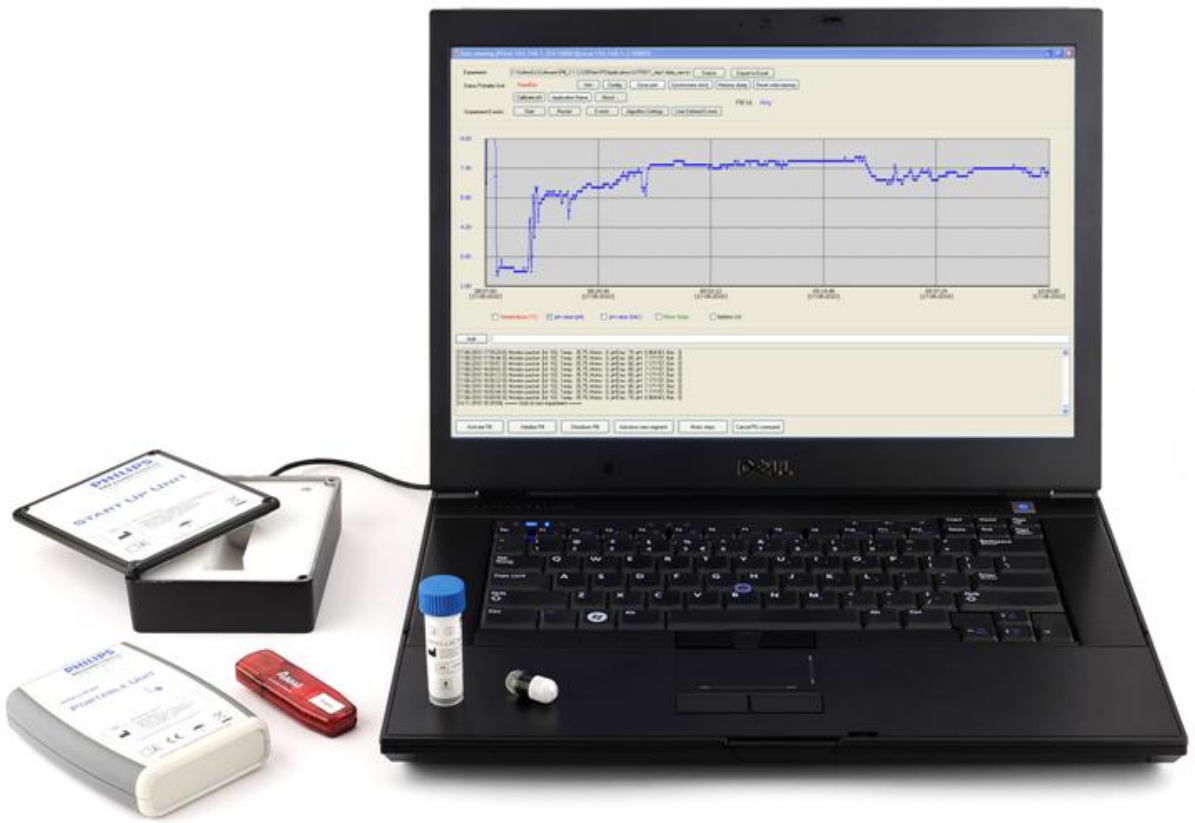
Review & approval

Name Reviewer	Function Reviewer	Review date	Signature
Olaf Weiner	CEO/GM *Medimetrics*	2010-11-29	O. Weiner

Name Approver	Function Approver	Approval date	Signature
Ventzeslav Iordanov	Director QA&RA *Medimetrics*	2010-11-29	

Name Author	Function Author	Date Signed	Signature
Jeff Shimizu	CTO/Director R&D *Medimetrics*	2010-11-29	

IntelliCap Drug Delivery and Monitoring System



User Manual

November 2010

Table of Contents

1. General Information

This user manual describes the constituent components and basic operation of the IntelliCap Drug Delivery and Monitoring System, alternatively referred to as the IntelliCap System.

Trademarks

- IntelliCap is a trademark of Philips
- Microsoft Windows® is a trademark of Microsoft Corporation
- Core2 is a trademark of Intel

The IntelliCap System is manufactured by Koninklijke Philips Electronics Nederland BV acting through Philips Research acting through Medimetrics.

Medimetrics
Philips Research
High Tech Campus 34 (WB.2-043)
5656 AE Eindhoven
The Netherlands

Telephone: +31 40 27 49268

Medimetrics
Philips Research
345 Scarborough Road
Briarcliff Manor, NY 10510

Telephone: +1 914 945 6628

2. Software License Agreement

Carefully read this SOFTWARE LICENCE AGREEMENT before continuing. By opening/using the Software you accept and agree to comply with the terms and conditions of this Agreement. If you do not agree with these terms and conditions, contact Medimetrics for directions on how to return your software package.

Software Licence Agreement

1. Software: As used herein SOFTWARE shall mean the IntelliCap Data viewing software supplied with and designed for use with IntelliCap System products.
2. Grant of License: Medimetrics grants you the right to use its software, which may include "online" or "electronic" documents.
3. Upgrades: If the SOFTWARE is an upgrade, the same GRANT OF LICENCE rules apply as if the SOFTWARE were an original installation.
4. Copyright: the SOFTWARE (including any images, configuration files, documents, text, resource files, photographs, animations, video, audio, or music incorporated into the SOFTWARE) is owned by Medimetrics and is protected by European Copyright laws and international treaty provisions. Therefore, you must treat the SOFTWARE like any other copyrighted material (e.g., a book or musical recording) except that you may either (a) make one copy of the SOFTWARE solely for backup or archival purposes, or (b) transfer the SOFTWARE to a single hard disk provided you keep the original solely for backup or archival purposes. You may only copy the printed materials accompanying the SOFTWARE after obtaining written permission exclusively from Medimetrics.
5. Other restrictions: You may not rent or lease the SOFTWARE, but you may transfer the SOFTWARE and user documentation on a permanent basis provided you retain no copies and the recipient agrees to the terms of the AGREEMENT. You may not reverse engineer, decompile, disassemble, or otherwise reduce the SOFTWARE to a human-perceivable form, nor permit anyone else to do so. You may not modify, distribute of create derivate works based upon the SOFTWARE in whole or in part without the written permission of Medimetrics.

3. Intended Use

The IntelliCap system is an in-vivo measurement system of pH and temperature in the gastrointestinal (GI) tract of humans and mammals, in order to facilitate delivery of a compatible compound in sections of GI tract, as a tool for premarket drug research.

The IntelliCap system is used as a tool for premarket drug research. The IntelliCap system is to be operated by trained physicians and personnel. All persons using or operating the equipment shall receive instruction and training from a member of Medimetrics. This manual serves as a reference for operation, technical information, and standardization of procedures.

4. Contraindications

The IntelliCap Capsule is an indigestible capsule-shaped object measuring 11 mm in diameter and 26.7 mm in length. Subjects who are unable to swallow the capsule or who present risk for retention of the capsule should be excluded for use. Further as the system operates with wireless RF communication the possibility for interference with implanted electro-medical devices should be avoided. The following contraindications apply:

- Subjects with known or suspected gastrointestinal strictures, including (suspected) Crohn's disease
- Subjects with swallowing disorders
- Subjects using acid reducing medication
- Subjects using NSAID' s
- Subject with known cardiopulmonary or any other gastrointestinal disorders
- Subjects with ASA > 1

5. Restrictions

The IntelliCap Capsule shall not be loaded with toxic or poisonous substances

The IntelliCap Capsule shall only be loaded with substances positively tested for compatibility and stability

The IntelliCap Capsule shall not be ingested by subjects with pacemakers or other implanted electro-medical devices

Subjects shall not be allowed to undergo MRI studies while the IntelliCap Capsule is in the body

6. Product Description

Each IntelliCap system consists of one Control Center, one or more portable units and one or more (up to 8 connected on one frequency channel) IntelliCap capsules. The Control Center is a personal computer that manages the environment. It provides the user interface for programming, initialization, interactive control, monitoring and evaluation of IntelliCap operation. The system structure is shown in Figure 1.

The Control Center communicates with each IntelliCap via a portable unit, which is placed in close proximity to the test subject. The portable units relay communication between IntelliCaps and the Control Center during the operation. The Control Center can communicate with multiple portable units. Nominally each portable unit addresses only one assigned pill. It is possible that more than one pill can be assigned to a given portable unit. This allows a single portable unit to handle more than one capsule in the body of a test subject. Additionally one capsule may communicate to more than one portable unit. This allows redundancy of receivers to reduce the chances of missed data packets.

The IntelliCap itself is an ingestible compound-delivery capsule containing a medication compartment, actuator, sensors, and wireless communication under control of a microprocessor. The IntelliCap consists of an electronic compartment and a drug medication compartment. The electronic compartment consists of a pH sensor, an integrated programmable microprocessor with a wireless transceiver, an antenna and a temperature sensor, an electrical stepper motor and batteries. The medication compartment consists of a 275 µl (nominal volume) drug

reservoir and a dispensing hole. The contents of the drug reservoir can be expelled by actuation of the stepper motor.

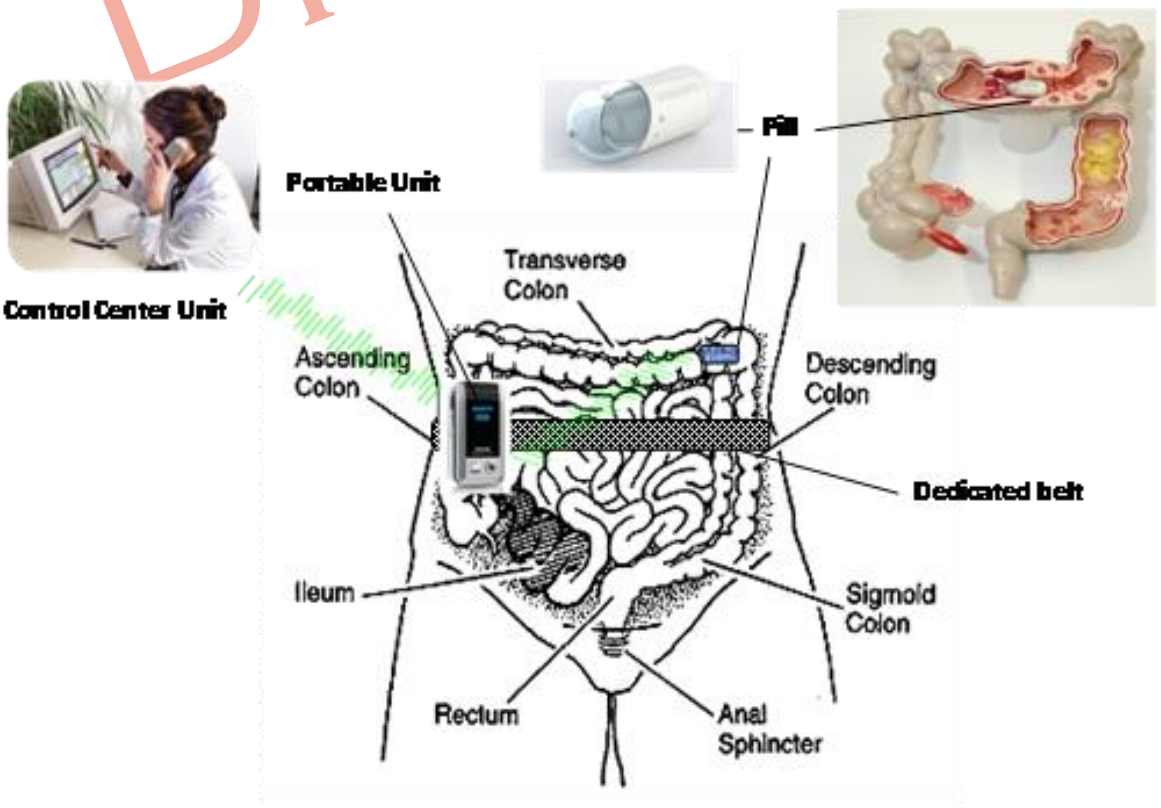


Figure 1: Schematic diagram of the IntelliCap system and communication channels.

A diagram of the IntelliCap capsule is shown in Figure 2. The diagram illustrates the mechanical layout of the capsule and identifies the main elements. The capsule house is made of a biocompatible polyethylene shell. A medication compartment is defined by the outer shell and flexible foil seal. An electrical motor pushes a piston forward thereby displacing the liquid drug out from an exit hole. The capsule is powered by a pair of primary cell silver oxide batteries. The batteries are not rechargeable and each IntelliCap capsule is a single use device. The capsule contains a pH sensor and a temperature sensor. A wireless transceiver is included for data communication between the IntelliCap inside the body and a portable unit (PU) which the patient carries outside the body.

The IntelliCap can be programmed to deliver a specific volume of drugs in a pre-set time frame, triggered by a change in pH. This change of pH presumably reflects transit of the IntelliCap from stomach (pH 1-4) to

duodenum (pH 7-8) and further on transit form ileum (pH 7-8) to cecum (pH 4-5). The IntelliCap can be programmed to expel its contents triggered by a change in pH, after a given programmable time at a given programmable rate. The IntelliCap's status (time, temperature, pH, expulsion status, battery voltage) can be monitored on a control station that is wirelessly connected to the IntelliCap through a portable unit worn by the test subject. The IntelliCap can be programmed to perform various release profiles such as single burst profile, dual burst profile or sustained release profile, triggered by a change of pH of >2 units.

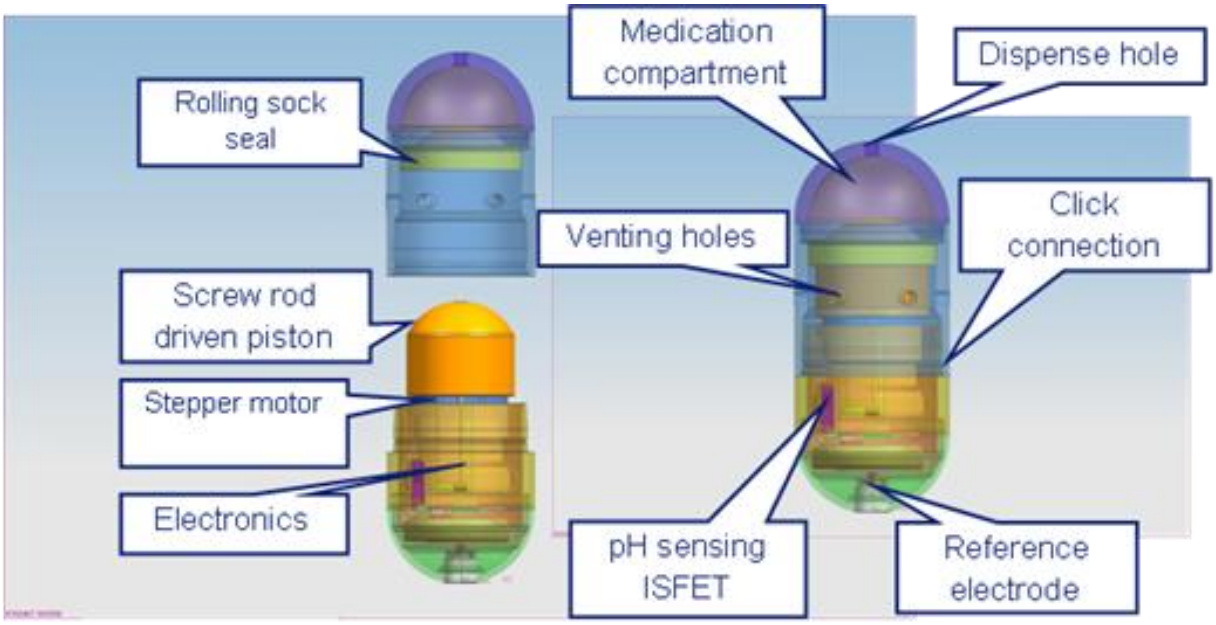


Figure 2: Diagram of the IntelliCap capsule showing mechanical layout and the main components.

The portable unit is the means for communication with the IntelliCap during an experiment. Communication between an IntelliCap and a portable unit uses RF frequencies nominally around 400-440 MHz (MICS band 402-405MHz or ISM band 432-434MHz). This range is chosen to limit attenuation of high frequency RF signals in the body. Since RF signals are strongly attenuated through the body, the portable unit must be in close proximity to the test subject. The portable unit has on-board recording memory so that all data can be retrieved even if real-time data transmission is interrupted.

The IntelliCap and the portable unit are battery powered devices and are designed in such a way that the operational lifetime is at least 48 Hours. In order to have an optimal power savings the communication links (Pill – Portable Unit and Portable Unit – Control Center) are not continuously present. In a normal operational situation the Pill measures data once in 10 seconds and sends it to the portable unit, and eventually receives commands back. The portable unit exchanges data with the Control Center also once in 10 seconds.

In normal operation commands from the control center are transmitted via the portable unit to the Pill. Due to substantial signal loss of RF signals propagating in body tissue, the signal strength is weak and pushes detection limits. Thus there exists the possibility for lost transmissions. Experimental design and software operation are made such that the loss of occasional transmissions shall not compromise the validity of the experiment (e.g. one out of six data packets received – i.e. one reliable data packet per minute).

Communication between the Control Center and a portable unit is accomplished by an AMBER module, which uses a well accepted wireless communication protocols in ISM (free bands). Separate modules are available operating at 868MHz or at 2.4 GHz. The used Amber module is a commercially one that works in a so-called transparent mode (all communication firmware already build in) and has a CE certification.

7. IntelliCap System Components

7.1 Control Center PC

The system is primarily controlled and operated from a notebook PC called the Control Center (CC). Software will be pre-installed by Medimetrics personnel who will check the specifications of the commercial notebook PC for compatibility. A notebook PC shall meet the following minimum requirement:

CPU 1.6GHz, RAM 2GB, Com ports: 4 USB, Operation System Microsoft Windows XP Professional Service Pack 3, with Microsoft .NET Framework 3.5 installed.

For example, control Center operation has been verified on a commercial notebook PC with the following characteristics:

Processor:	Intel Core2 Duo CPU P8700 @ 2.53GHz
RAM:	3.45 GB
Com ports:	4 USB ports
Operating System:	Microsoft Windows XP Professional, Service Pack 3

Software

The Data viewing software application is specifically designed to be used with the IntelliCap System. Additional information concerning detailed operation of the software may be found in separate documentation not included with this system user manual. Basic operation of the IntelliCap System is covered here. With the Data viewing software the user is able to:

- Initialize an IntelliCap Capsule with the behavior profile
- Establish a data communication link with a Portable Unit
- Activate an IntelliCap Capsule
- Enter pH calibration data for a given IntelliCap Capsule
- Continuously present the following parameters graphically and/or numerically on screen:
  - pH Data: ADC reading and calibrated value
  - Temperature of IntelliCap Capsule
  - Battery reading of IntelliCap Capsule
- Command an IntelliCap Capsule to advance to the next program segment
- Shut down an IntelliCap Capsule

- Import experiment data from previous data log files
- Export experiment data for analysis in external programs

7.2 Start Up Unit

The IntelliCap Capsules are initialized and activated by a Start Up Unit (SUU). The SUU is connected to the Control Center PC by a USB cable. The SUU incorporates a start up coil for inductively coupling energy to an IntelliCap capsule. Upon start up the IntelliCap Capsule closes a switch for connection to its internal battery power. The SUU is able to communicate wirelessly to an IntelliCap capsule. This communication link is also used to initialize the capsule. Initialization is the process of loading the capsule with the desired behavior profile. A photograph of a Start Up Unit is shown in Figure 3.

Figure 3: Photograph of a Start Up Unit used to activate and initialize IntelliCap Capsules.

7.3 Portable Unit

The Portable Unit (PU) is the main means for communication with an IntelliCap capsule during the execution of an experiment. The PU can communicate with both the IntelliCap capsule and the Control Center. As the communication range of the IntelliCap Capsule is limited a transceiver unit must be placed near the test subject. A photograph of a Portable Unit is shown in Figure 4.

Figure 4: Photograph of a Portable Unit used for communication between an IntelliCap Capsule and the Control Center PC. An Amber USB Adapter is used for wireless communication between the Control Center PC and a Portable Unit.

The PU is a relatively small and lightweight unit that may be worn by a test subject on a belt or specially designed holder. The holder may be fit comfortably about the waist of a person and contains a pocket for housing a PU. Data is stored locally on the PU and is additionally relayed to the Control Center for immediate visualization and analysis. Data stored in the PU memory is primarily for redundancy and to collect data when the subject exits the test environment. The data can be downloaded by direct connection via USB cable between the PU and Control Center. This operation is intended to occur after the end of an experiment as the PU cannot receive data from an IntelliCap capsule while downloading data via the wired connection.

Amber Module

An Amber Wireless M-Bus USB Adapter AMB8465 (868 MHz) or AMB2560 (2.4 GHz) is connected to the Control Center PC. The purpose of the Amber module is for low power wireless communication to the Portable Unit. The Portable Unit is configured with a matching module for wireless communication with the Control Center PC. The USB Adapter is a product of Amber Wireless GmbH, Colonge, Germany. The Amber USB Adapter and Control Center PC have been pre-configured for operation with the IntelliCap System. A photograph of an Amber USB Adapter is shown in Figure 4 as well.

7.4 IntelliCap Capsule

The purpose of the IntelliCap Capsule is to measure conditions of its local environment and to deliver the contents of a medicine reservoir. The IntelliCap Capsule is prepared by loading the medicine reservoir with the target medication and initializing it with the desired behavior profile. The IntelliCap Capsule is also calibrated for accuracy of the pH readings. The capsule is activated at a Start Up Unit and then used for an experiment. The capsule is swallowed by a test subject and passes naturally through the digestive tract. It is excreted. As needed the IntelliCap capsule will be recovered after excretion by the test subject. The recovered capsule can be cleaned and observed for properties such as condition of the medicine

reservoir or post-recovery calibration of the pH sensor. A photograph of an IntelliCap Capsule is shown in Figure 5.

Figure 5: Photograph of an IntelliCap Capsule used for drug delivery and monitoring in a test subject.

8. Data security and privacy

The IntelliCap System provides a secure repository for your information. The Control Center PC contains an encrypted hard drive and can only be accessed by an authorized user through password entry. The Data viewing Software stores data in a log file and can output data to a formatted Excel file. Collected data relates specifically to an individual test subject. Local laws governing the privacy and handling of data shall be followed. Data files should be noted by subject number only and should never contain direct information on the name or other personal information of the test person.

9. Warnings

- Clinical use of the IntelliCap System is restricted to trained personnel.
- Components and software of the IntelliCap System are optimized for use together. DO NOT CONNECT OTHER MACHINES, DEVICES TO THE START UP UNIT, PORTABLE UNIT, CONTROL CENTER PC OR ITS ACCESSORIES because damage to IntelliCap system, devices, the user or the patient may occur.
- NEVER USE THE PORTABLE UNIT ON A PATIENT WHEN CONNECTED TO THE MAINS FOR CHARGING OR ANY OTHER REASON. SERIOUS INJURY TO THE PATIENT MAY OCCUR.
- Safe and effective use of this device requires proper set-up and operation by trained personnel.
- The use of other cables and/or power supplies can cause damage to the IntelliCap System, the devices, the user or the patient.
- The IntelliCap System should only be used by trained personnel.
- Risk of electrical shock; do not attempt to service electrical components; refer servicing to qualified personnel.
- When handling the IntelliCap Capsule the operator shall put on a fresh pair of gloves. Failure to observe this procedure risks transmission of microbial contaminants to the patient who swallows the IntelliCap Capsule.
- After its use the IntelliCap Capsule shall not be reused.

10. Cautions

- Read all instructions prior to use.
- Physicians responsible for using the IntelliCap System must be trained in the system and be aware of the inherent risks of misinterpretation of the collected and displayed parameters.
- Do not use if any of the components is visibly opened or damaged.
- Check all parts prior to use.

11. Safety

Safety features for the IntelliCap System are monitored and controlled by internal hardware and software checks. These features provide an independent mechanism to monitor and react to system faults. Indications of system status are provided both at the Portable Unit and from the Software operating on the Control Center PC.

11.1 Portable Unit Indicators

The Portable Unit has LED indicator lights to monitor status and display to the subject or system operator. The Portable Unit may have the following indications:

- Power On/Off;
  - When power is switched on and the Portable Unit operating, the "Power" LED will be will be constantly lit.
  - When power is switched off, the "Power" LED will be off.

  WARNING: NEVER USE THE PORTABLE UNIT ON A PATIENT WHEN CONNECTED TO THE MAINS FOR CHARGING OR ANY OTHER REASON. SERIOUS INJURY TO THE PATIENT MAY OCCUR.

11.2 Control Center Indicators

Software running on the Control Center provides indicator messages to the operator to inform of system status and operation. The following messages should be monitored:

- Status Portable Unit;

- The main Data viewing form shows the status of the portable unit in a line in the top grouping see for example Figure 6.
- DestinationNetworkUnreachable: Communication with the network device cannot be established. The operator should check the Amber Unit and/or settings in the "Config" dialog box.
- TimedOut: Communication with the Portable Unit cannot be established. The operator should check the Portable Unit and/or settings in the "Config" dialog box.
- NotAvailable: Communication with the Portable Unit cannot be established. The operator should check the Portable Unit and/or settings in the "Config" dialog box.
- Available: Communication with the Portable Unit is operating normally.

• Pill Activated message box;

- When an IntelliCap is successfully activated at the Start Up Unit a message box pops up on the screen. The operator should click the "OK" button to dismiss.

12. Utilization of IntelliCap

The IntelliCap system is used for investigative studies with test subjects. The test subjects are evaluated for inclusion in the study. An attending physician nurse or other medical personnel trained in the use of the IntelliCap system directs the subjects for their use and interaction with the IntelliCap system components: the capsule, the portable unit, the belt, and any other ancillary equipment. Additionally the attending medical personnel are assisted by Medimetrics personnel with the set-up and operation of the IntelliCap system. The exact procedures will vary with each study as described in the protocol. Typical actions for use of the system are described below.

- Medimetrics personnel set up the IntelliCap system in the study environment
- Medimetrics personnel prepare the capsules for use including initialization, pH-sensor calibration, and activation of capsules
- A portable unit is prepared by Medimetrics personnel and placed into a belt
- The belt is given to the test subject for fitting around the abdomen
- Activated capsules are handed to the attending medical personnel
- Attending medical personnel provides the capsule to the test subject
- Test subjects swallow the capsule along with a glass of water
- Data is recorded at the control center PC
- The subject remains in a defined area near the control center PC
- Manual commands may be given from the control center PC to control action of the capsule if called for in the study design
- Depending on the study design the test subject may be allowed to leave the test area after a certain period of time. While the capsule is still in the body the belt with portable unit shall still be worn.
- The subject may remove the belt with portable unit for short periods of time for clothing change, bathing, etc. The belt and portable unit should not be submerged in water or worn in the shower.
- The belt with portable unit may be removed for sleeping and placed close to the subject's bed
- The subject may be requested to recover the capsule from feces after a bowel movement
- After the capsule is recovered from feces the belt may be removed

- The subject will report back to attending study personnel to confirm exit of the capsule from the body. At this time the belt and portable unit are returned.

WARNING: THE INTELLICAP SYSTEM IS EXCLUSIVELY FOR INVESTIGATION PURPOSES FOR USE IN A RESEARCH SETTING UNDER A PROPERLY APPROVED PROTOCOL. ALL SYSTEM COMPONENTS MUST BE RETURNED TO MEDIMETRICS PERSONNEL AT THE CONCLUSION OF THE STUDY.

13. Recovery and Disposal of the IntelliCap Capsule

In most cases the study protocol aims to recover the used IntelliCap capsule from the feces after excretion. As part of instruction test subjects will be taught how to recover capsules from the feces. In case the subject is allowed to leave the study premises ancillary equipment will be provided along with instructions on how to recover, isolate, and package the capsule for return to attendant personnel. A clean sealable container will be provided to house the recovered capsule. Any recovered capsule must be returned to attendant personnel. Medimetrics will take possession of used capsules and will process and dispose of the capsule in compliance to applicable regulations.

WARNING: THE INTELLICAP CAPSULE IS A SINGLE USE DEVICE. NO REUSE IS POSSIBLE. THE RECOVERED CAPSULE REPRESENTS A HAZARD AS BIOLOGICAL MATERIAL MAY BE ETRAINED. FURTHER THE CAPSULE MAY HOLD NON-EXPELLED DRUG SUBSTANCE THAT MAY POSE ADDITIONAL HAZARDS. MEDIMETRICS WILL TAKE POSSESSION OF PROCESS AND DISPOSE OF ALL USED CAPSULES.

14. Data Viewing Software

The IntelliCap system is designed to work with execution and control managed by a Control Center Personal Computer. A software application designed for the IntelliCap System is pre-installed on the Control Center. The software application is named PCApplications.exe. A shortcut to directory is provided on the desktop. Further details concerning the software are included in a separate IntelliCap Software manual. Instructions in this user manual cover the primary operations used in an IntelliCap System experiment.

Starting the IntelliCap Software

1. Locate the shortcut on the desktop named for example "PCApplications 2.0.0.NN", where NN is the current version number of the software. In case multiple versions exist and no other instructions are present use the latest version with the largest revision number. Open the folder by double clicking the icon.
2. Locate the file named PCApplications.exe.
3. Launch the IntelliCap Software by double clicking the application icon.
4. A window opens titled for example "Data viewing [PUnit aa][Local bb]" where aa is the assigned IP address of the Portable Unit and bb is the assigned IP address of the current window. In most cases connection is made to the Portable Unit with the Amber module operating on a serial COM port. When configured for this operation the window title is for example "Data viewing [PUnit serial COMn]" where n is the assigned COM port of the Amber USB adapter. The current software limits the maximum COM port number to 9.
5. Configuring and operating the IntelliCap System through the software interface is described in below.

Note: Multiple instances of the IntelliCap data viewing software can be opened simultaneously. This allows control of more than one portable unit from one PC. There is a one to one correspondence between an open Data viewing window and an active Portable Unit.

The main window for the IntelliCap System software is the Data viewing form. An example of this form and location of the main elements are illustrated in Figure 6. This main Data viewing form is groups into the following main areas:

- Title Bar: Windows title bar.
- Configuration Control: Grouping of information and control buttons to configure the Control Center for pairing with external equipment, storing data, calibrating pH, and controlling Experiment Events.
- Graphical Data Display: Current data is presented in graphical form. One data type at a time is displayed as selected from the check boxes.
- User Annotation Box: The use may add a text line annotation into the log file.
- Reporting Text Box: Actions and received data are reported in this text box with a time stamp.
- Command Buttons: Actions that may be commanded from the Control Center.

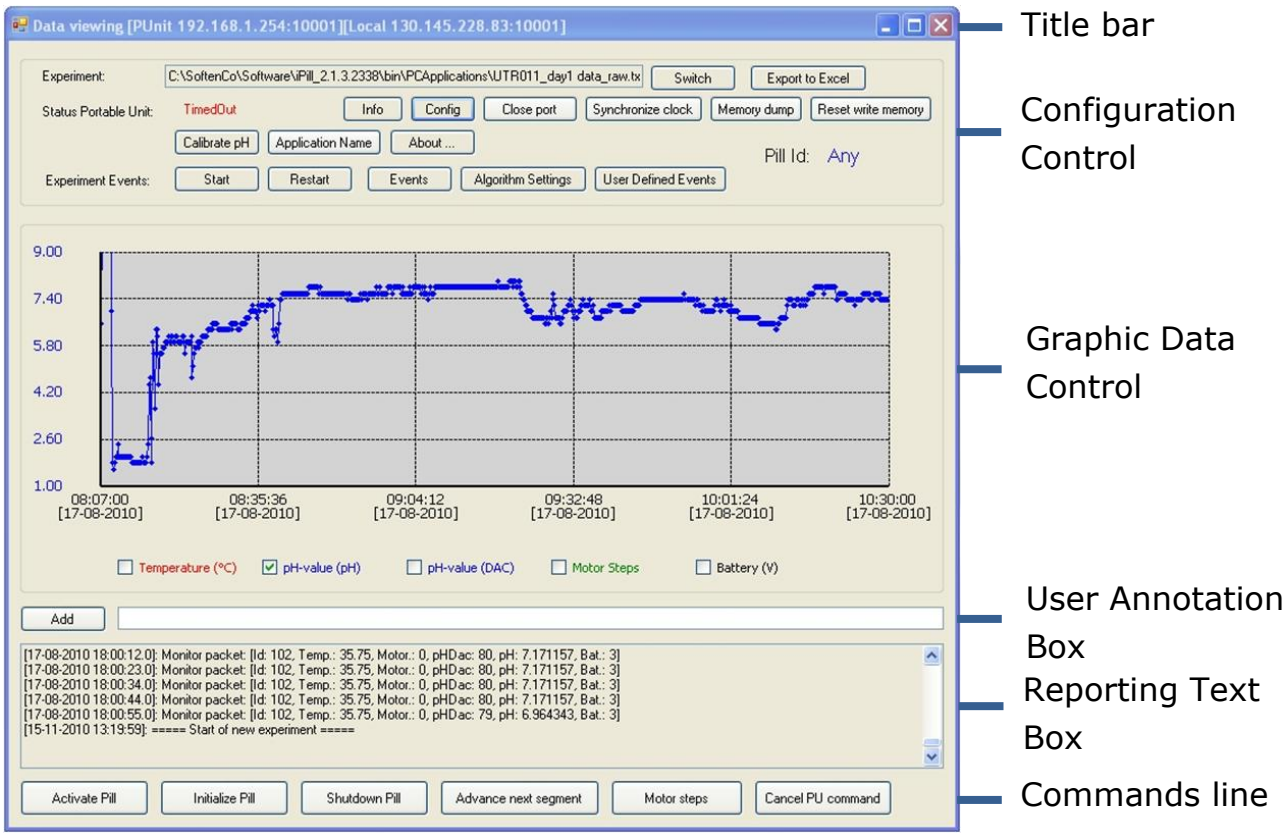


Figure 6. Example of the Data viewing form that is the main window for the IntelliCap System software.

15. Parts & Supplies

The IntelliCap System consists of several parts. Additionally, different accessories are available. These accessories are OPTIONAL.

PRODUCT CODE AND UNIT DESCRIPTION

Part number	Description	Number used per set up
PARTS		
Control Center PC	Personal Computer with installed IntelliCap Software	1
Amber adapter	USB dongle for communication to the Portable Unit(s)	1 per PU
Start Up Unit	Electronic unit for initialization and activation of IntelliCap capsules	1
Portable Unit (PU)	Electronic unit for communication with the IntelliCap Capsule and Control Center	Up to 4
IntelliCap Capsule	Swallowable capsule for monitoring and drug delivery	Up to 4
User Manual	IntelliCap System printed manual	1
ACCESSORIES		
Calibration buffers	Fluids for calibration of the pH sensor	1 to 3
Gloves	Gloves for handling of IntelliCap Capsules	
Holster for PU	Wearable holster for holding the PU near the body of a subject	1 per subject
Tweezers 70% IPA wetted wipes	Tweezers to for handling of IntelliCap Capsules Wipes for cleaning capsule body after calibration	

16. Capsule Preparation

The IntelliCap Capsule is manufactured, calibrated, and prepared for use in an experimental study. The initial pH calibration and loading of the medicine reservoir with the target payload are outside the scope of this user manual. The corresponding procedures are covered in separate standard operations procedure technical documents. A data sheet (produced within the calibration process) accompanies each IntelliCap capsule. The IntelliCap Capsule data sheet contains information including:

- IntelliCap Capsule serial number
- IntelliCap Capsule ID number used for programming and reporting
- Behaviour profile and communications frequency (or channel)
- Initial pH calibration
- Medicine payload information including type and weight

Capsules are delivered in dedicated storage vials as shown in Figure 7.

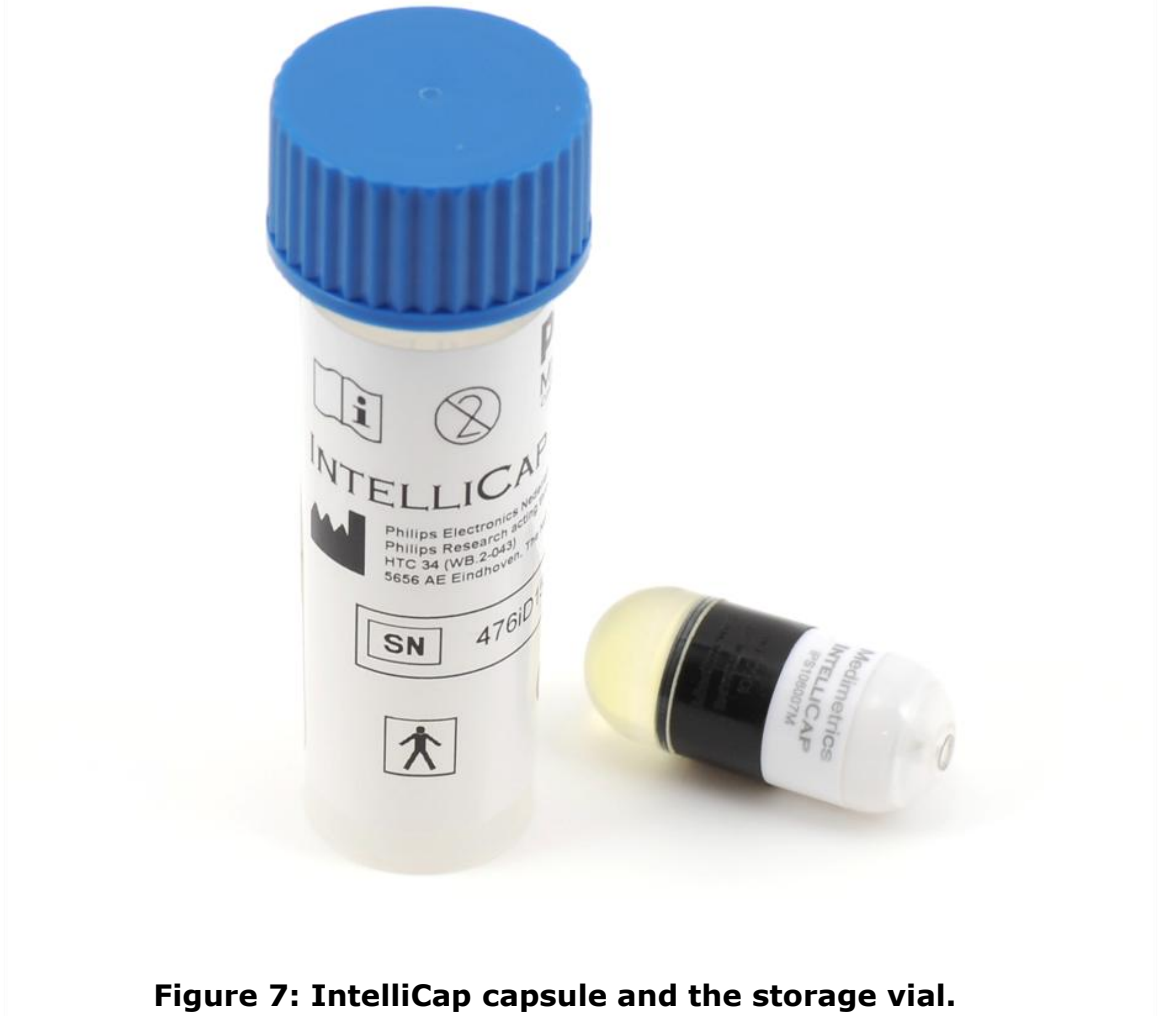


Figure 7: IntelliCap capsule and the storage vial.

17. Entering the pH Calibration Data

The pH calibration data can be entered at any time through the Data viewing application installed on the Control Center PC. The Control Center does not have to be connected to external equipment such as the Start Up Unit or a Portable Unit. Nor does the given IntelliCap Capsule need to be active. The pH calibration data is stored in the directory containing Data viewing software PCApplication.exe in a file named pHCalibration.csv. The pH calibration data is applied to all data displayed or exported according to ID of capsules. Data from the calibration file is read every time the Data viewing application is launched. So the calibration data does not have to be entered each time a Data viewing application window is opened. To enter or override the pH calibration data execute the following:

1. Open the directory PCApplications and launch the Data viewing application titled PCApplications.exe
2. Open the pH Calibration form by clicking the "Calibrate" button located in the upper control group.
3. Enter the ID of the IntelliCap Capsule. The ID number is given on the data sheet accompanying the IntelliCap Capsule. It is an integer between 0 and 255.
4. The pH data may be calibrated by 1, 2, or 3 points. Start entering data for Point 1 by clicking the check box and entering data for the pH DAC value and pH value.
5. Proceed to enter data for Points 2 and 3 if available. The order in which the data is entered does not matter. That is, for example, there is no assumption that Point 1 is the smallest value.
6. Click "Ok".

18. IntelliCap Capsule Initialization

The IntelliCap Capsule comes loaded with a pre-determined behaviour profile and operating communication channel. This behaviour profile may be changed if desired by the operator. The process of changing or programming the IntelliCap Capsule behaviour profile is called

Initialization. To initialize an IntelliCap Capsule the system must be configured with the following components:

- Control Center PC with IntelliCap data viewing application, PCApplications.exe pre-installed
- Start Up Unit connected to the Control Center PC by USB cable
- USB cable connected between the Control Center and Start Up Unit
- IntelliCap capsule

The procedure to initialize the IntelliCap Capsule and change the behaviour profile is as follows:

1. Open the directory PCApplications and launch the Data viewing application titled PCApplications.exe
2. Open the communications Configuration form by clicking the "Config" button located in the upper control group.
3. In the Portable Unit control group click the radio button titled "Portable Unit Serial". Select the appropriate COM port from the drop down list, for example COM8.
4. Click "Ok".
5. In the upper control group Status Portable Unit changes to Available.
6. Open the start up unit by removing the cover.
7. Place the IntelliCap Capsule while in the storage vial into the Start Up Unit. The pH sensor window (ISFET) of the IntelliCap Capsule should face towards the center of the start up coil as shown in Figure 8. Place the cover back on the Start Up Unit.
8. The command button group is at the bottom of the window. Click "Initialize Pill".
9. Choose the desired behaviour segments from the drop down lists in the InitializationForm.
10. Click "Initialize".
11. After a few seconds the IntelliCap Capsule starts up. Capsule activation is reported in the text box of the Data viewing form with a message such as: Activation packet: [Id: 147, Frequency 402.45 (MICS), Battery level: 3, Initialized: True, Profile segments: 1 0 1 0]
12. Next an acknowledgement of initialization is reported in a message box that pops up with a message such as: Pill initialized. Id: 147, Freq: 402.45 (MICS).

13. Click "Ok" to dismiss the message box.
14. Initialization is also reported in the text box of the Data viewing form with a message such as: InitializeAck Packet: [segments: 1, 0, 1, 0, frequency 402.45 (MICS)]
15. Next the IntelliCap Capsule shuts down and is reported in the text box with a message such as: Deactivation packet: [Id: 147, Motor Steps: 0, Temperature 10, Battery Level 3]
16. The IntelliCap capsule was successfully initialized (programmed for the behaviour profile).
17. If the messages were not reported successfully or as desired the process may be repeated.

Note: After shut down the IntelliCap Capsule cannot be immediately restarted. Wait 10 minutes after shut down before attempting to Initialize or Activate an IntelliCap Capsule after shut down.

Figure 8: Picture of IntelliCap Capsule in a storage vial on the SUU properly placed for capsule Initialization or Activation.

19. Pairing the Control Center to a PU

The basic set up of the IntelliCap system is shown in Figure 1. Typically there is a one-to-one pairing of a Portable Unit (PU) with an IntelliCap Capsule. Further there must be a one-to-one pairing of an active application window at the Control Center with a PU. So for example if the Control Center is controlling 3 PUs then 3 instanced of the Data viewing application, PCApplications.exe, will be running. The application window is paired to PU as follows:

1. Open the directory PCApplications and launch the Data viewing application titled PCApplications.exe
2. Connect an Amber USB dongle to the Control Center PC by inserting it into an available USB port.
3. Open the communications Configuration form by clicking the "Config" button located in the upper control group.
4. In the Portable Unit control group click the radio button titled "Portable Unit Serial". Select the appropriate COM port from the drop down list, for example COM5.
5. Click "Ok".
6. In the upper control group Status Portable Unit shows Not Available when the Portable Unit is not turned on.
7. Turn on the power to the Portable Unit that is matched to the Amber USB Adapter connected to the COM port selected in step 4.
8. In the upper control group Status Portable Unit changes to Available.
9. Repeat steps 1-8 for all desired Portable Units. Do not close the Data viewing application window for the previous application/PU pair.

20. Activating an IntelliCap Capsule

The IntelliCap Capsule is shipped in an inactive state consuming no power. The process of starting up an IntelliCap Capsule and connecting it to its internal power source is called Activation. To activate an IntelliCap Capsule the system must be configured with the following components:

- Control Center PC with IntelliCap data viewing application, PCApplications.exe pre-installed
- Start Up Unit connected to the Control Center PC by USB cable
- USB cable connected between the Control Center and Start Up Unit
- IntelliCap capsule

The procedure to activate the IntelliCap Capsule and change the behavior profile is as follows:

1. Open the directory PCApplications and launch the Data viewing application titled PCApplications.exe
2. Open the communications Configuration form by clicking the "Config" button located in the upper control group.
3. In the Portable Unit control group click the radio button titled "Portable Unit Serial". Select the appropriate COM port from the drop down list, for example COM8.
4. Click "Ok".
5. In the upper control group Status Portable Unit changes to Available.
6. Open the start up unit by removing the cover.
7. Place the IntelliCap Capsule while in the storage vial into the Start Up Unit. The pH sensor window (ISFET) of the IntelliCap Capsule should face towards the center of the startup coil. Place the cover back on the Start Up Unit.
8. The command button group is at the bottom of the window. Click "Activate Pill".
9. After a few seconds the IntelliCap Capsule starts up. Capsule activation is reported in a message box that pops up with a message such as: Pill activated. (id: 147)
10. Click "Ok" to dismiss the message box.
11. In addition the activation packet is reported in the text box of the Data viewing form with a message such as: Activation packet: [Id: 147, Frequency 402.45 (MICS), Battery level: 3, Initialized: True, Profile segments: 1 0 1 0]
12. Note the Frequency and Pill ID of the IntelliCap Capsule. This information should match the data sheet provided with the capsule. This information is needed to pair the IntelliCap Capsule to the Control Center through a Portable Unit.

13. Receipt of the activation packet automatically causes the Start Up Unit to switch to the proper channel for communication with the IntelliCap Capsule.
14. Depending on the behavior profile programmed onto the capsule, there will be a delay and then monitor packets will be received at the Control Center. The data will be reported in the text window and the graph updated every time a packet is received.
15. The IntelliCap Capsule is activated and continues to operate according to the programmed behavior profile.

Note: After shut down the IntelliCap Capsule can not be immediately restarted. Wait 10 minutes after shut down before attempting to Initialize or Active an IntelliCap Capsule after shut down.

21. Pairing the Control Center to an IntelliCap Capsule

The basic set up of the IntelliCap system is shown in Figure 1. Typically there is a one-to-one pairing of a Portable Unit (PU) with an IntelliCap Capsule. Further there must be a one-to-one pairing of an active application window at the Control Center with a PU. In order to view data from a given IntelliCap Capsule it must be paired with both the PU and the Data viewing application on the Control Center. This pairing is typically done manually where the Frequency and Pill ID of the IntelliCap Capsule is known.

21.1 Manual Pairing of IntelliCap Capsule / Portable Unit / Control Center

1. Pair the Control Center Data viewing application to desired Portable Unit as described above. Leave this Data viewing window open.
2. Activate an IntelliCap Capsule with the Start Up Unit as described above. Note the channel and Pill ID of the IntelliCap Capsule.
3. Switch focus to the Data viewing window paired with the desired Portable Unit.
4. Open the communications Configuration form by clicking the "Config" button located in the upper control group.
5. On top of the form enter the Pill ID.

6. In the Portable Unit field grouping click the check box at "Change PU frequency".
7. Choose the frequency from the drop down list.
8. Click "Ok".
9. After a delay of up to 20 sec confirmation of the frequency selection is reported in a message box with a message such as "Set frequency of Portable Unit. Ack received. Frequency: n", where n is the channel number selected.
10. Click "Ok" to dismiss the message box.
11. Data packets from sent from the IntelliCap Capsule will be reported in the text box and the graph updated.

Note: The Pill ID is used to filter the data displayed in the Data viewing window. Alternatively the Pill ID may be set to "Any". In this case data from any IntelliCap Capsule received by the PU will be reported in the application. The IntelliCap Capsule must be operating at the same frequency the PU is set to be received.

It is possible to automatically pair the Control Center and Portable Unit to an IntelliCap Capsule. To do this the Portable Unit must be able to receive wireless data from the IntelliCap Capsule while it is on the Start Up Unit.

21.2 Automatic Pairing on Activation

1. Link the Control Center PC to a Portable Unit as described above.
2. Pair a Control Center Data viewing window to the Portable Unit as described above.
3. Place focus on the Data viewing window associated with the Portable Unit.
4. Click Activate Pill.
5. Acknowledgment of the packet is confirmed in the text box with a data line such as [date time]: Portable unit Ack packet: 5.
6. Leave the Data viewing window associated with the PU open.
7. Launch another Data viewing window for the Start Up Unit and Activate the IntelliCap Capsule as described above.

8. The activation packet should be received and reported in both the Data viewing window paired with the Start Up Unit and the Data viewing window paired with the Portable Unit.
9. Data packets sent by the IntelliCap Capsule are recorded and reported in both Data viewing windows.

Note: When the Activate Pill command is sent to the Portable Unit that Portable Unit changes to Channel 0 and waits for an activation packet. The Portable Unit continues to wait for the activation packet until another command is sent including for example the Cancel PU command.

22. Data Storage and Review

All data received or actions commanded are reported in the Data viewing application on the Control Center PC in the text box near the bottom of the window. The last several lines of data are displayed and earlier data can be examined by control of the scroll bar. Further all messages displayed in the text box are recorded in a log file. The log file is a text file stored on the PC. By default the log file is named receivedPackets.txt and is stored in the same directory that contains the application file PCApplications.exe. The operator has the option of changing the name and location of the log file. Further the operator may export data to an Excel file for further analysis and data processing.

22.1 Changing the Data Log File

1. Place focus on an open Data viewing application window.
2. Near the top of the window click the "Switch" button.
3. A file selection form opens. Enter or select the desired file name.
4. Click "Open".
5. The location and name of the experiment log file is updated in the text box after Experiment: near the top of the Data viewing form.

Note: Changing the name of the data log files clears any past data from active memory and display. If an existing log file is chosen data from that file is read and displayed in the graph. In this manner past

experiment data may be reviewed and additional data may be appended to the log file.

22.2 Exporting Current Data to an Excel File

1. Place focus on an open Data viewing application window.
2. Near the top of the window click the "Export to Excel" button.
3. A file selection form opens. Enter or select the desired file name.
4. Click "Save".
5. The current data is saved in *.csv file.

Note: The current pH calibration values are applied to the pH data. New calibration or drift values can be applied to data in current memory. The new calibration and drift values are applied to data displayed on the pH-value (pH) graph but do not change data in the log file. They are applied to the data exported to the Excel *.csv file.

23. Commands to the IntelliCap Capsule

There are few of commands that can be sent to the IntelliCap Capsule from the Control Center. In order to send a command to an IntelliCap Capsule the Data viewing window must be paired to the capsule through a Portable Unit. Pairing the Control Center to an IntelliCap Capsule is described above. In order to send a command to an IntelliCap Capsule the correct Pill ID must be set. After setting the Pill ID the command may be issued from the Data viewing form. Available commands are grouped with the action buttons at the bottom of the window. Due to the power saving communications protocol a command is sent to the Portable Unit only after a monitor data packet is received or after a maximum wait period of about 20 sec. Further the command is held by the Portable Unit and send to the IntelliCap Capsule only after the capsule reports a data packet. Thus there is a built-in delay between sending the command from the Control Center and execution by the IntelliCap Capsule.

23.1 Setting the Pill ID

1. Place focus on the Data viewing application window paired with the desired Portable Unit.
2. Open the communications Configuration form by clicking the "Config" button located in the upper control group.
3. On top of the form enter the Pill ID.
4. Click "Ok".
5. The active Pill ID number is displayed in the top group on the right side.

23.2 Shutdown an IntelliCap Capsule

Shutdown of an IntelliCap Capsule disconnects the power source from the capsule electronics. The IntelliCap Capsule becomes inactive.

1. Place focus on the Data viewing application window paired with the desired Portable Unit.
2. Confirm or set the Pill ID for the desired IntelliCap Capsule.
3. At the bottom of the Data viewing form Click "Shutdown Pill".
4. Acknowledgement of command receipt at the Portable Unit is reported in the text box with a message such as [date time]: Portable unit Ack packet: 4.
5. A data monitor packet is received and displayed in the text box.
6. A deactivation packet is received and displayed in the text box.
7. The IntelliCap Capsule is inactive.

23.3 Advance to next program segment

The IntelliCap Capsule executes a behavior profile as programmed during Initialization. At any time the user may advance execution to the next program segment.

1. Place focus on the Data viewing application window paired with the desired Portable Unit.
2. Confirm or set the Pill ID for the desired IntelliCap Capsule.
3. At the bottom of the Data viewing form Click "Advance next segment".
4. Acknowledgement of command receipt at the Portable Unit is reported in the text box with a message such as [date time]: Portable unit Ack packet: 8.

5. A data monitor packet is received and displayed in the text box.
6. After a pause acknowledgement of program advance is reported in the text box with a message such as: MonitorAdvanceSegment packet: [Id: 147, CurrentSegmentCounter: 1, AutoAdvance: False]

23.4 Cancel command to the PU

Commands are first held at the Control Center and later at the Portable Unit before execution by the IntelliCap Capsule as described above. This command caching gives opportunity to cancel a command before it is sent to the IntelliCap Capsule.

1. Place focus on the Data viewing application window paired with the desired Portable Unit.
2. Confirm or set the Pill ID for the desired IntelliCap Capsule.
3. At the bottom of the Data viewing form Click "Cancel PU".
4. If the cached command is successfully canceled, a confirmation message is reported in a pup-up window. Otherwise, "Nothing canceled" is reported.

24. Maintenance of PU / CCU / SU unit

The following lists the recommended maintenance procedures should be followed:

Cleaning After Every Use

The IntelliCap System and its accessories should be cleaned after each use and/or after any spill of liquids. For routine cleaning, use only mild detergents and a humid soft cloth. The Portable Units should be disinfected after every use. For disinfecting wipe the equipment with an isopropyl alcohol solution or other proper surface disinfectant.

CAUTION: Ensure electrical power is **OFF** and line cord is disconnected from power source prior to cleaning. Do not use abrasive cleaning agents. Do not use solvents or strong alcohol solutions. Do not immerse any part of the interface or the accessories in liquids.

25. General Inspection Every Use

Visually check the condition of the all parts and the accessories before every use. Remove from service any unit and/or accessories that shows signs of physical damage.

26. Service

All service must be performed by Medimetrics or its authorized agents. For service, contact Medimetrics.

Medimetrics
Philips Research
High Tech Campus 34 (WB.2-043)
5656 AE Eindhoven
The Netherlands
Telephone: +31 40 27 49268

Medimetrics
Philips Research
345 Scarborough Road
Briarcliff Manor, NY 10510
Telephone: +1 914 945 6628

27. Product Changes

All products and product specifications are based upon information available at the time of publication. The right is reserved to discontinue any of these products or to change any such specifications without prior notice.

28. Technical Information

The IntelliCap System and its accessories are designed in accordance with the applicable harmonized international standards for medical devices.

29. Label

29.1 Capsule

Note: The IntelliCap serial number is formed by two numbers: the one on the electronic body (white part in the Figure 9) + the one on the medicine reservoir ring (black part in the Figure 9).

Figure 9: Laser engraving of the IntelliCap capsule

Laser engraving electronic body:

Medimetrics
INTELLICAP
iPSYYMXXXW

where

- "YY" – indicates the year (i.e. 00, …, 99)
- "M" – indicates the month (i.e. 1, 2, …, 9, A, B, C)
- "XXX" – indicates the serial number (i.e. 001, …, 999)
- "W" – indicates capsule type:
  - 'M' – test, PROTO, DEMO, mockup
  - 'F' – fully functional capsule

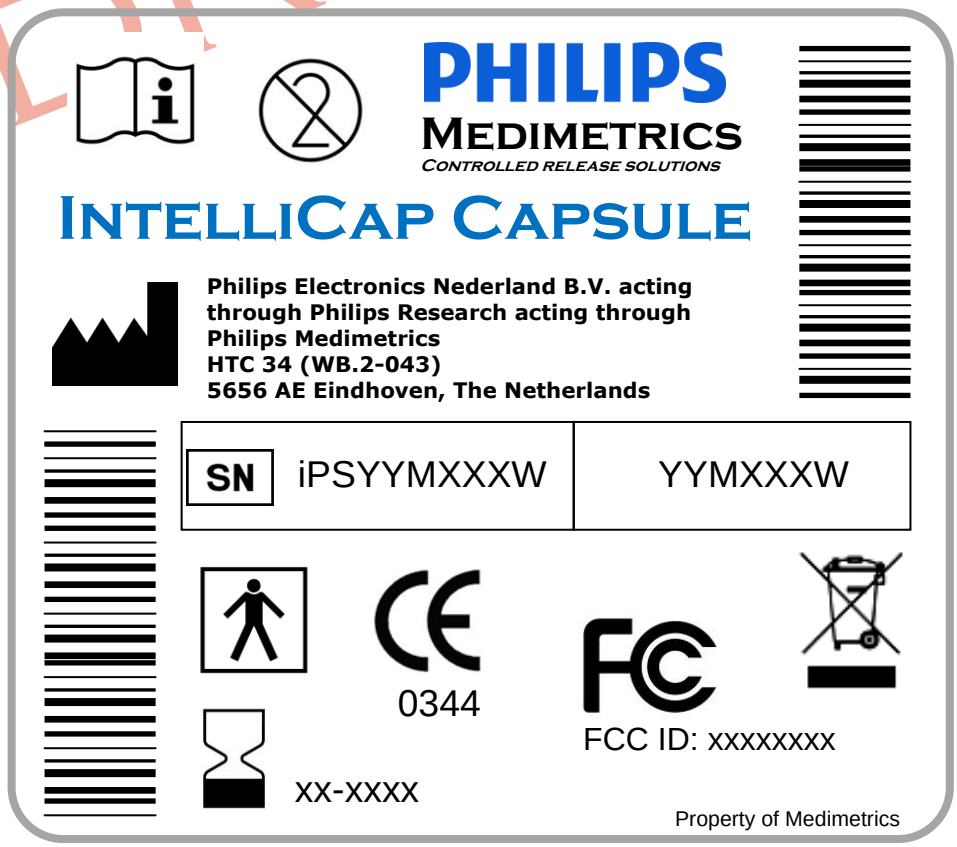
Laser engraving reservoir ring:

Medimetrics
INTELLICAP
YYMXXXW

where

- "YY" – indicates the year (i.e. 00, …, 99)
- "M" – indicates the month (i.e. 1, 2, …, 9, A, B, C)
- "XXX" – indicates the serial number (i.e. 001, …, 999)
- "W" – indicates capsule type:
  - 'M' – test, PROTO, DEMO, mockup
  - 'F' – fully functional capsule

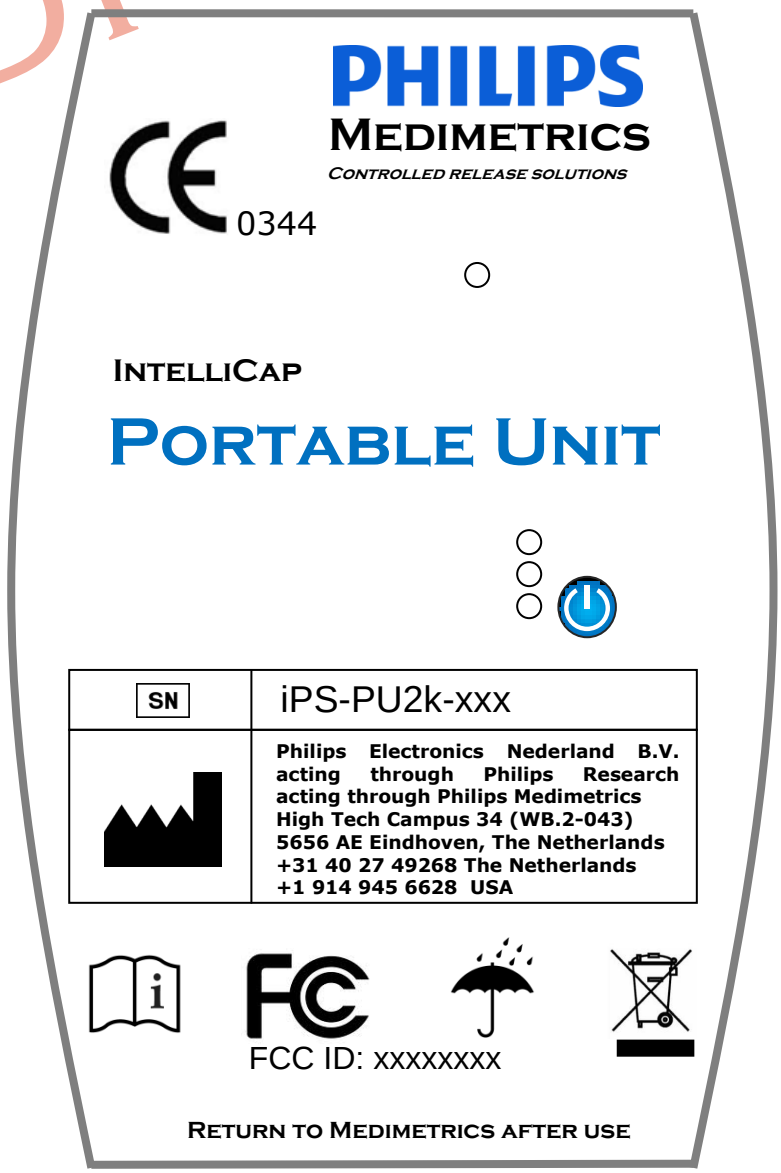
29.2 Storage Vial



Note: The vial is labeled with the same number as indicated on the capsule electronic body (first number). The medicine ring number (second number in the serial number line) is represented by the second number.

Note: The barcodes are optional and might not be present.

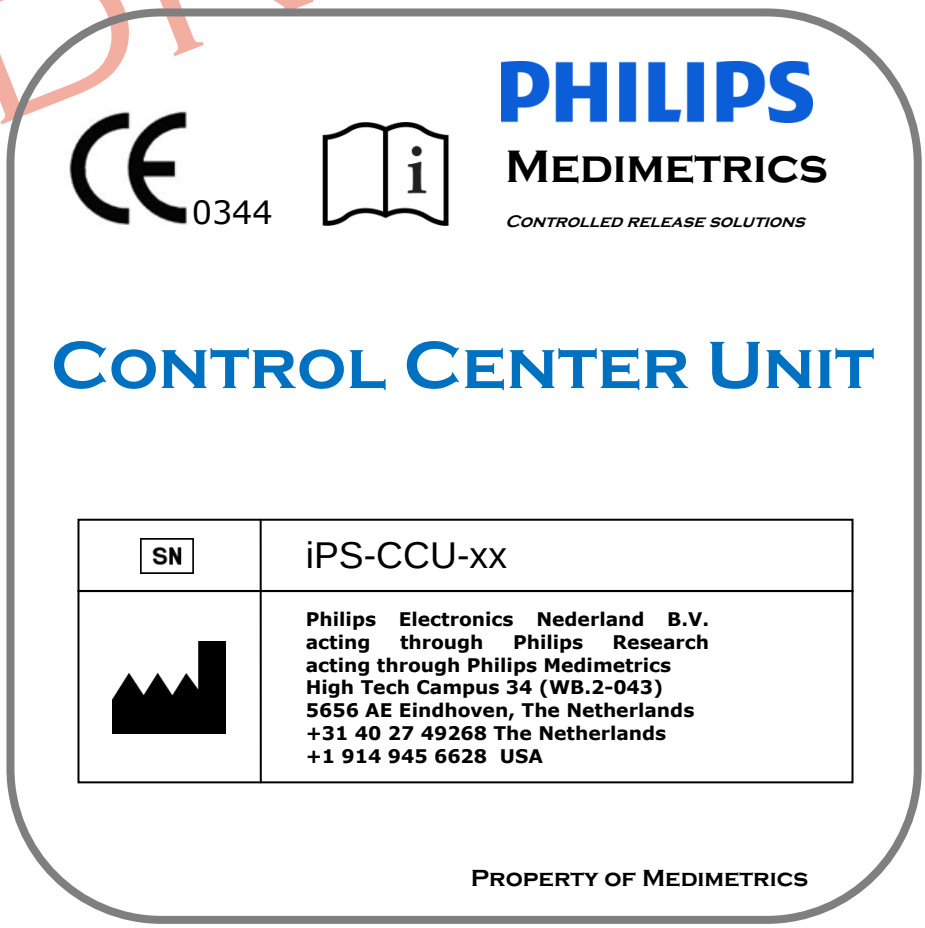
29.3 Portable Unit



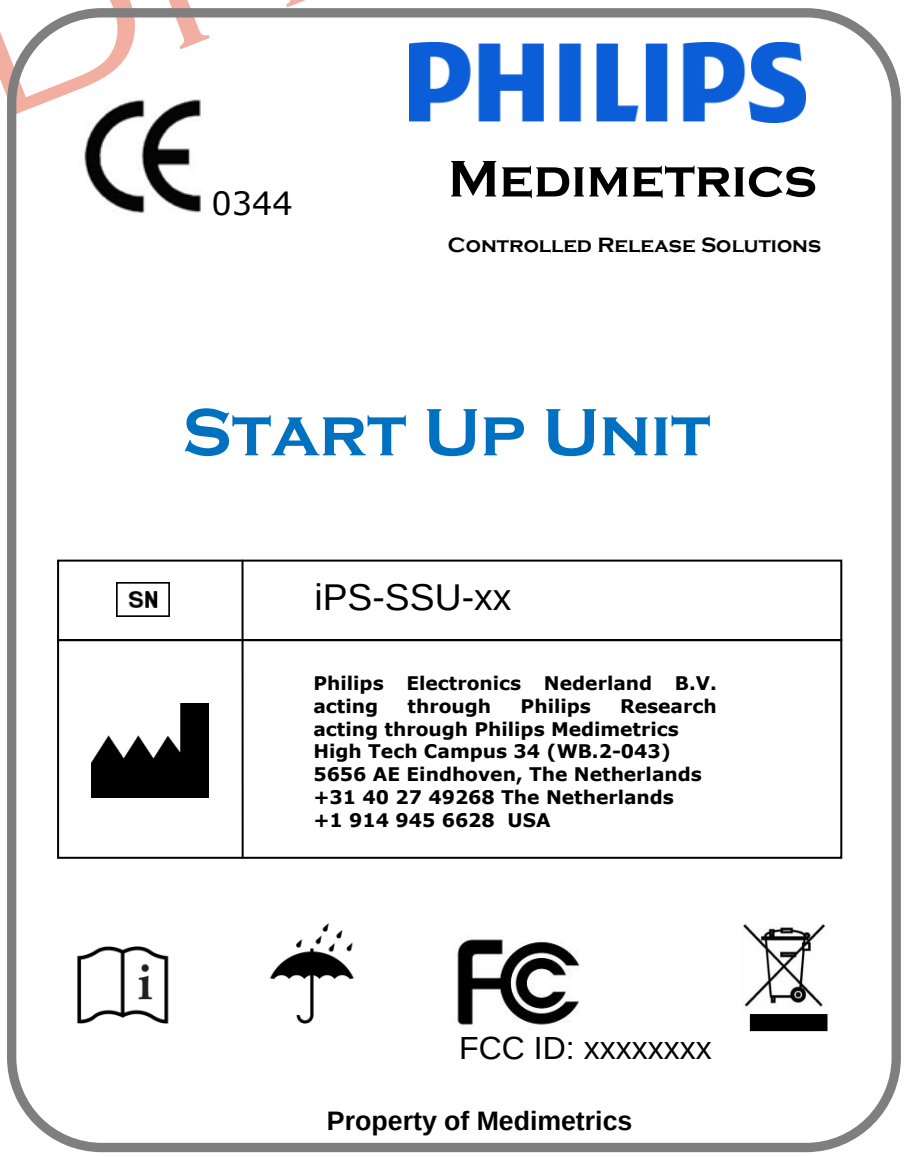
The letter "k" in the label indicates the difference on operational frequency:

- k = V → The module operates at 868MHz
- k = W → The module operates at 2.4GHz

29.4 Control Center Unit



29.5 Start-Up Unit



29.6 Symbols

Term	Definition
	Consult Instructions for Use
	Do not Re-use
	Shock Protection Type = BF
	Not for General Waste
	Keep Dry
	Manufacturer

Term	Definition
	Serial Number
	Use By
	Federal Communications Commission Certification
	Notified Body Certified Medical Product

1409

30. IntelliCap Capsule Specifications

CATEGORY	ITEM	PROPERTY	NOTE
Physical	Size (mm)	11 x 26.7	Diameter x Length
	Weight of unloaded pill (g)	3.2	Nominal
	Specific density of loaded pill (g/cm^3)	Between 1.5 – 1.6	1.5 Nominal, assuming medication at 1g/cm^3
Operational life	Duration	Up to 48 hour	Depends on the program
	Number of cycles	> 18000	Measure, transmit, and receive
Drug delivery	Medication capacity (µl)	275	Nominal
	Medication state	Liquid solution, suspension, or emulsion	
	Viscosity, maximum	1.0 Pa sec	
	Minimum dispensing volume (µ)	1.0	
Programmable Delivery Profile	Profile specification	User defined	Discrete segments, executed sequentially
	Dispense modes (segments)	1) Burst release 2)Sustained release 3) No release	1) Fastest dispense 2) Evenly distributed 3) Measure and report
	Burst release duration	<15 minutes	Empty full reservoir
Sensors	pH – accuracy calibrated	0.5 0.25	Absolute Resolution
	Temperature, range and accuracy	20-40 C, +/-1.0 C	Temperature of outside environment (or better)
Communication	IntelliCap to portable unit	400-440 MHz	Bi-directional MICS and ISM channels selectable at initialization
	Pill identification	ID code assigned	

31. Portable Unit Specifications

CATEGORY	ITEM	PROPERTY	NOTE
Physical	Size (mm)	117x79x24	Nominal
	Weight (g)	180	Nominal
	Housing	Plastic Enclosure	Closed with no accessible switches or connectors. No operation by the test subject.
	Portability	Cable-less during normal operation	Typical use is placement in a soft belt piece provided with the system
Power	Power source	Rechargeable battery	Normal operation
	Battery lifetime	> 48 hours	Full charged
	Charging source	Li-ion battery charger	1.3 A, 4.2 V output
	On/Off	Switch located internal on the PCB	Accessed by system operator. Torx driver required to open housing
Indicator LEDs	On/Off	Green	Continuous when on
	Optional	2 additional LEDs	Use not specified
Communication	IntelliCap to Portable Unit	400-440 MHz	Bi-directional MICS and ISM
	Control Center PC to Portable Unit	via Amber module	USB dongle at Control Center PC
	Range Control Center PC to Portable Unit	Up to 50m in open space	
	Stand alone operation	All data packets are recorded in local memory	Data capture continues when away from the control center area
	Wired communication	Optional USB connection for data download	For after an experiment. Housing must be opened.

32. Start Up Unit Specifications

CATEGORY	ITEM	PROPERTY	NOTE
Physical	Size (mm)	120x95x35	Nominal
	Weight (g)	290	Nominal
	Housing	Metal Enclosure	Removable lid attached with screws
Power	Power source	via USB cable	Connector provided
Pill Activation	Power coupling	via start-up coil	Internally mounted
	RF frequency range	18.5 – 21.5 MHz, frequency sweep	Nominal
	Capsule interface	Proximity to start up coil	Capsule may remain in the storage vial. ISFET window facing coil
Communication	IntelliCap to Start Up Unit	400-440 MHz	Bi-directional MICS and ISM
	Control Center PC to Start Up Unit	USB cable	Bi-directional
	Service channel	401.25 MHz	Used for activation reporting and initialization data exchange

1417 # 33. Document history

Version	Date	Author	Description of changes	CR
0.1	2010-01-20	Jeff Shimizu	First Draft - INCOMPLETE	N/A
0.2	2010-02-25	Jeff Shimizu	Second Draft - INCOMPLETE	N/A
0.3	2010-04-09	Jeff Shimizu	Draft – Complete for review	N/A
0.4	2010-04-26	Ventzeslav Iordanov	Reviewed version	N/A
1.0	2010-05-27	Jeff Shimizu	Final (major) version	N/A
1.1	2010-11-15	Ventzeslav Iordanov	Proposed new version (label information added; new figures; new structure)	N/A
2.0	2010-11-22	Jeff Shimizu	Final (major) version	N/A

1418

1419 END OF DOCUMENT.