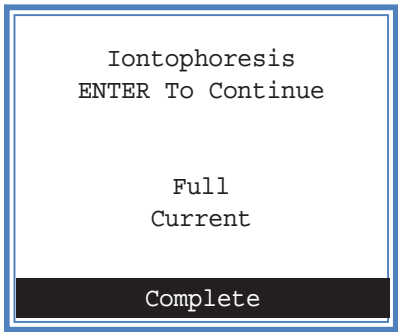
```
NANODUCT
2019-01-31 12:03

→Check Controls
 Iontophoresis
 Sweat Analysis
 Recall Reading
```

```
Iontophoresis


Increasing
Current
```

B. The display shows "Increasing Current." During this time, the induction/analysis module applies an increasing amount of current to the electrodes until reaching full current.



C. Once current has reached the full 0.5 mA, that level is maintained for 2 minutes. The display shows “Full Current” and a time bar at the bottom of the screen shows progress.



D. Current then decreases to zero (indicated by a short beep). The display shows “Complete” and “ENTER To Continue.”
Press ENTER to return to the main menu.

9 Remove the Red Electrode

While applying pressure to the red electrode with the index finger, rotate the upper ring approximately 90° clockwise until the cutouts align with the electrode flanges. Then remove the electrode. Immediately and properly dispose of the Pilogel disc from the positive (red) electrode.

⚠ **CAUTION**

Do not disturb or remove the red holder. It must remain in place during analysis. In addition, leave the negative (black) electrode, gel, holder and tape-downs in position to provide a ground contact for initial sweat rate determination.

⚠ **WARNING!**

Pilogel is considered harmful. Do not ingest. Consult the SDS sheet for more information.

⚠ **WARNING!**

Pilogel discs are a potential choking hazard. Make sure they are disposed of properly.

10 Clean and Dry the Skin in the Collecting Area

Use a cotton swab with a small amount of DI water to clean the entire skin area inside the holder, followed by clean dry swabs to completely dry the area. Without delay, proceed to the next step.

NOTE: *If the sensor is not inserted immediately, repeat the cleaning and drying procedure just before attaching the sensor.*

11 Insert Sensor Into Positive Holder

Insert the sensor (without being attached to the wiring harness) into the holder (red locking ring) as described in steps 7a and 7b, taking care not to disturb the holder or touch the bottom of the sensor.

Confirm that the instrument is ON.

12 Connect Sensor to the Red Sensor Connector

With the sensor in the holder, press the sensor connector fully onto the red sensor, so that the two electrode pins seat in the mating receptacles (orientation is not important).

NOTE: *The sensor cable should be securely taped to the patient's arm approximately 2 inches from the strain relief. Be sure to leave enough slack in the cable on the sensor side of the tape-down to protect it from inadvertent tugging. Make sure the tape-down doesn't disturb the sensor's even contact with the skin surface. Make sure the black electrode cable is still securely taped down.*

13 Activate Sweat Conductivity Analysis

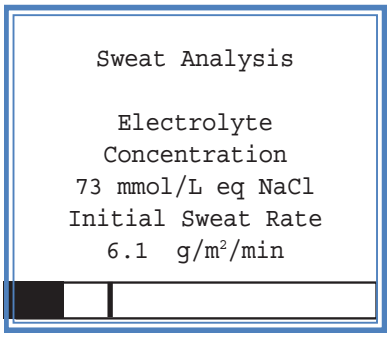
```
NANODUCT
2019-04-15 12:03

  Check Controls
  Iontophoresis
→Sweat Analysis
  Recall Reading
```

A. On the screen, the pointer should be pointing to Sweat Analysis. Immediately after the sensor is placed in the holder, press ENTER to begin the sweat conductivity analysis.

```
Sweat Analysis

→Suppress Readings
  Display Reading
```

B. The instrument prompts to display readings during testing or to suppress the reading for recall at a later time. Press SELECT to make your selection and press ENTER.

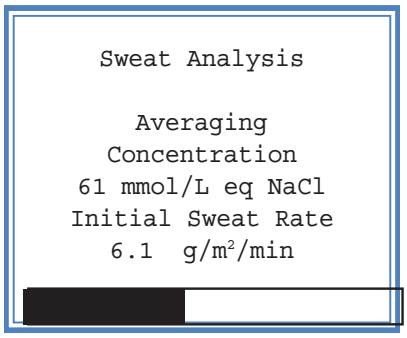
14 Record the Result



A. With the sensor and black electrode in place, the display indicates sweat contact with the first electrode within a few minutes.

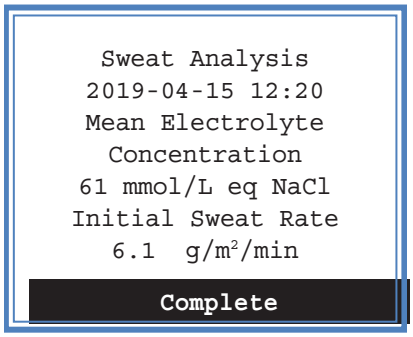
After another 2 to 6 minutes (all timing is approximate, depending on the initial sweat rate of the patient) the conductivity display should begin to show continuous data (if Display Reading has been selected). Simultaneously, the initial sweating rate in g/m²/min is displayed. The Initial Sweat Rate will be reported as Not Valid if the black electrode is removed before a value can be displayed. The result from the sweat test remains accurate, though there will be no indication if at least 1 g/m²/min sweat rate was achieved.

The Initial Sweat Rate will also be reported as Not Valid if calculated to be >50 g/m²/min.



B. The continuous data remains on display, and after 3 minutes, the display shows that averaging has commenced. The time bar at the bottom of the display indicates remaining time once sweat reaches the second electrode. The mean electrolyte concentration is displayed after another 5 minutes.

This value is compared with the established conductivity ranges for children under 16 years **(normal = below 50 mmol/L; equivocal = 50 to 80 mmol/L and CF = above 80 mmol/L)** for a diagnostic appraisal and becomes the reported test result.



C. Once the test is completed the display flashes “Complete” and the control module emits a short beep. The date and time the test was completed is displayed. Press ENTER to return to the main menu.

NOTE: *A patient should produce sufficient sweat within 30 minutes after iontophoresis. If the Nanoduct does not detect sufficient sweat to report “Sweat at First Electrode” within 30 minutes, or 30 minutes has elapsed between seeing “Sweat at First Electrode” on the display and seeing sweat testing data appear on the display, the test should be aborted due to insufficient sweat production.*

15 Remove Holders and Sensor, and Clean Electrodes

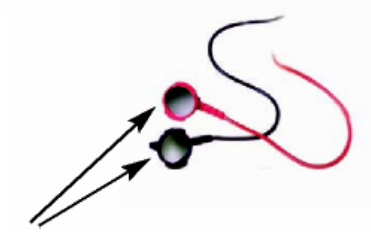
A. Disconnect the cable from the sensor. Remove the sensor from the holder and discard the used sensor. Immediately and properly dispose of the Pilogel disc from the negative (black) electrode.

⚠ **WARNING!**

Due to possible biological contamination, Nanoduct sensors are single use only and must be discarded after use.

B. Disconnect the cable plug from the socket of the instrument and turn OFF the power.

C. Remove the holders from the patient and gently wash and dry the entire skin areas involved in the test.



Wash and Dry Metal Plates

D. Wash and dry the electrode plates.

```
NANODUCT
2019-04-15 12:32

Check Controls
Iontophoresis
Sweat Analysis
→Recall Reading
```

16 Recall the Display Reading

If you selected “Suppress Readings,” or if the control unit powers off, the last reading can be recalled by selecting Recall Reading from the main menu and pressing ENTER.

Recall Reading also outputs the last reading to the serial port where it can be printed if a serial printer is connected to the port. The output includes the date and time of the last reading and the reading in mmol/L eq NaCl.

```
Recall Reading
2019-04-15 12:20
Mean Electrolyte
  Concentration
61 mmol/L eq NaCl
Initial Sweat Rate
  6.1  g/m²/min
ENTER To Continue
```

3.2 Interpreting the Sweat Test

Units of Conductivity

Electrical conductivity–essentially an electrical measurement–should properly be measured in siemens/cm. However, we use conductivity to indirectly measure electrolyte concentration. Since medical professionals are more familiar with standard chemical units (such as mmol/L) for concentration, the siemens/cm units have not been used for conductivity values in the practice of clinical chemistry, to prevent confusion. ELITechGroup has retained the mmol/L (equivalent NaCl) unit used by other sweat conductivity instruments in the past. Unfortunately, this unit has also produced confusion in some quarters.

It is therefore important to define and explain the meaning of this expression. The readout, both as displayed continuously and as the electronically averaged value is expressed in mmol/L (equivalent NaCl).

This means that the sweat sample has an electrical conductivity that is equivalent to that of an NaCl solution of the displayed mmol/L concentration (at the same temperature). **THE READINGS IN SUCH UNITS DO NOT REPRESENT THE ACTUAL CONCENTRATION OF EITHER SODIUM OR CHLORIDE IN THE SWEAT.**

The level of electrical conductivity is a function of the molar concentration of ionized molecules in a solution. Sweat samples are made up of sodium, potassium, and a small contribution by ammonium, as the cation contribution. The anions balancing these are mainly chloride, with lactate and bicarbonate. Thus, the conductivity can be seen as a measure of the total electrolyte in mmol/L.

Clinical trials have amply demonstrated that sweat total electrolyte and sweat chloride are equally effective analyses in the diagnosis of CF. As there are other ions contributing to the conductivity other than sodium and chloride, the mmol/L (equiv. NaCl) value of a sweat sample always exceeds the actual molar sodium or chloride concentration as analyzed specifically. The diagnostic range is therefore different from that established for chloride.

The electrolyte selected for calibration reference happens to be sodium chloride, but it could have been any other salt. The chemical nature of the calibration solution is immaterial, because the reference ranges for sweat conductivity is based upon comparison with the calibration value, and is valid whatever electrolyte is used as a reference.

For example, if lithium nitrate had been selected as the reference salt, it may have produced a possibly different but equally reliable and effective reference range. Conductivity values would then have been expressed as mmol/L (equivalent $LiNO_3$). Though such an alternative calibration option is not recommended, it would have had the advantage that since no mention of sodium or chloride is made, the results would not be mistakenly seen as representing actual sweat sodium or chloride levels.

Automatic Averaging

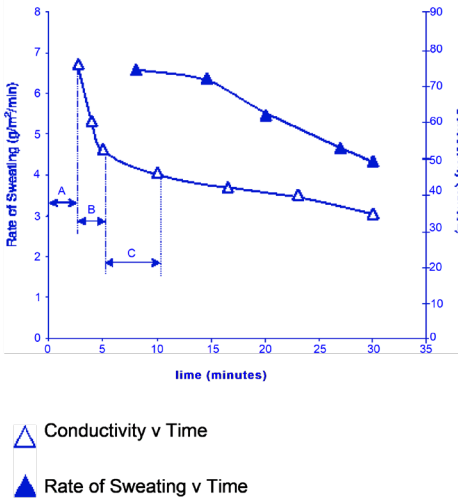
Examination of the data showing the relationship between sweat conductivity and time after attaching the sensor, obtained on all the subjects in the original test of the system, and typically shown in Fig.1, allowed the selection of optimal settings for the averaging circuitry. After a variable lapse of time (Period A, Fig.1) during which the sweat is gradually filling the channel in the sensor, it reaches the second electrode, thereby completing the conductivity cell circuit and producing a displayed conductivity reading. During the next 3 minutes (Period B, Fig.1), this reading usually falls sharply, and then assumes a steady rate of decrease that is maintained thereafter.

This initial rapid change has been termed the “first sample phenomenon” and the reason for it is not yet clear. In the steady phase of decrease of conductivity, the average rate of decrease is about 15% per 10 minutes (during the period 10 to 20 minutes after the first reading). The best time period for averaging commences after the initial rapid fall stabilizes, that is at 3 minutes from the first reading, thus avoiding the “first sample phenomenon.”

It then continues for the next five minutes (Period C, Fig 1) during which the sweating rate is still near-maximal.

The induction/analysis module is therefore programmed to make an average conductivity assessment by noting the time at which the first conductivity result is displayed, allowing a time lapse of 3 minutes and then commencing a 5-minute averaging period, after which the mean value is displayed.

Fig. 1



Diagnostic Ranges

Normal = below 50 mmol/L*

Equivocal = 50 to 80 mmol/L*

CF = above 80 mmol/L*

*equivalent NaCl

Using the data displayed in Fig 1, which show both sweat rate and conductivity variation with time after stimulation, the Nanoduct averaged value (over period C) was obtained (46 mmol/L).

This can be compared with the value (47 mmol/L) that would theoretically have been obtained using a Macroduct-obtained mixed sweat yield over 30 minutes, the standard collection time used in the clinical trial that provided the basic results for the selection of the currently-established normal, equivocal, and CF diagnostic ranges. It is clear that the Nanoduct results may confidently be evaluated with reference to these ranges, for children under 16 years of age, **normal below 50 mmol/L, equivocal 50 to 80 mmol/L, and CF above 80 mmol/L (equivalent NaCl).**

In non-CF adults, the normal range is frequently extended into the equivocal levels, but never sufficiently to provide a false positive diagnosis.

Initial Sweat Rate

One advantage of the unique continuous-flow sensing device of the Nanoduct System is that it allows computation of the initial sweat rate. The volume of the sensor channel from the first electrode to the second electrode contact is precisely known, as is the collecting surface area. After the sensor is attached to the arm, the time taken for this volume to be filled with sweat is measured by the Induction/Analysis module.

Applying an algorithm with the fill time as the sole variable allows a display of the initial sweating rate in the conventionally accepted units of grams of sweat per square meter of skin surface per minute. This datum is available when the first reading is displayed on the continuous record of conductivity.

Notes Regarding Sweat Rate

Established sweat testing guidelines specify a minimum sweat rate of 1 g/m^2/min for a sweat test to be considered valid in the diagnosis of cystic fibrosis. ELITechGroup recommends that a physician be consulted before interpreting sweat test results if a sweat rate of at least 1 g/m^2/min is not achieved. To provide the most information for subsequent consideration, the Nanoduct 1030 will display an initial sweat rate reading even if it is below 1 g/m^2/min and provide a sweat electrolyte concentration measurement.

Section 4: Troubleshooting and Preventive Maintenance

4.1 Troubleshooting

General Troubleshooting and Diagnosis

Symptom	Probable Causes / Possible Solutions
Nothing happens when the On button is pressed, display remains blank, or is not responsive when buttons are pressed.	Probable Causes: Low or dead batteries. Potential malfunction causing a lock-up condition. Possible Solutions: Replace all four batteries. Reset the Nanoduct.* If the problem persists, contact ELITechGroup for further instructions.
Nanoduct immediately shuts off after pressing On button or shuts off during a test.	Probable Causes: Low battery voltage. Possible Solutions: Replace all four batteries. Repeat the sweat test one time.† If problem persists, there may be an issue with the Nanoduct. Contact ELITechGroup for further information.
During Sweat Analysis, the display does not change from “Please Wait…”	Probable Causes: No sweat detected, possibly due to sensor cell not properly latched with locking ring or holder not adequately secured to patient. Cable may have become detached from sensor cell or Nanoduct. Damaged electrode cable assembly. Orifice on sensor cell blocked. Possible Solutions: Ensure sensor cell is latched with locking ring and that holder secured with adequate tightness to the patient’s limb. Do not overtighten and impede blood circulation. Ensure that the cable is properly connected to both sensor cell and Nanoduct. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. Replace electrode cable assembly. Repeat the sweat test one time using a new sensor cell.† The patient’s sweat rate may be very low (see next row). Wait sufficient time to allow sweat to flow. (Not to exceed 30 minutes.)

Symptom	Probable Causes / Possible Solutions
Insufficient sweat rate or insufficient sweat for Sweat Analysis to complete. (See also Error Message Troubleshooting below.)	Probable Causes: Insufficient sweat may occur for a variety of reasons and varies depending upon patient. Physiological factors, such as the patient's age, weight, race, and hydration level may contribute to insufficient sweat, as well as other physiological factors (e.g. anhidrosis, hypohidrosis). Possible Solutions: If an adequate sweat sample is not obtained, repeat testing should occur as soon as is practical. This could be the same day or the following day. The sweat test should only be repeated once on any given day.† The patient should be well hydrated and free of acute illness. Check that the Pilogel is within the expiration date.
Nanoduct resets during a test.	Probable Causes: Low battery voltage. Electrostatic discharge to the Nanoduct's face, enclosure, connectors, or electrodes may cause the Nanoduct to reset (see Appendix J). Possible Solutions: Replace all four batteries. Repeat the sweat test one time.† If the problem persists, contact ELITechGroup for further instructions.
Iontophoresis process stops prematurely.	Probable Causes: Low battery voltage. Electrodes not properly latched with locking ring or cable becoming detached from Nanoduct. Holders not adequately secured to patient. Damaged electrode cable assembly. Possible Solutions: Replace all four batteries. Ensure both electrodes are latched with locking ring and that the cable is properly connected to the Nanoduct. Ensure holders are secured with adequate tightness to the patient's limb. Do not overtighten and impede blood circulation. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. Repeat the sweat test one time.† If the problem persists, contact ELITechGroup for further instructions.

Symptom	Probable Causes / Possible Solutions
Communication problems or incorrect information sent to Nanoduct Lab Report or printer.	Probable Causes: Communication settings are not correct. Damaged communication cable. Nanoduct hardware or software problem. Possible Solutions: Check RS-232 communication settings on the computer or printer. Inspect the communication cable and replace if necessary. Restart Lab Report software, printer, or computer and retransmit the data. Reset the Nanoduct and retransmit the data.* Repeat the sweat test one time.†
Data appears to be missing or corrupted when reviewing Recall Reading.	Probable Causes: Potential malfunction with the Nanoduct. Possible Solutions: Reset the Nanoduct.* Retry recalling the information or exporting it to a printer or Nanoduct Lab Report. Repeat the sweat test one time.†
Date and time revert to “2000-01-01 00:00” each time the Nanoduct is turned on.	Probable Cause: Internal clock battery is dead. Possible Solutions: Contact ELITechGroup to have the internal clock battery replaced.‡

Error Message Troubleshooting and Diagnosis

Error Message Displayed	Screen	Probable Causes / Possible Solutions
Low Battery	Main Menu	Probable Causes: Battery voltage is below the low battery threshold. Possible Solutions: Replace all four batteries. After replacing the batteries, if the same problem persists, contact ELITechGroup for further instructions.
Fault Calibration Not Completed	Check Controls	Probable Causes: An attempt to calibrate to a value other than 80 mmol/L. Damaged electrode cable assembly or calibration plate. Possible Solutions: Repeat calibration using the 80mmol/L position on the calibration plate. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. If fault continues to occur, contact ELITechGroup for further instructions.

Error Message Displayed	Screen	Probable Causes / Possible Solutions
Open Loop Fault Check Electrodes	Iontophoresis	Probable Causes: No Pilogel discs under electrodes. Dirty electrodes. Electrodes not properly latched with locking ring or cable not connected to Nanoduct. Holders not adequately secured to patient. Damaged electrode cable assembly. Possible Solutions: Ensure that a Pilogel disc is under each electrode. Clean electrodes if necessary. Place a drop of deionized water directly on the clean skin beneath each Pilogel disc. Ensure both electrodes are latched with locking ring and that the cable is properly connected to the Nanoduct. Ensure holders are secured with adequate tightness to the patient's limb. Do not overtighten and impede blood circulation. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. Repeat the sweat test one time.† If fault occurs on a regular basis, contact ELITechGroup for further instructions.

Error Message Displayed	Screen	Probable Causes / Possible Solutions
High Resistance Fault Moisten Skin	Iontophoresis	Probable Causes: No Pilogel discs under electrodes. Dirty electrodes. Electrodes not properly latched with locking ring or cable becoming detached from Nanoduct. Holders not adequately secured to patient. Damaged electrode cable assembly. Patient's skin resistance is too high for proper iontophoresis current. Possible Solutions: Ensure that a Pilogel disc is under each electrode. Clean electrodes if necessary. Place a drop of deionized water directly on the clean skin beneath each Pilogel disc. Ensure both electrodes are latched with locking ring and that the cable is properly connected to the Nanoduct. Ensure holders are secured with adequate tightness to the patient's limb. Do not overtighten and impede blood circulation. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. Replace electrode cable assembly. Repeat the sweat test one time.† If fault continues to occur, contact ELITechGroup for further instructions.
Fault Check Instrument	Iontophoresis	Probable Causes: Operational error has been encountered by the system. Possible Solutions: Reset the Nanoduct.* Perform a Self Test on the Nanoduct. If the problem persists, discontinue use of the Nanoduct and contact ELITechGroup for further instructions.
Over Current Fault Check Instrument	Iontophoresis	Probable Causes: Iontophoresis current exceeds allowed threshold. Nanoduct may be damaged. Discontinue use of the Nanoduct. Possible Solutions: Contact ELITechGroup for further instructions.

Error Message Displayed	Screen	Probable Causes / Possible Solutions
Initial Sweat Rate Not Valid	Sweat Analysis Recall Reading	Probable Causes: Black electrode removed during sweat analysis. Red sensor connector not connected to the sensor cell before sweat flows into sensor cell. Damaged electrode cable assembly. Possible Solutions: Black electrode must remain attached during sweat analysis for the Nanoduct to display a sweat rate value. Connect red sensor connector to sensor cell immediately after inserting sensor cell into the positive holder. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. Replace electrode cable assembly. Repeat the sweat test one time.† If fault continues to occur, contact ELITechGroup for further instructions.

Error Message Displayed	Screen	Probable Causes / Possible Solutions
Fault Sweat Analysis Was Not Completed	Sweat Analysis Recall Reading	Probable Causes: Insufficient sweat collected for analysis due to sensor cell not properly latched with locking ring or holder not adequately secured to patient. Insufficient sweat collected for analysis due to iontophoresis not properly completed prior to starting sweat analysis. Cable may have become detached from sensor cell or Nanoduct. Damaged electrode cable assembly. Nanoduct may have been inadvertently powered off or batteries died during sweat analysis. Process may have timed out due to patient producing very low sweat rate or insufficient sweat to fill sensor cell. Possible Solutions: Ensure sensor cell is latched with locking ring and that holder secured with adequate tightness to the patient's limb. Do not overtighten and impede blood circulation. Ensure iontophoresis is properly completed before starting sweat analysis. Ensure that the cable is properly connected to both sensor cell and Nanoduct. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. Replace electrode cable assembly. Replace all four batteries (if necessary) and repeat the sweat test one time.† If fault continues to occur, contact ELITechGroup for further instructions.

Error Message Displayed	Screen	Probable Causes / Possible Solutions
Fault Sweat Analysis Was Not Valid	Sweat Analysis Recall Reading	Probable Causes: Insufficient sweat collected for analysis or air bubbles present in sensor cell due to sensor cell not properly latched with locking ring or holder not adequately secured to patient. Cable may have become detached from sensor cell or Nanoduct. Damaged electrode cable assembly. Orifice on sensor cell blocked. Possible Solutions: Ensure sensor cell is latched with locking ring and that holder secured with adequate tightness to the patient's limb. Do not overtighten and impede blood circulation. Ensure that the cable is properly connected to both sensor cell and Nanoduct. Inspect the electrode cable assembly for any damage. Do not use electrodes if there is any damage to the cable insulation or if there are exposed bare wires. Replace electrode cable assembly. Repeat the sweat test one time using a new sensor cell.†

**Reset the Nanoduct by doing the following: (1) Remove the two Phillips screws from the battery door located on the bottom of the Nanoduct, then remove the door. (2) Remove one of the batteries from the battery holder, wait for one minute, reposition the battery with correct polarity in the battery holder. (3) Return the door to original position, insert the two Phillips screws and tighten. (4) Turn the Nanoduct on by pressing the ON key.*

†The sweat test should only be repeated one time within any 24-hour period. Consult a physician before performing multiple tests on a patient within a 24-hour period.

‡The lithium coin cell backup battery used to power the clock is not accessible to the user and should only be replaced by qualified service personnel.

***NOTE:** This instrument is designed and tested to meet IEC CISPR 22 / EN55022 and IEC/EN 60601-1-2 standards for electromagnetic compatibility for medical electrical equipment. However, if you suspect electromagnetic susceptibility or interference, reorient or relocate the equipment to correct the problem.*

4.2 Cleaning the Instrument

When needed, the induction/analysis module surfaces and accessories should be wiped down using a soft cloth dampened with mild detergent or 10% household bleach solution.

Electrodes must be cleaned following each iontophoresis procedure as follows:

1. Remove any remaining gel from electrodes.
2. Use a cotton ball or swab moistened with purified water to clean each electrode thoroughly.
3. If the electrode appears dirty after an extended idle period, or does not clean with steps 1 and 2, use a small round piece of light duty cleaning pad (such as 3M Scotch-Brite™ #7445) to buff the electrode surface.

CAUTION

Never use harsh abrasives such as steel wool, sandpaper, or emery cloth to clean electrodes. Never scrape electrodes with metal tools. If the electrode surface is scratched or pitted it does not perform as specified and must be replaced.

Use the following options to clean Nanoduct straps, holders and attachment strap retainers or any other parts that come into contact with a patient:

Option A:

1. Soak the straps for 30 minutes in a freshly prepared 10% dilution of household bleach.
2. Rinse soaked straps thoroughly in tap water.
3. Allow to air dry.

Option B:

1. Autoclave the straps for 30 minutes at 121 °C.

⚠ **CAUTION**

Do not autoclave the Nanoduct holders (red or black) or the attachment strap retainer post. Autoclaving destroys these parts.

Option C:

1. Treat straps as disposables.
2. Discard straps after each use.
3. Purchase new straps from ELITechGroup.

4.3 Calibration and Checking Control Values

Patient Simulator

ELITechGroup offers the AC-111 Patient Simulator as an accessory to the Nanoduct for those who wish to measure unknown samples as part of a proficiency study or to verify or validate the function and accuracy of the Nanoduct instrument. Contact ELITechGroup or your sales representative for additional information.

Calibration Plate

NOTE: *This instrument uses an extremely stable single set point calibration. The calibration plate verifies that the instrument is functioning properly and allows for recalibration when necessary.*

The calibration plate has one calibration value, 80 mmol/L (equivalent NaCl) and three control values: 40, 60, and 120 mmol/L (equivalent NaCl).

Instructions

1. Select “Check Controls” on the menu and press ENTER. Note that the date and time indications are in the format yy-mm-dd hh:mm. Dates, times and other data shown are for example purposes only. Actual data during use varies.

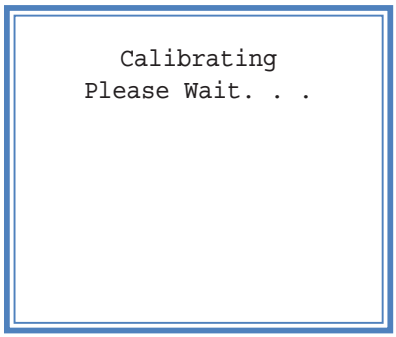
```
NANODUCT
2019-03-24 22:45

→Check Controls
 Iontophoresis
 Sweat Analysis
 Recall Reading
```

2. The display shows the date and time when the last calibration was performed. This information gets displayed for a few seconds. At the same time, the calibration date and time gets sent to the serial port.

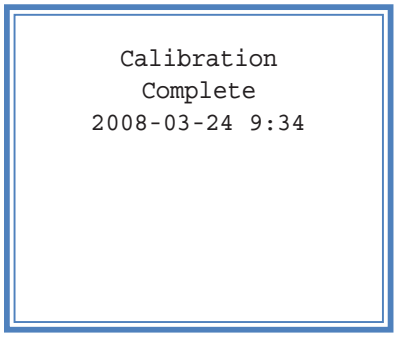
```
Check Controls
Calibration Date
2019-01-29  09:32
```

3. Connect the electrode cable assembly to the electrode socket.
4. Connect the sensor cell connector to the 80 CAL connection on the calibration plate. The selected value shows corresponding mmol/L eq NaCl ±1.
5. Select “Calibrate” and press ENTER. The instrument calibrates to 80 mmol/L and displays “80 mmol/L eq NaCl” when completed.

```
Check Controls

 Electrolyte
Concentration
80 mmol/L eq NaCl

  Exit
→Calibrate
```

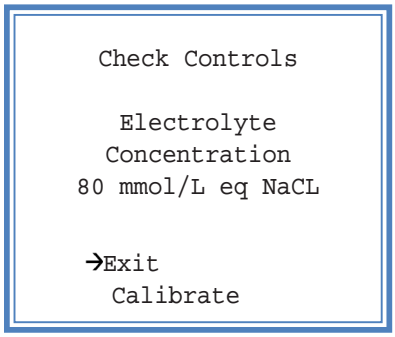


6. The Nanoduct calibrates to the 80 mmol/L (equivalent NaCl). The screen indicates that the instrument is calibrating and to please wait. When the calibration has been completed, the screen advances to the next screen.

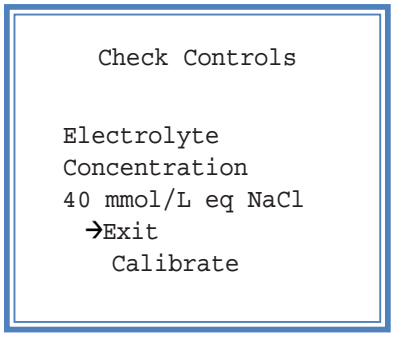


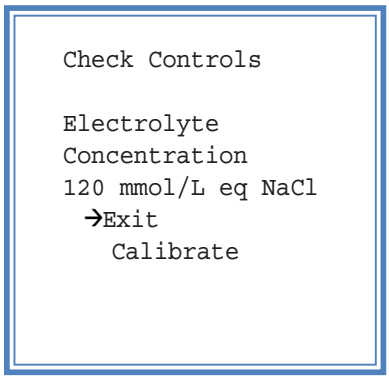
7. When the calibration is completed, a Calibration Complete screen is displayed for a few seconds. The time of the calibration also gets displayed.

   Data is sent to the serial port.



8. Optionally for checking control values, connect the sensor cell connector to any of the 3 control values (40, 60, 120). The value gets displayed as shown below:
   Select Exit and press ENTER to exit Check Controls.





Appendix A: Instrument Specifications

<table>
<tr><th colspan="2">Instrument Specifications</th></tr>
<tr><td>Readout</td><td>128 x 64 LCD graphic display (non-backlit). Supports up to 8 lines of 18 characters or numerals, with multi-lingual support (English, French, German, and Spanish).</td></tr>
<tr><td>Sound</td><td>Alert signals.</td></tr>
<tr><td>Keyboard</td><td>ON, OFF, SELECT and ENTER keys.</td></tr>
<tr><td>Electrode Connection</td><td>6-pin locking medical connector to mate with induction/conductivity cell, cable.</td></tr>
<tr><td>Serial Outputs</td><td>RS-232 (ASCII format)

9-pin D-Sub male connector.

Data Protocol: 9600 Baud, 1 Start Bit, 8 Data Bits, No Parity, 1 Stop Bit.

<table>
<tr><th>Pin #</th><th>Signal</th><th>Description</th></tr>
<tr><td>1</td><td>N/C</td><td>No Connection</td></tr>
<tr><td>2</td><td>RXD</td><td>Receive Data (output)</td></tr>
<tr><td>3</td><td>TXD</td><td>Transmit Data (input)</td></tr>
<tr><td>4</td><td>N/C</td><td>No Connection</td></tr>
<tr><td>5</td><td>GND</td><td>Signal Ground</td></tr>
<tr><td>6</td><td>N/C</td><td>No Connection</td></tr>
<tr><td>7</td><td>N/C</td><td>No Connection</td></tr>
<tr><td>8</td><td>CTS</td><td>No Connection</td></tr>
<tr><td>9</td><td>N/C</td><td>No Connection</td></tr>
</table>

USB – Device

Type B Receptacle.</td></tr>
<tr><td>Electrical</td><td>Four AA Alkaline batteries (NEDA 15A, IEC LR6).

Typical solid-state, over-current circuit protection.

3.0 VDC lithium coin cell for the real time clock. Expected battery life of lithium cell is >5 years.</td></tr>
<tr><td>Sweat Induction Control</td><td>Current profile controlled for use with Pilogel Discs for Nanoduct (or fiber pilocarpine reservoirs) with multiple fail-safe circuits to limit current. Nominal current is 0.5 (± 0.02) mA for 120 (±2) seconds. Total iontophoresis time is ~2.5 minutes including current ramping. Maximum fail-safe current limited to <4 mA.</td></tr>
<tr><td>Real Time Clock</td><td>± 2 minutes per year (battery backed).</td></tr>
<tr><td>Operating Temperature</td><td>15 to 30 °C (59 to 86 °F).</td></tr>
<tr><td>Operating Relative Humidity</td><td>≤ 85%, non-condensing.</td></tr>
<tr><td>Operating Atmospheric Pressure</td><td>≥ 79.5 kPa (≤ 2000 m).</td></tr>
<tr><td>Storage Temperature</td><td>0 to 60 °C (32 to 140 °F).</td></tr>
</table>

Appendix A: Instrument Specifications

Instrument Specifications	
Transport Temperature	0 to 60 °C (32 to 140 °F).
Transport Relative Humidity	≤ 85%, non-condensing.
Instrument (H x W x D)	7.5 x 5 x 2 in (19.1 x 12.7 x 5.1 cm).
Weight	1.2 lb (0.5 kg).
Carrying Case	13.5 x 10.5 x 4 in (34.3 x 26.7 x 10.2 cm).
(Weight with instrument)	4.0 lb (1.8 kg).
Sweat Analysis	
Conductivity Readout	mmol/L (equivalent NaCl).
Conductivity Range	3 to 200 mmol/L.*
Error	1% or less from 25 to 150 mmol/L (equivalent NaCl).
Initial Sweat Rate	Up to 50 g/m^2/min.
Calibration	Single point automatic calibration at 80 mmol/L (equivalent NaCl) using the AC-081 Calibration Plate.

* Solutions with a conductivity of less than 3 mmol/L are reported on the instrument as ≤ 3 mmol/L (equivalent NaCl).

Appendix B: Accessories, Supplies, and Replacement Parts

Accessories	
AC-081	Calibration Plate
AC-111	Nanoduct Patient Simulator
AC-175	Nanoduct Lab Report
AC-177	Seiko Printer (9600 baud) Power Supply and Cable

Supplies	
SS-043	Nanoduct Supply Kit for 6 sweat tests

Replacement Parts	
RP-359	Electrode Cable Assembly
RP-353	Strap Retainer Post
RP-357	Positive Red Electrode and Sensor Cell Holder
RP-358	Negative Black Electrode Holder
RP-354	Holder Attachment Strap, Small, 1 each
RP-355	Holder Attachment Strap, Medium, 1 each
RP-356	Holder Attachment Strap, Large, 1 each
RP-238	Clock Battery, 1 each
RP-444	Nanoduct 1030 User's Manual

Appendix C: Serial Data Ports

RS-232 Serial Port

⚠ WARNING!

Do not connect a line powered printer or computer when the instrument is attached to a patient.

The Nanoduct RS-232 port uses a DB9 connector located on the top of the instrument. This port is for serial communication with a printer. Data is automatically sent out on the serial port whenever “Recall Reading” or “Check Controls” is selected from the main menu. Data output is in ASCII characters. The following are examples of the data printed.

Data from the recall Reading selection:

```
2009-10-20  14:24
41 MMOL/L EQ NACL
```

Data from the Check Controls menu selection:

```
CAL2009-10-19 12:15
80 mmol/L eq NaCl
```

Data from the Self Test mode:

```
2009-10-19 12:15
PRINT TEST
```

Data from the Recall Reading menu includes the date, time, and result from the last completed sweat test. Data from the Check Controls Menu includes the prefix CAL followed by the date, time, and calibration value from the last calibration. If a new calibration occurs, the new date, time, and calibration values are sent to the printer. Data from the Self Test mode includes the date, time, and the text “Print Test.”

Connecting to a Printer

The serial port is configured as Data Communications Equipment (DCE), however the 9-pin connector is male instead of the traditional female connector. The required cable is null-modem with a male connector on one end and a female connector on the other. We recommend that you purchase the ELITechGroup Printer Cable (AC-049).

Data protocol: 9600 Baud, 1 Start Bit, 8 Data Bits, No Parity, 1 Stop bit.

USB Port

⚠ WARNING!

Electrical Shock Hazard. Do not connect to a line powered computer when the instrument is attached to a patient.

The Nanoduct has a Universal Serial Bus (USB), used in conjunction with Nanoduct Lab Report software to record data from the Nanoduct. The port is configured as a USB device (not a host) and uses a standard USB type receptacle. The port cannot be used with a USB printer. Always install the Nanoduct Lab Report software before connecting the Nanoduct to a computer. This allows the computer to correctly recognize the Nanoduct when it is connected. Refer to the Nanoduct Lab Report Manual for additional information.

Appendix D: Critical Components

Pilogel Discs for Nanoduct (part of SS-043 Supply Kit for NANODUCT)

Product(s)	Critical Components
Pilogel Discs for Nanoduct contain:	Pilocarpine Nitrate= 1.4 % (USP grade) Methyl Paraben (Methyl p-Hydroxybenzoate) [preservative] = 0.06% Propyl Paraben (Propyl p-Hydroxybenzoate) [preservative] = 0.03%

SS-043 Supply Kit for NANODUCT

Hazard Pictogram	
Signal word	**Warning**
Hazard statements	**H302 - Harmful if swallowed.**
Precautionary Statements	**P102 - Keep out of reach of children** **P264 - Wash hands, forearms and face thoroughly after handling.** **P270 - Do not eat, drink or smoke when using this product** **P301+P312 - If swallowed: Call a POISON CENTER, a doctor if you feel unwell** **P330 - Rinse mouth** **P501 - Dispose of contents/container to an authorized waste collection point**

For areas in which Pilogel discs are not available, users should check with ELITechGroup for the availability of fiber pilocarpine reservoirs of the same size as Pilogel discs, for use with pilocarpine solutions supplied by the user. Unless otherwise indicated, any mention of Pilogel discs in this manual applies equally to the fiber pilocarpine discs.

Appendix E: Pilogel Information

PILOGEL® DISCS FOR NANODUCT® (sold in Supply Kits for Nanoduct)

This information also applies to fiber pilocarpine reservoirs when containing pilocarpine solution supplied by the user.

Proprietary Name:

Pilogel® Discs for Nanoduct®

Single Use Only: possible biological contamination; pilocarpine exhaustion.

Composition:

See Appendix D, Critical Components.

Indications:

Pilogel/pilocarpine is used under iontophoresis to induce sweating for sweat analysis for the laboratory confirmation of a clinical diagnosis of cystic fibrosis.

Contraindications:

- Do not apply to broken or damaged skin surface.
- Do not use on patients that have a known sensitivity or allergy to any ingredient.

Identification:

A translucent off-white gel disc. (Fiber pilocarpine reservoirs are not translucent.)

Side Effects and Special Precautions

The typical and well-known side effects associated with pilocarpine use during iontophoresis onto the skin are adverse skin reactions. Most individuals that exhibit a sensitivity to pilocarpine experience mild erythema (redness) of the skin at the electrode locations. In some cases, one or more blister-like welts may also form. Such “blisters” invariably disappear within 2 to 3 hours, leaving no aftereffects. But, some patients may also experience skin burns in various degrees. Minor skin burns have been an unwelcome, adverse side effect of pilocarpine iontophoresis from the beginning of sweat testing with the Gibson and Cooke method. While the apparent burn rate with the original ELITechGroup Macroduct 3700 system is less than 1 in 50,000 tests, based on current data and reported events, there have been no reported burns using Pilogel Discs for Nanoduct and the original Nanoduct system or the Nanoduct 1030. Burn descriptions vary from “tiny black pinholes in the skin” to “crater-like, third degree burns two to three millimeters in diameter.” In most of the reported incidents, the children have exhibited no sign of pain or discomfort during iontophoresis, and the burn was not discovered until the electrodes were removed.

ELITechGroup carefully records any side effects reported with its pilocarpine iontophoresis systems.

Consult a physician before performing multiple tests on a patient within a 24-hour period.

Storage Instructions:

Refrigerate at 2 to 10 °C. Do not Freeze. Keep locked up and out of reach of children. (Not applicable to fiber pilocarpine reservoirs.)

Appendix E: Pilogel Information

Reference Numbers:

SS-043 Supply Kit for Nanoduct with

32-0100 Pilogel® Discs for Nanoduct®

Name and Business Address of Manufacturer:

ELITechGroup Inc.
370 West 1700 South
Logan, Utah 84321-8212
USA

Appendix F: Storage and Handling Conditions

Storing the Instrument

Before storing the Nanoduct do the following:

Wipe down the induction/analysis module surfaces and accessories using a soft cloth dampened with mild detergent or 10% household bleach solution.

Electrodes must be cleaned as follows:

1. Remove any remaining gel from electrodes.
2. Use a cotton ball or swab moistened with purified water to clean each electrode thoroughly.
3. If the electrode appears dirty after an extended idle period, or does not clean with steps 1 and 2, use a small round piece of light duty cleaning pad (such as 3M Scotch-Brite™ #7445) to buff the electrode surface.

⚠ **CAUTION**

Never use harsh abrasives such as steel wool, sandpaper, or emery cloth to clean electrodes. Never scrape electrodes with metal tools. If the electrode surface is scratched or pitted it does not perform as specified and must be replaced.

Refer to Section 4.2 for instructions for cleaning Nanoduct straps, holders and attachment strap retainers or any other parts that come into contact with a patient:

If storing for an extended period of time, remove the batteries and place the instrument in a plastic bag or other type of container to keep dust or other particles from collecting on the instrument.

Store the instrument in a location within the storage temperature range of 0 to 60 °C and less than 85% non-condensing humidity.

Appendix G: Shipping and/or Disposal Instructions

Shipping the Nanoduct

Instruments must be cleaned before returning them to an authorized service center. A charge is assessed if an instrument must be cleaned or decontaminated at the service center.

⚠ **WARNING!**

During decontamination, use universal precautions: eye protection, gloves, lab coat, and ventilation.

1. Wipe down the induction/analysis module surfaces and accessories using a soft cloth dampened with mild detergent or 10% household bleach solution.

   Electrodes must be cleaned as follows:

   A. Remove any remaining gel from electrodes.

   B. Use a cotton ball or swab moistened with purified water to clean each electrode thoroughly.

   C. If the electrode appears dirty after an extended idle period, or does not clean with steps 1 and 2, use a small round piece of light duty cleaning pad (such as 3M Scotch-Brite™ #7445) to buff the electrode surface.

2. Obtain a Return Maintenance Authorization (RMA) number from ELITechGroup or an authorized service center.
3. Enclose the instrument in a container comparable to its original packaging. You may use the packaging from the loaner instrument if you received one or request a new shipping container from the service center. With a black marker, boldly write the RMA number on at least two sides of the container.
4. Return the instrument to ELITechGroup or an authorized service center. The customer is responsible for the cost of shipping and insurance covering the value of the device.

Disposal of the Instrument

This instrument should be completely decontaminated and disposed of as follows:

Under Directive 2012/19/EU (WEEE), this instrument cannot be disposed of in a normal landfill. Instead, the instrument must be disposed of either by:

1. Routing to an authorized local facility approved for handling hazardous materials, or
2. Returning the instrument to ELITechGroup or an authorized service center.
3. Dispose of batteries according to local laws.

Appendix H: Supplemental Information

Cystic Fibrosis: A Brief Description of the Disease

Cystic fibrosis of the pancreas (or mucoviscidosis) is due to one of the many known 'inborn errors of metabolism' that are fundamentally the result of aberrations in the structure of the genetic material. It is classed as lethal because of the very poor prognosis afforded to sufferers. The inheritance is autosomal recessive, so that an affected child must inherit one defective gene from each of the parents to be homozygotic. Such parents must then at the least be carriers (heterozygotes). The distribution of the genetic anomaly varies with racial types. It is predominantly associated with Caucasians in whom it occurs in about 1 in every 1500 to 2000 live births.

The symptoms of the disease are manifold; however, they are not strictly specific and hence physicians often have difficulty in distinguishing CF from other childhood diseases on the basis of medical diagnosis alone. The most serious clinical features are the pulmonary problems stemming from abnormally viscous exudates in the lungs, requiring urgent physiotherapy and antibiotic treatment to offset the ever-present risk of pneumonia. The pancreas is also affected by over-viscous secretions that reduce its output of digestive enzymes; thus, the child tends to fail to thrive because the food ingested passes through the alimentary canal without the normal enzymic breakdown necessary for absorption of nutrients. Fortunately, the latter problem is relatively easily corrected by the addition of animal pancreatic extracts to the diet. The use of "pancreas" in the disease name arose because of the identification (in 1938) of pancreatic abnormalities during post-mortem examination of children that had died with a set of symptoms that were not as yet associated with a specific illness. It should be noted here that CF sufferers may differ quite widely in the degree to which they exhibit the various symptoms. Some may be relatively less affected in the respiratory airways; others may show more serious pancreatic problems. A feature of the inheritance is that carriers do not exhibit the symptoms of CF.

In 1953, it was found that children afflicted by the disease are prone to acute hyponatremia during hot weather. Investigations on the cause of the loss of sodium showed that the eccrine sweat of children with CF contains 3 to 4 times as much salt as that of unaffected subjects. Subsequent work showed that this salt increase is not observed in presumed carriers. This was the first intimation that a laboratory test for the disease was conceivable. The sweat test was born and remains to this day the principal laboratory diagnostic test for this disease. In recent years the discovery of "the CF gene" promised a new laboratory diagnostic approach. Intensive studies of this gene have revealed hundreds of variants that may, or may not, produce the typical CF symptoms.

There is no doubt that in the future, this research will illuminate the effects of different genetic abnormalities on the biochemical patterns of the individual. However, the sweat test will remain the definitive laboratory diagnostic test for some time yet.

The Evolution of Sweat Test Methods

The sweat test has traditionally involved three separate, sequential procedures — stimulation of the sweat glands, collection of their secretion, and sweat analysis. Early stimulation procedures involved total body heating followed by placing the patient in a bag, or, later by heating followed by collection from a limited area of skin covered by a hermetically sealed absorptive pad. Both of these methods endangered the infants and proved unsatisfactory.

The heating was eventually avoided by using pilocarpine iontophoresis to induce the glands to sweat maximally. Following this, the sweat was collected in a pre-weighed pad and re-weighed, eluted and analyzed.

The method is usually known as the Gibson and Cooke[1] pad absorption sweat test or the QPIT (quantitative pilocarpine iontophoresis test). This procedure has persisted over the years and is still being performed, particularly by CF centers. It is time-consuming and tedious, requiring many manipulations where human error may intervene, and in one particular step offers technical difficulties that virtually ensure some degree of error, particularly when the sweat sample size is very small.

Laboratorians in CF centers who specialize in this method develop the requisite skill to maintain reasonably accurate results, but this is generally not the case in outlying clinics and hospitals, where the test is only occasionally requested, leading to unacceptably high risk of false results.

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While the iontophoretic transport of pilocarpine into the glands has remained the universally preferred method of sweat stimulation to this day, the need for a simpler method of collection and analysis spawned the development of alternative procedures during the late 60's and early 70's. Principally among these were the cup-collection systems, which used electrical conductivity for analysis, and the direct skin chloride electrode system.

These methods were highly innovative, procedurally simpler than the Gibson and Cooke method, and were initially commercially successful. They nevertheless failed in their objective to eliminate false diagnostic results. The adoption of these new procedures on a wide scale exacerbated the problem, evoking a storm of criticism in the professional literature, with calls for a return to the original pad-absorption which was now regarded as the "reference method."[2, 3, 4] In fact, CF referral centers in the United States, operating under accreditation of the Cystic Fibrosis Foundation were forbidden to use any sweat test method other than the QPIT.

These early attempts to simplify the sweat test failed for two principal reasons: (1) error intrinsic to the method of collection and beyond the control of the operator, or (2) extreme susceptibility to variations in operator technique. The direct skin chloride electrode, though offering unrivaled simplicity, was very prone to operator variability in manual skill, and gave poor results due mainly to great difficulties experienced in the control of evaporation error.

The cup collection method was examined for potential intrinsic error by Webster[5] who found that the phenomenon of condensate formation on the walls of the plastic cups was the principal cause of the trouble. His quantitative measurements of the degree to which this occurred in unheated plastic cups showed that the error was always significant and very often reached proportions sufficient to produce false positive results. The error was avoided by using a metal collector cup that was maintained at above skin temperature throughout sweat collection, condensation was prevented, and the error disappeared.

In 1978, Wescor (now ELITechGroup)introduced the Model 3500 Webster Sweat Collection System that employed an electrically-heated metallic collector cup.[6] It was the first "simplified" sweat collection system worthy of comparison with the Gibson and Cooke method, it enjoyed considerable success, and was free from any criticism by users and related professionals. It was however burdened by a problem common to all cup-collection systems, that is, the need to "harvest" the sweat accumulated beneath the cup during collection.

Wescor's determined commitment to resolve this problem eventually led to the invention of the MACRODUCT® Sweat Collector.[7] This innovation completely supplanted the heated cup, while retaining its advantages by the use of a collector that anaerobically collected sweat by using the hydraulic pressure of the sweat glands to pump the secretion directly from the ducts into a fine-bore capillary tube. This system has been very successfully employed both in the US and internationally since 1983.

Vested in ELITechGroup's scientific and engineering staff is a combination of many years of experience in laboratory sweat testing and in the development of modern electronic instrumentation. The ELITechGroup aim in the field of sweat testing has always been to provide quality instrumentation to meet a number of criteria.

1. Elimination of all intrinsic sources of error concomitant to previous collection methods.
2. Ensuring impeccable accuracy in the diagnostic result by reducing human error potential to the lowest possible level.
3. Maximization of patient safety and comfort.
4. Maximization of operator convenience within the strictures imposed by objectives 1, 2 and 3.

These objectives have led to considerable innovative improvements in all aspects of sweat testing, iontophoretic safety measures, collection methods and also in the analytical phase of the test. With the introduction of the Model 3600 Macroduct Sweat Collection System in 1983, all of the comprehensive objectives had been accomplished. Paramount among the system's several unique features was the innovative Macroduct disposable sweat collector.

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Development of the Nanoduct Neonatal Sweat Collection System

During almost twenty years of successful deployment of the Macroduct Sweat-Chek System it began to be realized that a truly neonatal sweat test was needed, one that preserved the error-free anaerobic handling of the sweat sample employed in Macroduct, yet at the same time was particularly designed to meet the special requirements of the newborn infant during the first two weeks of life.

In the interests of effective early management of newborn CF patients, it is highly desirable that a definitive laboratory diagnosis be made as early as possible, allowing prompt initiation of appropriate medical procedures, especially those correcting malnutrition due to pancreatic deficiency and those protecting the infant from airway problems. The frequency of “insufficient sweat,” or “no sweat” reports from laboratories has been unsatisfactorily high throughout the history of sweat testing on very young infants. Recent years has seen increasing emphasis on “screening tests” to newborns, particularly the combination of immuno-reactive trypsin assays and genotype analysis. Both of these have been very useful, but have not reached the status of a definitively diagnostic procedure as has the sweat electrolyte test.

The reason for sweat test failures is well understood by those professionally charged with sweat test performance. The size of iontophoretic electrodes and collection paraphernalia is usually inappropriately large for effective use on the extremely small and frail limbs of the newborn. Many technologists are wary of attempting this daunting task due to the distinct possibility of causing a burn, and also because of the risk of producing a false result in the pad absorption test by inability to control evaporation and condensation errors, particularly when handling tiny infants and dealing with low sweat yields. The Macroduct System, which employs the smallest electrodes and collector of all methods used up to 1998, is nevertheless frequently found to be inappropriately-sized for tests with neonates. It is obvious that any attempt to devise a sweat test for newborn babies must involve, as a fundamental requirement, equipment for iontophoresis and collection that is scaled down to minimal dimensions, enabling their effective application to extremely small limbs.

It is also evident that this approach, taken alone, would merely aggravate the problem by limiting even further the number of sweat glands involved and thereby reduce the sweat yield to as little as 3-6 microliters in 15 minutes collection. In such cases the traditional methods for gathering the sample, storing it in a sealed container, and taking aliquots for presentation to an instrument for analysis would clearly not be feasible, because the potential for serious error would be very difficult, if not impossible, to control.

Such limitations could be avoided if no attempt was made to collect the minute sweat yield. Instead, the sweat is channeled from the sweat duct openings in such a way that it passes directly and anaerobically into a conical collecting interface, just as it does in the Macroduct device, and thence to a microbore tube within the collector that is equipped with electrodes and becomes a conductivity cell for analysis of electrolyte concentration.

Research and development at ELITechGroup (formerly Wescor) provided evidence that this approach was feasible, and sweat tests using the prototype equipment illustrated the simplicity and ease of operation of the method and the speed at which definitive results could be obtained.

In effect, the apparatus, called the Nanoduct Neonatal Sweat Analysis System,[8] incorporates a flow-through conductivity cell that provides, in situ, continuous readings as the sweat enters it from the sweat ducts. This type of data has not been available in any test method to date, making the Nanoduct unique. All other methods involve analysis of a mixed sample obtained over the whole collection period. The sweat is not seen, nor is it collected as a visible sample.

With the development of this neonatal procedure, the opportunity presented itself to make desirable modifications with the aim of improving the safety and shortening the time of iontophoresis, and to provide the electrode gels with protection against accidental freezing.

This method was first published in the Annals of Clinical Biochemistry in 2000.[8]

Subsequent publications have shown that the Nanoduct Neonatal Sweat Analysis System can reliably differentiate between patients with and without Cystic Fibrosis.[9, 10]

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References

1) Gibson, L. E., Cooke, R. E., A test for concentration of electrolytes in sweat in cystic fibrosis of the pancreas utilizing pilocarpine iontophoresis. Pediatrics 1959; 23: 545-9.

2) Gibson, L. E., The Decline of the Sweat Test. Comments on Pitfalls and Reliability. Clin Pediatr. 1973; 12: 450-3.

3) Rosenstein, B. J., Langbaum, T. S., Gordes, E., and Brusilow, S. W., Cystic fibrosis: problems encountered with sweat testing, JAMA, 240, 1987, 1978.

4) Gibson, L. E., Cooperative study comparing three methods of performing sweat tests to diagnose cystic fibrosis.

5) Webster, H. L., and Lochlin, H., Cystic fibrosis screening by sweat analysis. A critical review of techniques, Med J. Aust., 1, 923, 1977.

6) Webster, H. L., and Barlow, W. K., New approach to cystic fibrosis diagnosis by use of an improved sweat-induction/collection system and osmometry, Clin. Chem., 27, 385, 1981.

7) Barlow W. K., and Webster H. L., A simplified method of sweat collection for diagnosis of cystic fibrosis. Proceedings of the 9th International Cystic Fibrosis Congress. Brighton, England, June 9th-15th 1984. Lawson D. (ed), John Wiley & Sons, New York; 1984; 204.

8) Webster H. L., Quirante C. G., Micro-flowcell conductometric sweat analysis for cystic fibrosis diagnosis. Ann Clin Biochem, 2000 Vol. 37, 399-407.

9) Barben J., Ammann R.A., Metlagle A., Shoeni M. H., Conductivity determined by a new sweat analyzer compared with chloride concentrations for the diagnosis of cystic fibrosis. J Pediatr (2005);146:183-8.

10) Desax M., Ammann R.A., Hammer J., Shoeni M.H., Barben J., Nanoduct®sweat testing for rapid diagnosis in newborns, infants and children with cystic fibrosis. Eur J Pediatr (2008) 167:299-304.

Appendix I: Pilocarpine Iontophoresis: Requirements and Risks

In common with all sweat test procedures for the diagnosis of cystic fibrosis since the inception of the sweat test, sweat must be induced in order to be analyzed. In modern medical practice the sweat glands in a limited area of the skin are stimulated by local application of cholinergic drugs, particularly pilocarpine. These substances are introduced to the glands by iontophoresis (in the case of pilocarpine).

These drugs act by mimicking the action of the natural physiological gland stimulator, acetylcholine, which is liberated at the gland by signals from the autonomic nervous system. The iontophoretic procedure depends upon the application of a small and brief direct current to the skin via electrodes, the anode of which, being positive, drives the positively-charged pilocarpine from the reservoir of drug sufficiently to reach the glands.

The requirements for Pilocarpine, as defined in the ELITechGroup Quality Procedures, are primarily that the form and source of the drug be pilocarpine nitrate and the purity being that specified by the United States Pharmacopeia (USP Grade). The concentration of aqueous pilocarpine nitrate solution should be sufficient to initiate a maximal sweat-yielding response from the glands. The ELITechGroup concentration for Nanoduct meets this requirement at a minimal level of 1.5%. Where positively- charged salt ions (acting as iontophoretic transport competitors) are absent from the drug solution, the requirement may be met by 1.0% pilocarpine. The literature on pilocarpine shows no evidence of allergic sensitivity to the drug.

ELITechGroup gel drug reservoirs are quality controlled to meet these requirements in Pilogels manufactured in-house, using spectrophotometric procedures to check the pilocarpine content of the gels in each batch.

Burns Under Iontophoresis

Minor skin burns have been an unwelcome, adverse side-effect of pilocarpine iontophoresis from the beginning of sweat testing with the Gibson and Cooke method. Unusual sensitivity to pilocarpine has sometimes been assumed to be the cause of “burns” but there is no firm evidence for this contention.

Majority opinion seems to support the proposition that some types of stimulating apparatus are prone to cause burns, particularly when associated with procedural error.

ELITechGroup sweat stimulating systems use a sophisticated microprocessor controller with a very low total delivery current (0.5 milliamperes in the Nanoduct System). Pilocarpine is contained in unique gel reservoirs. Pilogel Discs for Nanoduct also include compounds that further protect the patient from skin damage by preventing acid accumulation, by minimizing the risk of gel breakage, and by substantially reducing the time of electrical drug transport.

These features markedly reduce, but do not entirely eliminate, the possibility of skin burns. Most individuals that exhibit a sensitivity to pilocarpine experience a mild erythema (redness) at the skin stimulation site.

In some cases, one or more blister-like welts may also form. These are often mistaken for burns, but are more likely to be a temporary reaction to the passage of electrical current. Such “blisters” invariably disappear within 2 or 3 hours, leaving no aftereffects.

While the apparent burn rate with the original ELITechGroup Macroduct 3700 system is less than 1 in 50,000 tests, based on current data and reported events, there have been no reported burns using the original Nanoduct system or the Nanoduct 1030.The low rate is due to ELITechGroup’s insistence on proper test procedures together with built-in equipment safety provisions that minimize the risk of even mild skin injury. It is highly unlikely that patients will suffer a burn during the stimulation phase of the sweat test.

Appendix J: Electromagnetic Compatibility (EMC)

Medical Electrical Equipment, in general, needs special precautions regarding EMC and needs to be used according to the EMC information provided in the accompanying documents. Portable and mobile RF communications equipment can affect Medical Electrical Equipment.

The Nanoduct instrument is not susceptible to some types of electrical interference, because it is battery-powered and doesn't connect to power lines that might conduct high frequency noise along with the power. However, it could be affected by radio emissions from other devices. Like all digital electronic equipment, it also emits some radio frequency energy when it operates. Use of accessories or cables other than those supplied with the Nanoduct or supplied by the manufacturer as replacement parts could result in increased emissions or decreased immunity of the Nanoduct.

The tables below show the test results for both EMC emissions and immunity.

Guidance and Manufacturer's Declaration – Electromagnetic Emissions
The Nanoduct system is intended for use in the electromagnetic environment specified below. The customer or the user of the Nanoduct system should assure that it is used in such an environment.

Emissions Test	Compliance	Electromagnetic Environment - Guidance
RF Emissions CISPR 11	Group 1	The Nanoduct system uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF Emissions CISPR 11	Class B	The Nanoduct system is suitable for use in all establishments including domestic. It is battery-powered and does not connect to the public power supply network.

The Nanoduct system should not be used adjacent to or stacked with other equipment. If adjacent or stacked use is necessary, the Nanoduct system should be observed to verify normal operation in the configuration in which it will be used.

Guidance and Manufacturer's Declaration – Electromagnetic Immunity
The Nanoduct system is intended for use in the electromagnetic environment specified below. The customer or the user of the Nanoduct system should assure that it is used in such an environment.

Immunity Test	IEC 60601-1-2 Test Level	Compliance Level	Electromagnetic Environment - Guidance
Electrostatic discharge (ESD) IEC 61000-4-2	+/- 2, 4, 8 kV contact +/- 2, 4, 8, 15 kV air	+/- 8 kV contact +/- 15 kV air	The Nanoduct system is isolated from ground. Any typical flooring may be used.

Appendix J: Electromagnetic Compatibility (EMC)

Guidance and Manufacturer's Declaration – Electromagnetic Immunity							
The Nanoduct system is intended for use in the electromagnetic environment specified below. The customer or the operator of the Nanoduct system should assure that it is used in such an environment.							
Immunity Test	**IEC 60601-1-2 Test Level**			**Compliance Level**			**Electromagnetic Environment - Guidance**
	Frequency (MHz)	**Level (V/m)**	**Modulation**	**Frequency (MHz)**	**Level (V/m)**	**Modulation**	
Radiated RF Immunity IEC 61000-4-3	800 – 2700	10	1 KHz 80% Amplitude Modulation	800 – 2700	3	1 KHz 80% Amplitude Modulation	Recommended minimum separation distance (m) 1.2√P (80 – 800 MHz) 2.3√P (800 MHz – 2.7 GHz). Where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey a, should be less than the compliance level in each frequency range. b Interference may occur in the vicinity of equipment marked with the following symbol: 
	385	27	Pulse Modulation 18 Hz	385	27	Pulse Modulation 18 Hz	
	450	28	FM ± 5 Hz deviation 1 KHz sine	450	28	FM ± 5 Hz deviation 1 KHz sine	
	710 745 780	9	Pulse Modulation 217 Hz	710 745 780	9	Pulse Modulation 217 Hz	
	810 870 930	28	Pulse Modulation 18 Hz	810 870 930	28	Pulse Modulation 18 Hz	
	1720 1845 1970	28	Pulse Modulation 217 Hz	1720 1845 1970	28	Pulse Modulation 217 Hz	
	2450	28	Pulse Modulation 217 Hz	2450	28	Pulse Modulation 217 Hz	
	5240 5500 5785	9	Pulse Modulation 217 Hz	5240 5500 5785	9	Pulse Modulation 217 Hz	

NOTE 1: *At 80 MHz and 800 MHz, the higher frequency range applies.*

NOTE 2: *These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.*

[a]Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the Nanoduct system is used exceeds the applicable RF compliance level above, the Nanoduct system should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the Nanoduct system.

[b]Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

Appendix J: Electromagnetic Compatibility (EMC)

Recommended separation distances between portable and mobile RF communications equipment and the Nanoduct System
The Nanoduct is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the operator of the Nanoduct can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the Nanoduct as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter (Watts)	Minimum separation distance (m) between portable and mobile RF communications equipment and the Nanoduct system.		
	150 kHz to 80 MHz d(m)= 1.2 √P	80 MHz to 800 MHz d(m)= 1.2 √P	800 MHz to 2.7 GHz d(m)= 2.3 √P
.01 Watts Maximum	.1 m	.1 m	.2 m
.1 Watts Maximum	.4 m	.4 m	.7 m
.5 W Maximum (typical mobile phone)	.8 m	.8 m	1.6 m (mobile phone)
1 Watts Maximum	1.2 m	1.2 m	2.3 m
10 Watts Maximum	3.7 m	3.7 m	7.4 m
100 Watts Maximum	11.7 m	11.7 m	23.3 m

For transmitters rated at a maximum output power not listed above, the recommended separation distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

NOTE 1 At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

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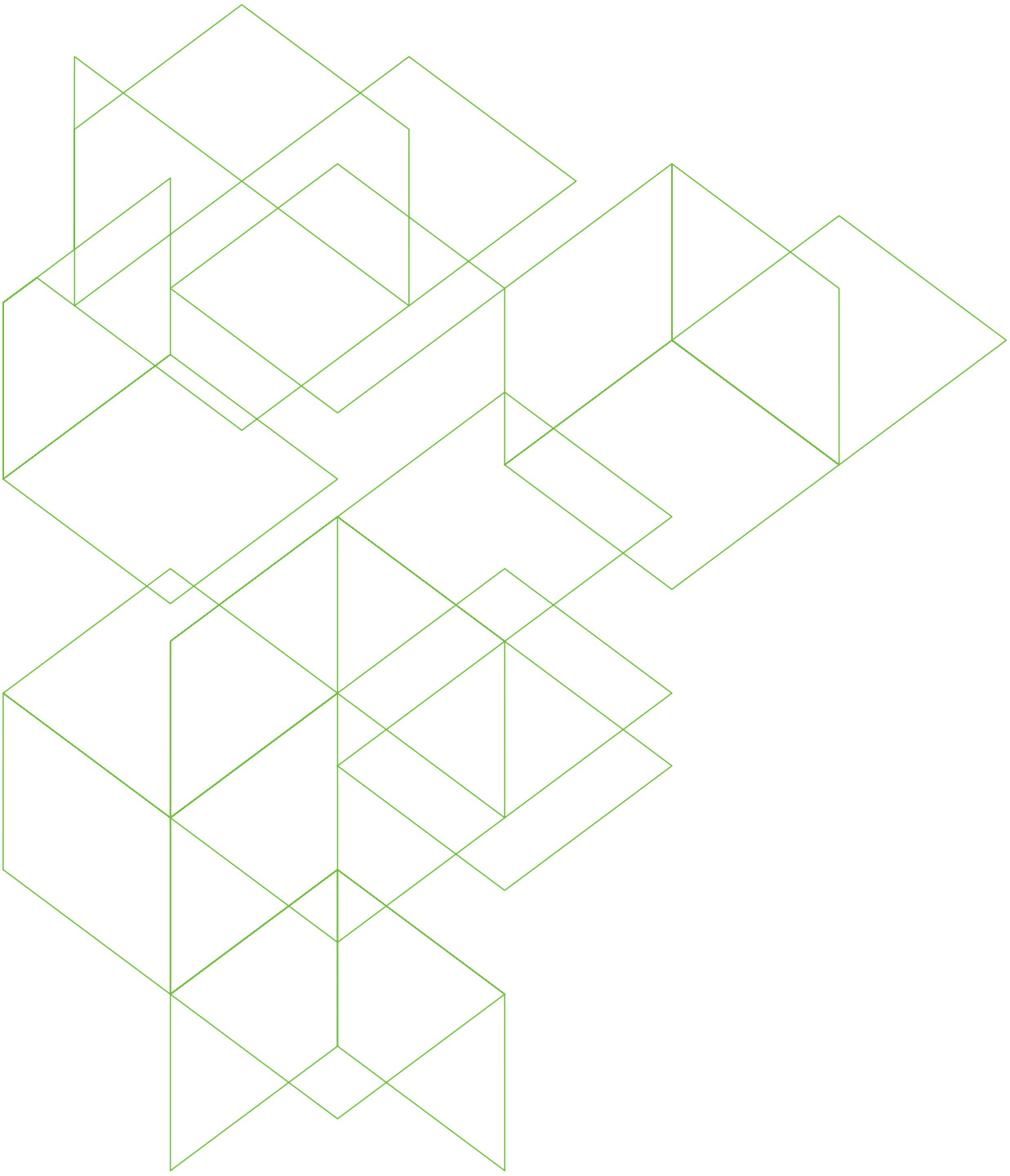

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