INSTRUCTIONS FOR USE

Instructions for use hyborg Dx RED2 V005

IVD CE

November 2024

hyborg Dx RED2, hyborg software (Version 1.8)	**REF / UDI-DI**	*09120127730015*

Analysis system for processing multiplexed hybcell tests including software.

System Liquid	**REF / UDI-DI**	*09120127730022*
PE-Buffer	**REF / UDI-DI**	*09120127730138*
Waste Bottle	**REF / UDI-DI**	*09120127730046*
Rack	**REF / UDI-DI**	*09120127730220*

Buffers and Accessories

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Document history

CUBE-MA-16025-V01-E CE-IVD hyborgDx - **CUBE-MA-16025-V01-E CE-IVD hyborgDx V02**
First draft, introduction of the disclaimer. The removal of the symbol for liquids used by the hyborg. Use of images from the updated hyborg software. Added chapters, “Diagnose the status of device hardware or electronics” and “Granting a Support member remote access to the device”

CUBE-MA-16025-V01-E CE-IVD hyborgDx V02 - **CUBE-MA-18003-V01-E CE-IVD hyborg-DxRED2**
Formatting of the first page to include better images and the month of document release. Modified disclaimer report. Added images to chapters, “Diagnose the status of device hardware or electronics” and “Granting a Support member remote access to the device”. Improvement of the troubleshooting chapter to add more images on handling the hyborg, added a new subchapter “Empty Liquids / Full Waste” and finally, the removal of the subchapter involving the error lamp.

CUBE-MA-18003-V01-E CE-IVD hyborgDxRED2 - **CUBE-MA-20009-V03-E CE-IVD hyborg-DxRED2**
Introduction to subchapters “Manage Liquids (buffers)”, “Check system pressure”, “Control hybcell and quality assurance” and “Show log, usage and this manual” whilst removal of subchapter “Granting a support member access to the device” from the Tools chapter. The Troubleshooting subchapter now has added subchapters “Granting a support member access to the device” and “Empty Liquids / Full waste”.

CUBE-MA-20009-V03-E CE-IVD hyborgDxRED2 - **CUBE-MA-21010-V04-E CE-IVD hyborg-DxRED2**
The chapter “Basic hybcell processing” now has updated images as a result of hyborg software updates. Accompanied with the rearrangement of some subchapter content.

hyborgDxRED2_instruction for use_E_2022_05_18
Renaming of the documents instead of manual, now called instructions for use. The previously named chapter “Switching on” is now referred to as “Preparatory treatment”. This chapter now has additional information. Introduction of the subchapter “Serious Incidents / vigilance” into the Troubleshooting chapter

hyborgDxRED2_instruction for use_E_2023_04_25
Introduction of the GTIN into the main page and page

hyborgDxRED2_instruction for use_E_2023_10_13
The buffers and rack are now introduced in the main page of the IFU including their REF numbers, together with that, GTIN is now referred to as UDI-DI.

hyborgDxRED2_instruction for use_E_2024_01_03
Updated images throughout the IFU related to the hyborg software updates and year 2024. Reports have also been updated both software and PDF versions. Into the chapter Troubleshooting, a new subchapter “Barcodes on liquid bottles not readable” has been introduced.

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hyborgDxRED2_instruction for use_E_2024_04_25
The chapter Troubleshooting, subchapter “Barcodes on liquid bottles not readable” now has introduced barcodes in multiple languages, French, German, Italian, Spanish, and UK. Lastly, an appendix “Pre-installation form Cube Dx hyborg connectivity” is now added into the last page of the IFU.

hyborgDxRED2_instruction for use_E_2024_11_07
The chapter “hyborg packaging for transport” is renamed, and it now has step by step instructions on how to pack the hyborg for transportation. Introduction of a new Chapter “Connectivity” which was previously in the appendix.

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Ask Cube Dx GmbH or your local distributor for a more recent version of this manual.

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Table of Contents

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1. Warnings and Safety Information

Please read this user manual carefully before you using the device for the first time!

Intended for **professional IVD usage only**. The product bears the **CE mark** according to **(EU) 2017/746**.

Handling the device in a manner not in accordance with this user manual can detract from its intended level of protection and / or device performance. In addition, the device's warranty becomes invalid if not used as intended.

The device has to be checked annually according to ÖVE/ÖNORM E8701 or DIN VDE 0701-0702 by the operator.

Note that the hyborg meets standards of emissions and immunity in accordance with EN 61326-2-6, electrical safety standards in accordance with EN 61010-1, EN 61010-2-010, EN 61010-2-051, EN 61010-2-101 as well as laser safety standards in accordance with EN 60825-1.

When working with hyborg, please adhere to the **generally accepted rules of conduct in laboratories**.

Replacement parts and accessories may only be supplied by the manufacturer and its distribution partners. The use of non-OEM replacement parts and other accessories will lead to a forfeit of warranty.

Installation of the hyborg may only be carried out by authorized personnel. Note that (premature) installation and commissioning of the device by the user is not permitted and will lead to a forfeit of warranty.

Always wear **disposable gloves** when operating the device, and also **safety glasses** when handling hyborg liquids. It is recommended to wear a **lab coat** as well. The liquid in the waste container (marked with red dot) is potentially infectious.

Within the hyborg are **moving parts**. You may jam your fingers in the device drawer if you handle the device carelessly. Keep your hands and fingers out of the device's drawer when it is closing!

Also comply with the **test-specific user manuals** relevant for the respective product.

The **housing** of the hyborg protects users from laser radiation, moving parts and contact with the heater bars of the device. Note that you must not remove the housing during routine operation! Safe and proper operation of the hyborg is guaranteed only when the provided housing is in place.

Do not use the hyborg close to sources of strong electromagnetic radiation, since this may disrupt proper operation.

Make sure to interpret the analysis result in combination with the patient history, before stating a diagnosis.

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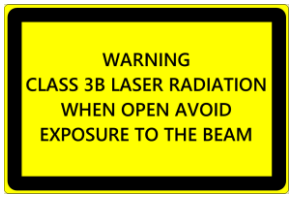
2. Explanation of Symbols

Symbol	Explanation
	**Follow the instructions for use!** The instructions for use include information for safe use. Position: device front.
	**Biological hazard!** Samples processed by the hyborg are potentially infectious. Position: device front and waste bottle position.
	**Hot surface!** Heater bars mounted in the device might be hot during operation. These bars are located inside the device and are accessible, if the cover is removed (for maintenance, error handling…). Position: cover of optical module.
	**Attention, general hazard area!** The device processes samples that are potentially infectious. Wear disposable protective gloves and safety glasses when handling the waste. Moving parts within the device might inflict injuries. Be careful not to jam your fingers or hands in the drawer. Position: device front.
	The laser beam is completely covered within the device. The cover has no outlet openings through which laser light can penetrate. The laser is constantly on during the scanning process. Position: device front.
	**Attention, laser radiation!** The device contains a laser source. Position: cover of optical module.
	By removing the case of the optical module, exposure to laser radiation of class 3B is possible. Position: cover of optical module.

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CE IVD	CE mark. In vitro diagnostic medical device.
	Manufacturer.
EXP	Expiry date.
REF	Catalog number.
SN	Serial number.
	Reference to the instructions for use.
	Use by date.
	Temperature limit for storage.
	Sufficient for <n> tests.
	Expires 2 months after opening.

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3. Hyborg Packaging for Transport

Before carrying out the work steps, ensure that:

- all required equipment and tools are available and maintained,
- all required materials and solutions are available in sufficient quantities, and
- the description of the work steps has been understood so that a smooth execution is guaranteed.

3.1. Required devices, accessories or auxiliaries

- 1 *hyborg Dx RED2* device (REF/UDI-DI 09120127730015)
- carrier box (wooden)
- 7 x 40cm angle profiles
- 2 x lashing strap
- bag
- transport instructions (form)
- 2 x shock indicator
- 2 x tilt indicator
- Optional: stretch film

3.2. Execution:

1. Disconnect accessories and cables and put them in a bag: e.g. keyboard, mouse, WIFI stick (USB), barcode scanner, power cable. Empty all bottles (e.g. System Liquid, PE-Buffer, Wash Buffer) and put the bottles back in their positions. Empty the waste.

2. Thread the lashing straps into the provided holes of the bottom of the carrier box. If there are no such holes provided, the straps are routed around the outside.

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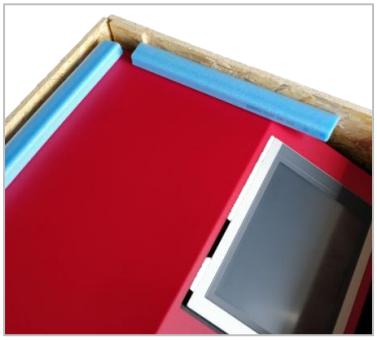
3. Place the hyborg in the middle of the bottom of the carrier box and position the 40cm angle profiles under each side of the hyborg (4x).

4. Arrange the side panels around the hyborg. Pay attention to the orientation of the handles so that they can fold down. The lashing straps are on the outside of the side panels.

5. Place three 40cm angle profiles at the top edges (on both sides and at the back).



6. Put the bag with the accessories onto the slant holding the device's screen. Before doing that, put some soft packaging material on the slant to protect the surface of the device.

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7. Thread the lashing straps into the provided holes of the top cover and put the top cover onto the carrier box. If there are no such holes provided, the straps are routed around the outside.

8. Attach the transport instructions on the top cover of the carrier box and tighten the lashing straps (using the attached ratchet spanners). If available, you can attach two shock indicators (No. 1, ‘SHOCKWATCH’) and tilt indicators (No. 2, TILTWATCH’) each. Place the shock indicators on diagonally opposite corners. Place the tilt indicators on a long and a short side each.

No. 1 

No. 2 

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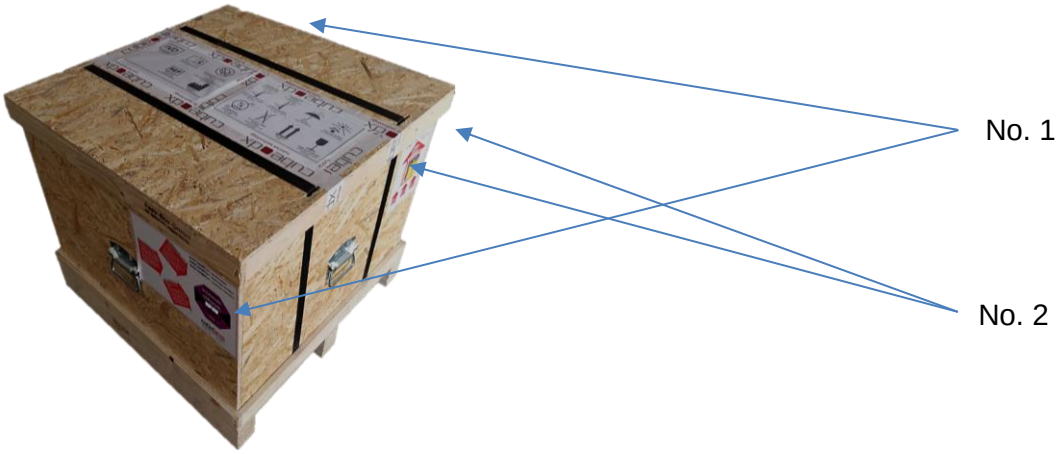

optional: Wrap the box with stretch film in multiple layers.

The checklist below summarizes the most important steps to prepare the hyborg for transportation.

Checklist	Outcome
hyborg Dx RED2 placed in the middle?	☐
7 x 40cm angle profiles placed?	☐
Accessories added?	☐
Transport box firmly lashed?	☐
Shock indicator attached?	☐
Tilt indicator attached?	☐

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4. hyborg Receipt / Storage / Product Components

hyborg Receipt

When you receive your hyborg device, please check the packaging for visible damage. Please report any damage of the packaging immediately.

The packaging is equipped with one impact and two tilt indicators. These are located on the outside of the packaging, and indicate whether the product experienced any shocks:

- Shockwatch L 65: If the force of any shock applied to the packaging exceeds the defined limit, the indicator tears and the released liquid irreversibly changes colors of the indicator (to red).
- Tiltwatch: The indicator field turns red when the packaging is inclined more than 7°.

The indicator is – in case of proper transportation – not colored red. If the indicator is colored red, accept the delivery but make sure the carrier confirms the activation of the transportation indicator in written form.

Until the device is installed, store the hyborg in a dry location free at an ambient temperature (between 0 and 40°C).

If you need to transport the hyborg for yourself, please note that it weighs approximately 70 kg (with its packaging). Use the handles on the packaging or other appropriate transportation aids (e.g., a lift truck) to move the hyborg with its packaging. When moving or lifting the hyborg without packaging, lift the device by grabbing the base plate on the bottom of the device.

If you want to transport the hyborg device after commissioning the drawer must be closed.

Before disposing the device, you should decontaminate it (see *Maintenance, Cleaning and Decontamination*).

In case of further questions, please contact:

- 

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  Westbahnstraße 55, 4300 St. Valentin, Austria
  Contact data: www.cubedx.com

Product Components and Storage

The Device and its Accessories:

- 1 *hyborg Dx RED2* device (REF/UDI-DI 09120127730015): store at **0 to 40°C**
  - 1 barcode scanner
  - 1 power cable
  - 4 bottles (1 waste, 3 empty bottles for liquids)
  - 1 hyborg manual

Buffers:

- *System Liquid* (REF / UDI-DI 09120127730022): store at **8 to 25°C**
  - 1 L of system liquid in a plastics bottle
- *PE-Buffer* (REF / UDI-DI 09120127730138): store at **8 to 25°C**
  - 1 L of PE buffer in a plastics bottle

Accessories:

- *Waste Bottle* (REF / UDI-DI 09120127730046): store at **8 to 25°C**
  - 1 L plastics bottle to collect liquid waste
- *Rack* (REF / UDI-DI 09120127730220): store at **8 to 25°C**
  - 5 x rack to hold up to 8 hybcells each.

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5. Intended Use and hybcell technology

The hyborg Dx RED2 (device) and its Software are intended to process and analyze different hybcell tests. The device and the software enable the user to automatically perform hybcell tests according to configured workflows - coded in software protocols – with little variations in timing, heating, liquid dispensing or scanning.

hyborg

These protocols are imported to the software.

The hyborg provides possibilities for heating and cooling the sample, to add liquids, to stir the solution by rotating the hybcell and fluorescence scanning the hybcell surface (a cylindrical microarray).

The device is not intended to be used with any accessories other than those provided by the manufacturer. Only educated and trained laboratory staff may operate the device.

5.1. hybcell technology

hybcell enables both challenging immunologic (protein) as well as comprehensive genetic (DNA) tests on one platform. Fundamental to the quality of any test is molecular interaction under defined and reproducible physical and chemical conditions. The hybcell technology provides fast results with reduced hands-on time which results in quicker diagnosis and direct patient benefit.

Microarrays are an established core technology within the R&D community and are a very powerful method for the detection of molecular interactions. In principle, certain detector molecules, such as antibodies or DNA Oligos are immobilised on a surface, which can either be a simple glass slide or a proprietary chemical or biological coating. The detector molecules bind certain compounds in the test sample and a biological readout is made which detects this interaction. A core component of all microarray systems is software packages which are able to interpret the large amount of data which can be generated in parallel by the large number of spots included in current microarrays.

The hybcell is the world's first cylindrical microarrays. Advantages of the hybcell are a very reproducible and fast process which is easy to use, as the hyborg processes the samples automatically. As opposed to carrying out the incubation and reaction between analytes and detector molecules in a standard two-dimensional format, the hybcell is made up of following components:

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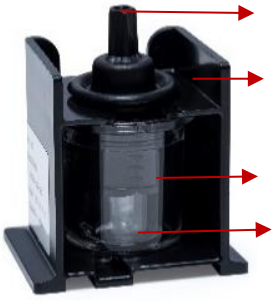

Lid: The lid is used to seal the hybcell and to prevent cross-contamination

Tray: The tray holds the other components together and mechanically protects the hybcell.

Core: The core is the heart of the hybcell and includes test-specific spots on its surface.

Tube: This transparent cylinder holds the liquid sample. The core rotates within the tube (and therefore within the sample).

The hybcell

5.2. Required Accessories

Accessories to be used in combination with hyborg include particular liquids (System Liquid, PE-Buffer), a waste container (Waste Bottle) and a device holding the hybcells in position (Rack) which can be purchased at Cube Dx or respective distribution partners. However, note that DNA-based hybcell tests may require additional processing with devices such as thermocyclers or qPCR machines to amplify sample DNA. Make sure to use only third-party devices which are validated for the use in combination with Cube Dx products.

Consumables and wear parts (hybcells, buffers, tubing, racks, etc.) may only be obtained from Cube Dx and respective distribution partners. Service and maintenance may only be done by authorized personnel.

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6. Technical Description

hyborg Dx RED2 (device) and hyborg Software	
Weight	Device: ~ 45 kg (without liquids) Device and box for transport: ~ 70 kg
Dimensions (depth / width / height)	Device: 620 / 574 / 503 mm Box for transport: 740 / 670 / 700 mm
Ambient conditions	indoor use, not for wet locations, pollution degree 2 ambient temperature 0 to 40° C, humidity 30 to 80 % rHu altitude < 2000 m sea level
Electromagnetic compatibility (EMC)	Moderate disturbances accepted (laboratory environment)
Power supply	100 to 240 VAC (16 A) (overvoltage category II) 50 - 60 Hz
Power consumption	Max. 480 W
Appliance class	Class I
Fuses	10A delay-action fuse
Liquids	Maximum 4 liquids: ▪ Liquid 1 and 2 for PE-Buffer and / or custom solutions (e.g. Wash Buffer) ▪ Waste ▪ System Liquid
Automatic cleaning	After each run
Heating	4 to 95° C
Optic module (laser)	Laser class 1, classified in accordance with IEC 60825-1:2014. Laser output power: <0.39 mW; wavelength: 640 nm. The light source itself can be classified as class 3B in accordance with IEC 60825-1:2014. The device has no outlet openings through which laser light can penetrate. The laser is constantly on during the scanning process.
Sound pressure level during operation	< 70 dB
Rated operating pressure	~ 100 mbar

Technical data

The hyborg is designed for 24 hours / 7 days operation. It is intended to be used multiple times for multiple samples.

24 hybcells can be processed per run. Processing time is test-specific.

The device may only be used by properly trained operators (authorized training by Cube Dx or its distributors).

6.1. Device Access / Connections

The hyborg provides different accesses for the user, as indicated in the picture below. The drawer is the main access and opens to load and unload the up to 3 racks, holding up to 8 single hybcells / samples. On the left-

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hand side of the device the liquids are connected / refilled (Liquid 1, Liquid 2 and System Liquid) or disconnected / disposed (Waste). The cover is not intended to be removed during routine operation. However, it can be opened with a tool for service and maintenance reasons (unscrew 4 screws and remove).

Connectors are located on the right of the device. They are used to connect the barcode reader or additional peripheral devices (e.g., keyboard, computer mouse, ethernet cable, etc.)

The power connector and main switch is on the right side of the device as well.

The pictures below show the opened drawer and a rack with hybcells. Opening and closing of the drawer is controlled by the software.

As the samples within the hybcells are potentially infectious, wear disposable gloves at any time when inserting and removing racks!

The barcodes on the hybcells have to face the inside of the device. Different shapes on both sides of the rack should safeguard, that the rack is inserted with the right orientation. **Therefore, do not use excessive force to insert racks!**

Open drawer.

Rack with hybcells.

The device is connected to the power grid using the power cable included within the scope of the product.

Disconnect the hyborg from the power grid, if you intend to remove the housing for any repairs! Do so by removing the power cable.

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The device can be connected to the Intra-/Internet using either a standard patch cable (CAT5), or a wireless adapter.

6.2. Electronic Interfaces

The device provides following electronic interfaces:

- USB 2.0 (for validated accessory only)
- Ethernet (RJ-45) (for maintenance and service activities only)

The USB interfaces are used to connect accessories to the device. Make sure to use only the accessories, which are supplied with the device and validated for the use with hyborg Dx RED2 (especially barcode reader). The use of any other accessories may inhibit the correct functioning of the device!

The device does not need to be connected to a network in order to achieve its intended use. The network interface may be used for maintenance or service activities by authorized personnel only!

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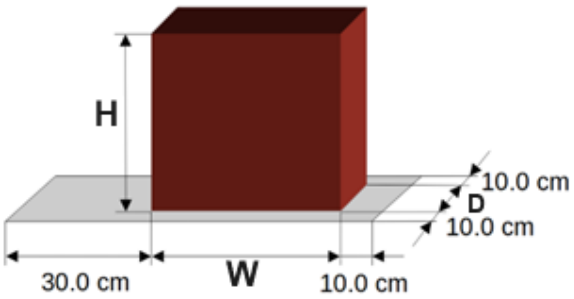
7. Installation

Installation must be done by authorized personnel only!

7.1. Requirements

The hyborg has to stand on an even, dry, and stable area near a wall socket. It requires approximately 100 cm bench (depth approximately 70cm) – see footprint on the right.



There should be at least 10 cm of free space towards the top. Make sure to keep 10 cm distance at the back of the device for air circulation. At least 60cm of space should remain to the left of the device to allow the exchange of liquid bottles.

Electrical power supply (100 to 240 VAC, 50 to 60 Hz, 16 A) – equipped with a protective conductor - is required to operate the hyborg.

The device stands on 4 pedestals. Each of these pedestals is carrying a weight of up to 12 kg. Make sure to keep the distance between the ground plate of the device and the work bench clear for air circulation.

7.2. Installation Procedure

Following, the basic steps during installation and (first) power-up are described.

- Unpack the device by removing the lashing straps and lifting the top of the wooden box. Then remove the side parts of the wooden box. Check for visible damages.
- Place the hyborg on its workspace.
- Connect the power cable.
- Connect the barcode reader.
- Fill in the buffers:
    - System Liquid, yellow (must be filled),
    - Wash Buffer, green (for tests based on proteins, not included in CE-IVD),
    - PE-Buffer, blue (for tests based on RNA or DNA),
    - Waste Bottle red (must be empty).
- Optional: connect the PC to the Ethernet (Intra- / Internet).
- Do a performance qualification according to the instructions by Cube Dx.

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- Receive an operator training by Cube Dx or its authorized distributors.

8. Connectivity

The Hyborg Dx RED2 device uses a network connection for the following use cases:

8.1. Remote support

CubeDx is using Anydesk as remote support application. Anydesk enables CubeDx and its sales partners to provide fast and targeted support. With direct remote access, many questions relating to hybcell tests can be answered in a customer-friendly way.
AnyDesk uses TLS 1.2 with authenticated encryption. Every connection is secured with AES-256. When a connection can be established, the session is endpoint encrypted and its data is not routed through third-party servers. AnyDesk clients use the TCP-Ports **80**, **443,** and **6568** to establish connections. It is however sufficient if just one of these is opened.

8.2. Automatic protocol download

Automatic protocol download is a part of hyborg software. It is connecting to https://www.cubedx.com/protocols over TCP-Port **443** and checks every 24 hours or at system startup for new protocols. Without automatic protocol download, the user must download and import the hybcell test protocols himself for each new hybcell production.

8.3. HL7 internal result upload

The hyborg software can upload hybcell test results to an internal hospital or laboratory information system by configuring the HL7 interface (server name or IP address and port) on the Options tab of the hyborg software. In this case, the hyborg software sends an HL7 ORU R30 Unsolicited Point-Of-Care Observation Message to the specified destination.

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9. Maintenance, Cleaning and Decontamination

9.1. Maintenance

Cube Dx recommends an annual inspection and preventive maintenance done by authorized service personnel. Repairs are without exception only authorized if done by trained service personnel. If the device is repaired or modified by non-authorized personnel, any warranties are waived.

Operators in Austria and Germany are obliged to execute recurring safety checks according to the *Medical Device Operator Regulation.* These checks have to be executed by the operators themselves (visual check, measurement of earthing and insulation resistance as well as leakage currents).

9.2. Cleaning and Decontamination

The device might come into contact with bio-hazardous materials, so it's crucial to wear appropriate protective gear when cleaning it.

The tubing inside the device undergoes automatic cleaning with System Liquid after each device run. Clean the device's surface at suitable intervals and before transporting it. To clean these surfaces, use detergents containing only **alcohol or aldehyde cleaning agents**. Avoid using detergents that could damage or harm any parts of the device.

Before cleaning, ensure the device is switched off to prevent unintended actions if controls are accidentally operated. For cleaning the touchscreen exclusively, utilize a cloth dampened with water, detergent, screen cleaning solution, or ethanol. Apply the liquid to the cloth first and refrain from spraying it directly onto the device. Avoid using harsh solvents, chemicals, abrasives, compressed air, or hot steam on the device.

In case of potential contamination due to spills of infectious material on the device, decontaminate the hyborg. Additionally, decontaminate it before maintenance, repair, transportation, or after prolonged periods of inactivity (e.g., 3-4 weeks).

Start by removing all bottles, then use an ethanol solution and a cloth to wipe down the entire exterior and the opened drawer of the hyborg. If any internal parts might be contaminated, follow the same procedure for those affected areas (refer to Troubleshooting for instructions on accessing the front).

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10. Preparatory Treatment

After installation, the hyborg should be ready for operation.

- Switch on the device, using the main switch (and wait until boot and initialization routines are completed).

Main switch on right side of device

The hyborg starts with its initialization routine (homing all axis, check for “lost” hybcells and flushing the tubing). This routine lasts for approximately 3 minutes. After the initialization process the hyborg is ready for operation.

In order to ensure full functionality of the device, Control hybcells can be processed. See section *Control hybcell and Quality Assurance* for further information.

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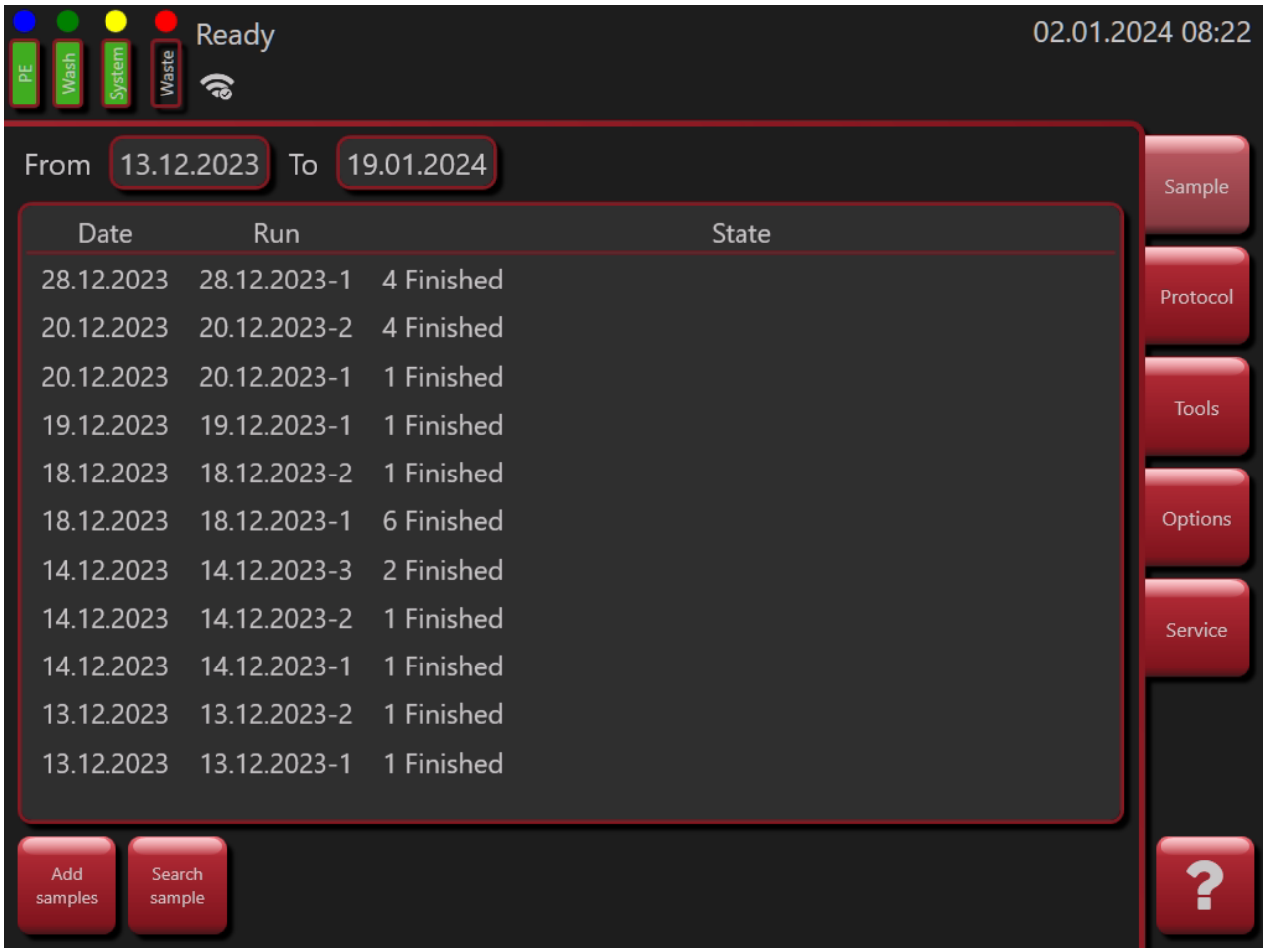
11. Basic hybcell Processing

After start-up of the software and initialization of the device, the Sample screen is shown to the user. This view initially gives an overview of all created runs.



Sample screen of hyborg software.

Status Information

The top line of the top-level screens (*Sample, Protocol, Tools and Options*) contains status information:

- Level of all four liquids (Waste, System Liquid, Liquid 1, Liquid 2) as bar graphs, if these liquids are activated (see *Options*).
- Device status
- Date and Time.

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Navigation to top-level screens

On the right-hand side of all top-level screens, navigation buttons to all other top-level screens are provided. The top-level screens are:

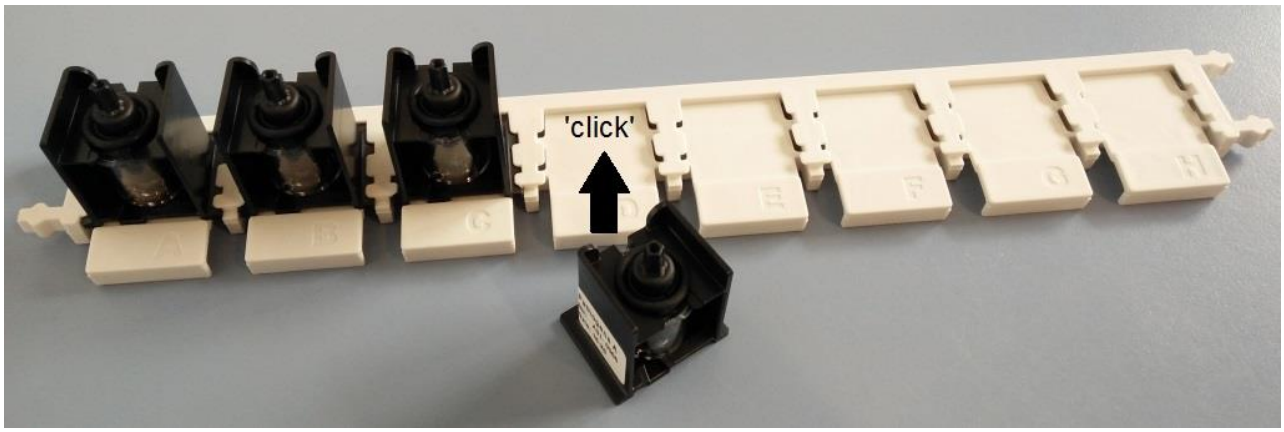
- *Sample* (see screen above): Create and manage samples and hyborg runs.
- *Protocol*: Check, import and delete protocols.
- *Tools*: Different functions like cleaning liquids, QA, operation of drawer, analyze scans and shut-down.
- *Options*: Set different device and report options.
- *Service*: for service purposes only, restricted access (password protected), not further considered in this manual.

Content-specific operators

On the bottom of the top-level screens, specific operators (buttons) are displayed to trigger different actions.

11.1. Creating New Samples for Processing

Each hybcell has to be fixed to a rack (8 positions each). The barcode of the hybcell is facing to the direction of insertion. The rack holds the hybcell tightly at its bottom. When the hybcell reaches its final position, you will hear a ‘click’.



Each hybcell has to be inserted into a position of the rack.

To define new samples within a run, make sure the Sample-screen is opened and press the *Add samples* button.

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Screen to create new samples (or to edit already created samples).

Barcode (mandatory)

Each hybcell is assigned to a unique identifier, printed as a barcode on the hybcells tray. This barcode contains a reference to the protocol which will be processed (has to be loaded in hyborg software before), the expiry date (calendar week) and a serial number. The barcode is most easily read with an attached handheld barcode scanner (USB), but can be typed in with the virtual keyboard as well (see below).

Sample (mandatory)

The sample ID is chosen by the user (or is predefined by the user's organization), it identifies the sample and is stated on the result. This ID must be unique for the particular run. The ID can be as well read from a barcode on the sample container.

Remark (optional)

A remark can be added by the user. This remark will be displayed on the later report.

Profile (optional)

For some tests, profiles might be defined. A profile is a subset of possible results, that will be presented on the report (if positive). In other words, some possible results are not displayed, to avoid possible "confusion". This

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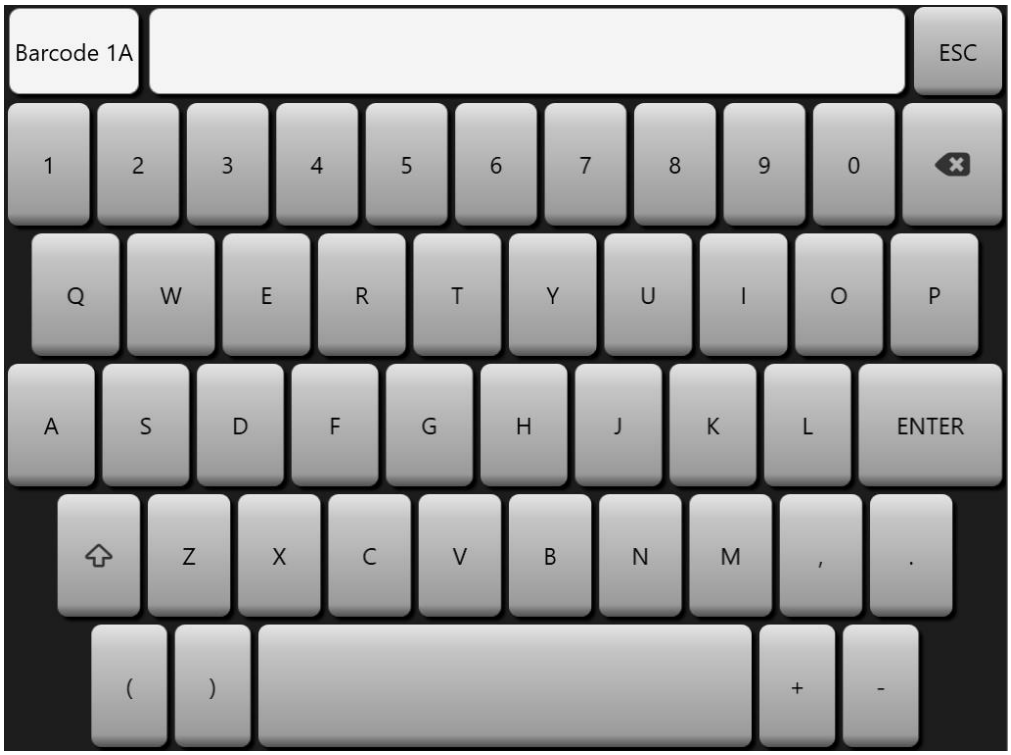
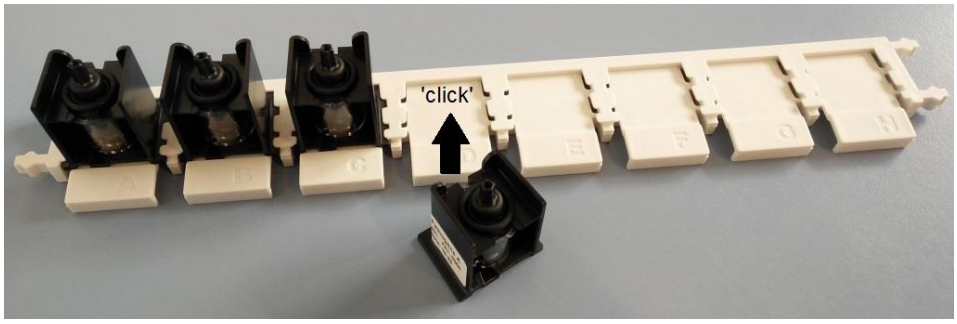
can make sense, if broad tests deliver possible results, that might not be of clinical relevance for certain types of samples.



Virtual keyboard (presented on the touchscreen).

The order of data input is from sample 1 (barcode, sample, remark, profile) to sample 2 (barcode, sample, remark, profile) to sample 3 and so forth. For reasons of streamlining the workflow, the user can choose to enter all barcodes (hybcell IDs) first, by pressing the *Edit Rack* and *Barcode* button. Same can be done for sample and remark by pressing the *Sample* button, respectively the *Remark* button.

After up to 24 hybcells are assigned with at least its barcode and sample ID the run can be started by clicking the *Start* button. The drawer will open and the racks with the prepared hybcells can be placed on their designated positions. To avoid sample mix-up, ensure that the positions of the hybcells in the rack and the position of the racks in the drawer matches the assigned positions.



The rack is inserted into the device, with the hybcell barcodes facing towards the device.

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The barcodes of the hybcells in the rack have to face the inside of the device.

After loading the racks into the drawer, the run is started by clicking OK. The device will close the drawer and start the sequential processing of the hybcells.

11.2. Selecting, Editing or Deleting Samples and Starting Processing

To edit or delete already defined samples, select the samples.

Select more than one sample by using the *Multiple Selection* button from the *Sample* screen. All selected samples can then be deleted by pressing the *Delete samples* button.

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- To edit the selected samples, press the *Edit samples* button. The same screen as for adding new samples will appear. To delete the selected run, press the *Delete run* button.

- To start processing the samples, enter the Edit-view (by pressing *Edit samples*) and press the *Start* button – all hybcells within the same run will be analyzed.

- To export the results of several samples as a PDF file and as a summary in a csv file, press *Export samples*.

- You can end the multiple selection by pressing the *End selection* button.

While performing the analysis, the user can abort the whole run, skip the current hybcell or stop the run after finalising the processing of the current hybcell.

- *Abort analysis* button: The complete run is aborted immediately. If a hybcell is processed, the processing of this hybcell is aborted as well. The remaining hybcells (not processed) keep their status 'ready' and can be processed later. Results from samples that have already been processed are retained.

- *Abort sample* button: Processing the current hybcell is stopped and the next hybcells of the run are processed.

- *Stop analysis* button: After completing the analysis of the current hybcell, the run is stopped.

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11.3. See Results, Check Plausibility and Print Report

After processing, the samples are marked with *Successful* (green indicator). In case of an error during processing or if the user aborted processing, the samples are marked *Aborted* (red indicator).

Most hybcell tests define internal controls – coded within the imported protocol. If such internal control failed, the sample is marked with *Control failed* (yellow indicator).

To see results for one sample, click on the sample.

Processed samples with a valid report.

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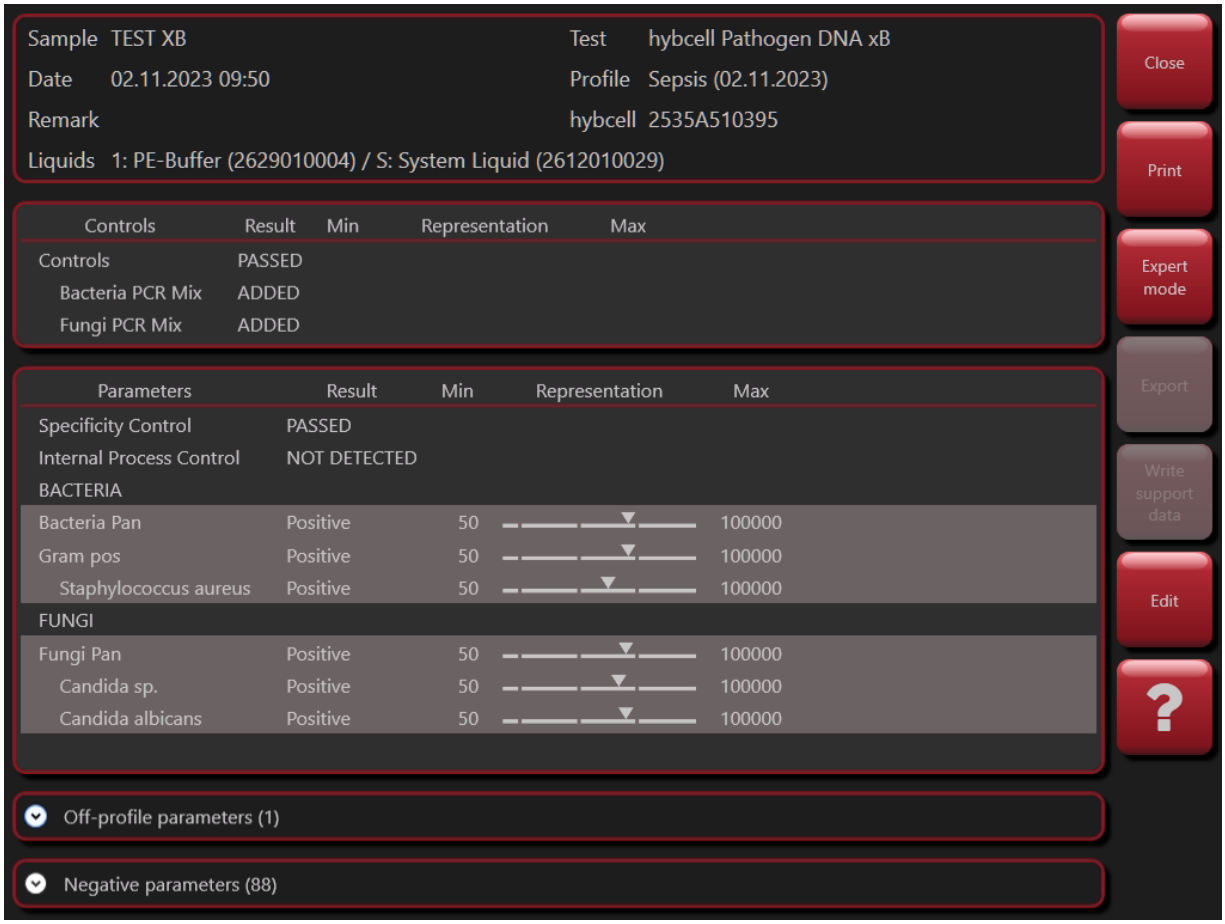

Possible result of a processed sample.

All reports are divided into three sections:

The header section with general information regarding the hybcell and the sample,

the controls section with the results of internal controls (single controls are only shown, if they are invalid)

and the result section, a table with following columns:

- **Parameter:** Name of the tested criteria, as defined in the protocol (e.g., bacterial species, inflammatory marker, etc.)
- **Result:** Test-specific results like qualitative result as an expression like positive / negative, yes, no. Quantitative result: Quantity and unit.
- **Representation (test specific)** of measurement with minimum value, maximum value and a graph indicating, where the actual value lies within that logarithmic range (indicated by a triangle).

Expert users can check plausibility of results by checking the scan (raw data) of the sample by pressing the *Expert mode* button.

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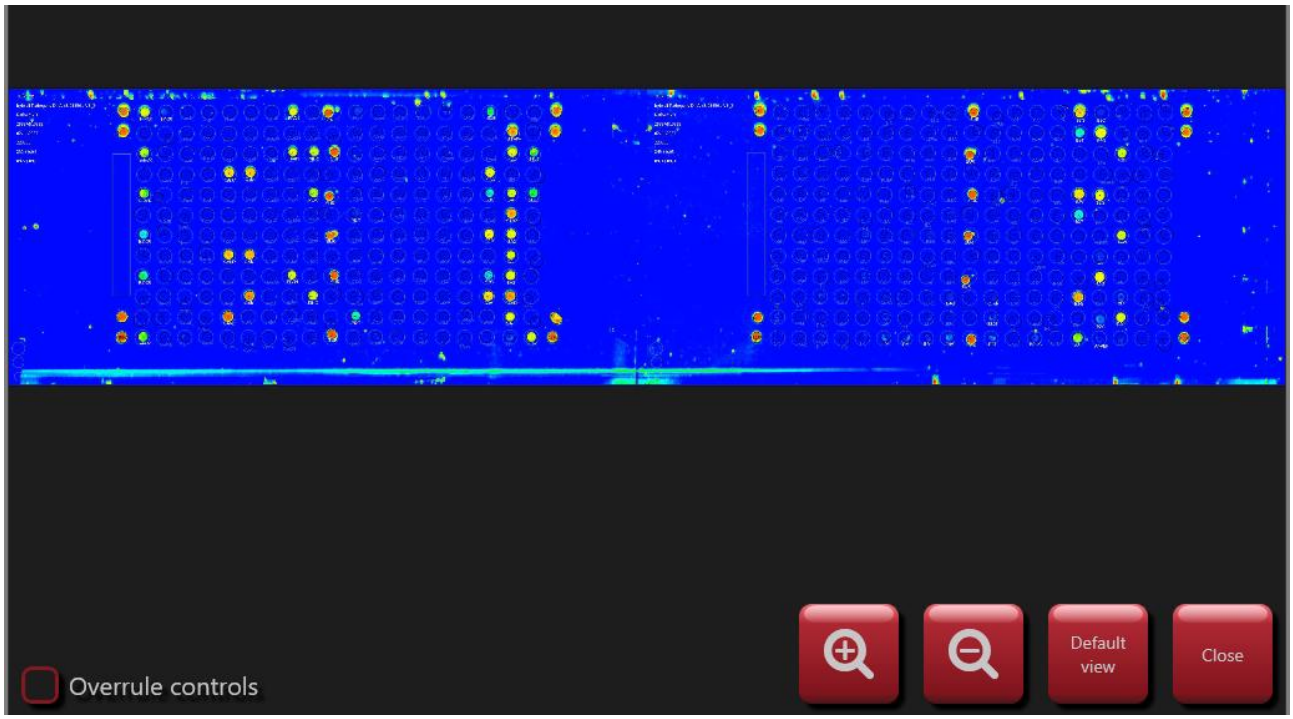

Scanned image of hybcell surface (false colour presentation and indication of probes).

The user can zoom in and out by pressing the + and - buttons. Original size is restored by pressing the *Default view* button. You can return to the report by pressing the *Close* button.

To print out the report, press the *Print* button. The print is directed to the standard printer defined in the settings (Windows) of the device (in the example below: printout to pdf).

The *Export* button saves the result in pdf file format to a USB drive.

With the *Write support data* button, all analysis-related files can be saved to a USB drive and shared for further assistance.

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cube dx
hybCell technology

Sample	TEST XB	**Test**	hybcell Pathogen DNA xB (3)
Date	02.11.2023 09:50	**Profile**	Sepsis (02.11.2023)
Remark		**hybcell**	2535A510395
Liquids	1: PE-Buffer (2629010004) / S: System Liquid (2612010029)		

Controls		
Controls	PASSED	
Bacteria PCR Mix	ADDED	
Fungi PCR Mix	ADDED	

Parameters	Result	Representation
Specificity Control	PASSED	
Internal Process Control	NOT DETECTED	
BACTERIA		
Bacteria Pan	Positive	50 — 10000
Gram pos	Positive	50 — 10000
Staphylococcus aureus	Positive	50 — 10000
FUNGI		
Fungi Pan	Positive	50 — 10000
Candida sp.	Positive	50 — 10000
Candida albicans	Positive	50 — 10000

Off-profile parameters	Result	Representation
Staphylococcus sp.	Positive	50 — 10000

Negative Parameters

Abiotrophia defectiva, Acinetobacter baumannii, Actinobacillus pleuropneumoniae, Anaerococcus sp., Aspergillus clavatus, Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Aspergillus sp., Aspergillus terreus, Bacteroides fragilis, Bordetella pertussis, Borrelella burgdorferi, Borrelella sp., Brucella sp., Burkholderia cepacia complex, Burkholderia pseudomallei, Campylobacter sp., Candida dubliniensis, Candida parapsilosis, Candida tropicalis, Carbapenemases, Citrobacter freundii complex, Citrobacter koseri, Corynebacterium diphtheriae, Corynebacterium jeikeium, Corynebacterium sp., Corynebacterium ulcerans, Cryptococcus gattii, Cryptococcus neoformans, CTX-m1/m3, Enterobacter cloacae, Enterobacter cloacae complex, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Extended Spectrum beta Lactamases, Finegoldia magna, Fusarium oxysporum species complex, Fusarium solani species complex, Fusobacterium necrophorum, Fusobacterium nucleatum, Fusobacterium sp., Gram neg, Granulicatella adiacens, Haemophilus haemolyticus, Haemophilus influenzae, Helicobacter pylori, IMP, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, KPC, Legionella pneumophila, Listeria sp., Methicillin, Methicillin Type A, Methicillin Type C, Moraxella catarrhalis, Morganella morgani, NDM, Neisseria meningitidis, OXA-48, Pasteurella multocida, Pichia kudriavzevii, Pneumocystis jirovecii, Pneumocystis murina, Prevotella buccae, Prevotella intermedia, Proteus mirabilis, Proteus sp., Providencia stuartii, Pseudomonas aeruginosa, Salmonella enterica, Scedosporium, Serratia marcescens, Staphylococcus non-aureus, Stenotrophomonas maltophilia group, Streptococcus agalactiae, Streptococcus anginosus group, Streptococcus dysgalactiae, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus salivarius group, Vancomycin, Vancomycin Type A, Vancomycin Type B, Yersinia enterocolitica

Example of printout of a report (pdf).

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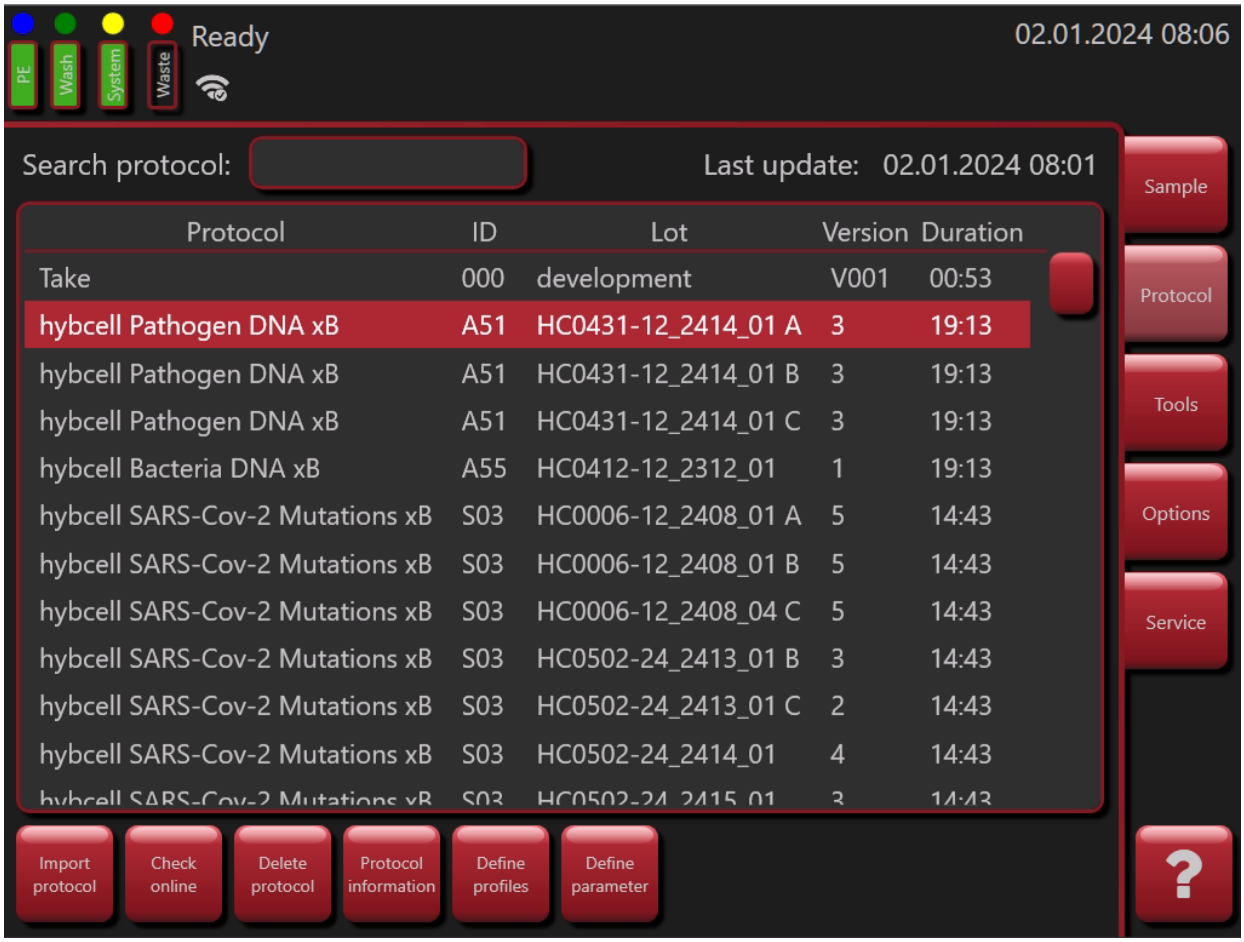
12. Managing Protocols

Protocols are xml-files, that are configured by Cube Dx. They contain information on the processing steps undertaken by the hyborg (software), e.g., heating and cooling cycles, rotation of the hybcell, exchange of liquids or fluorescence scanning. Furthermore, the protocol contains information on the microarray grid on the hybcell's surface. Any parameter (e.g., bacteria species, a single inflammatory biomarker) is represented by one or more spots of that grid. Which spots are associated with which parameter is as well coded in the specific protocol, along with rules how to calculate the parameters value from the raw data (fluorescence signal).



The protocol screen with the currently available protocols (on that specific hyborg).

A protocol has a name as well as a unique ID – which is part of the hybcell barcode. Besides that, a version of the protocol might apply. For any new production lot, a new protocol version is issued. On the *Protocol Screen* the approximate duration of the processing of the hybcell is indicated.

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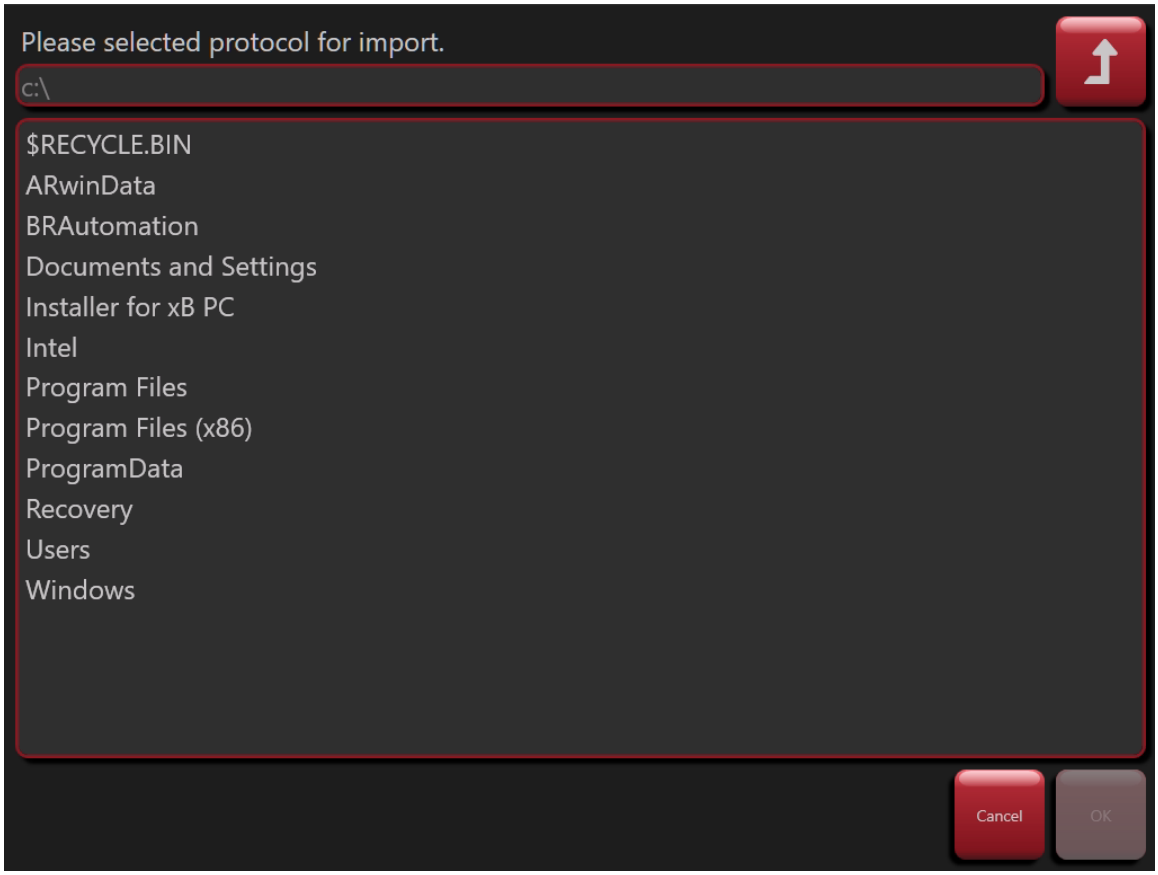
12.1. Import New and Delete Outdated Protocols

To import a new protocol, press the *Import protocol* button. A file selection dialogue appears.



File selection of protocol to be imported (file extension .hyb).

The imported files must have the extension .hyb.

To delete an outdated protocol, select the protocol by clicking on it. Press the *Delete protocol* button.

Click on the *Protocol Information* button to see further details of the protocol (e.g., short name or the protocol, author, duration, etc.)

12.2. Define Profiles and Parameters

Some hybcell tests might be used for different diagnostic uses and not all parameters (e.g., bacterial targets, biomarkers, etc.) are relevant for all uses. Therefore, it is possible to narrow the scope of results of a report within the hyborg software. This narrowing is done by defining profiles and to select the parameters which should be considered for the report. The remaining parameters are then termed as off-profile parameters and can be shown in a different section of the report (dependent on the settings, compare *Options*).

To create a profile, press the *Define profiles* button. Assign a name to the profile (to be able to select a profile for the hybcell test) and select the parameters that should be included (by checking the checkbox of the parameter).

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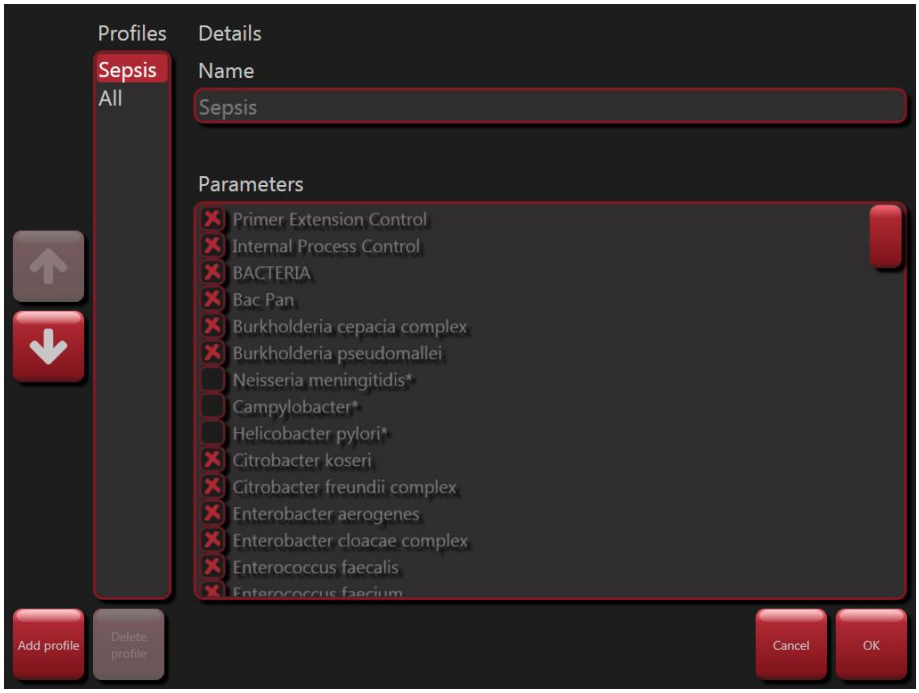
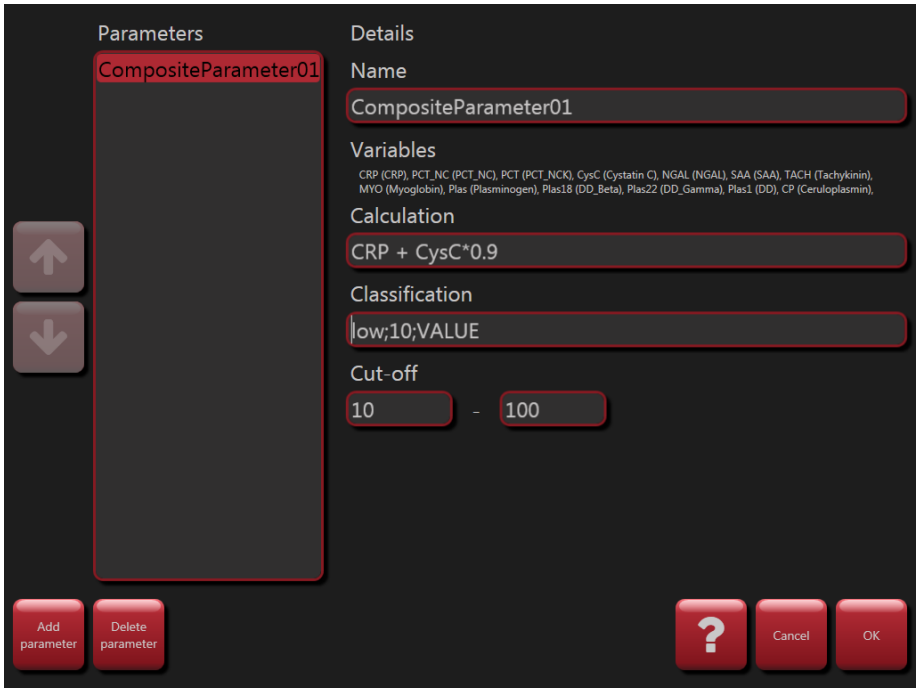


Definition of profiles.

You can define your own parameters by combining available parameters (with help of basic arithmetic operators) and classifying them (defining two or more classes).

To define your own parameters, click the *Define parameter* button. Assign a name to the parameter and define the combination and classification. Cube Dx provides a quick manual for defining own parameters.



Definition of own parameters.

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13. Tools

The hyborg software offers a few tools to maintain the hyborg as well as to analyze scans offline (or from other sources), for example with modified protocols.

The Tools screen.

13.1. Operating the Drawer Manually

To operate the drawer manually (opening or closing it), press the *Open drawer* button. The software prompts the user to wait, until the drawer is opened. After pressing the *Ok* button, the drawer is closing again.

13.2. Cleaning and Emptying the Tubing

To prevent the tubing from blocking (due to sediments of salts from the buffers, etc.), a regular cleaning (flushing) of the tubing is done after every run. However, to repeat such cleaning, click the *Clean tubing* button to start the cleaning routine. The tubing will be emptied after the cleaning procedure.

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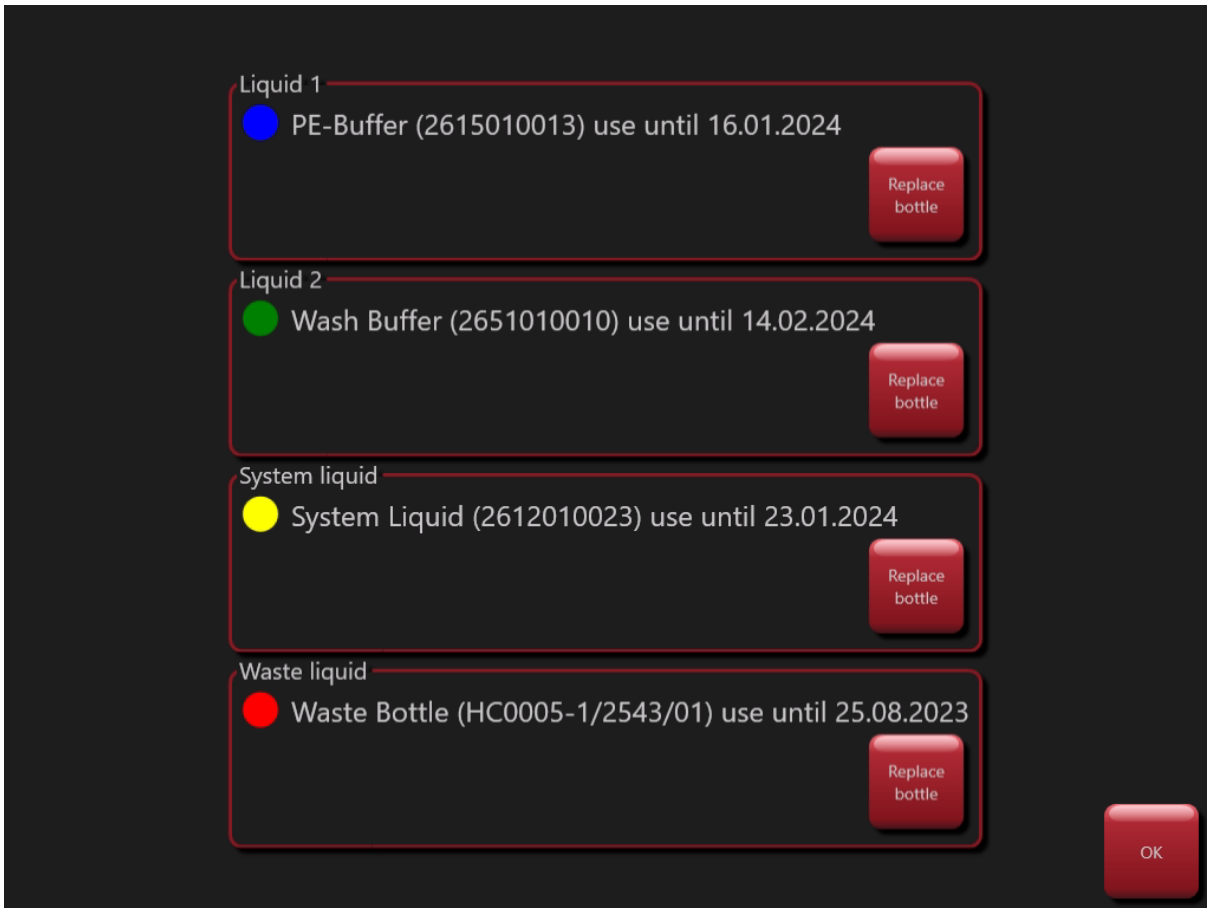
13.3. Repeating the Initialization Routine

After an error occurred, or to move the axis back to the initial position, the initialization routine (described under *Switching On*) can be repeated. Press the *Initialize device* button to initialize the device once again.

13.4. Manage Liquids (buffers)

To exchange buffers and manage liquids and bottles of the hyborg, click the *Manage liquids* button.



The Manage liquids screen.

This screen helps to define the used buffers and the System Liquid (the positions and the software association of the liquids are colour-coded (blue, green, yellow and red). Click on the respective *Replace bottle* button and scan the liquid barcode from the label of the bottle. The expiry date of the liquids is coded in the liquid barcodes and the software checks the expiry of the liquids.

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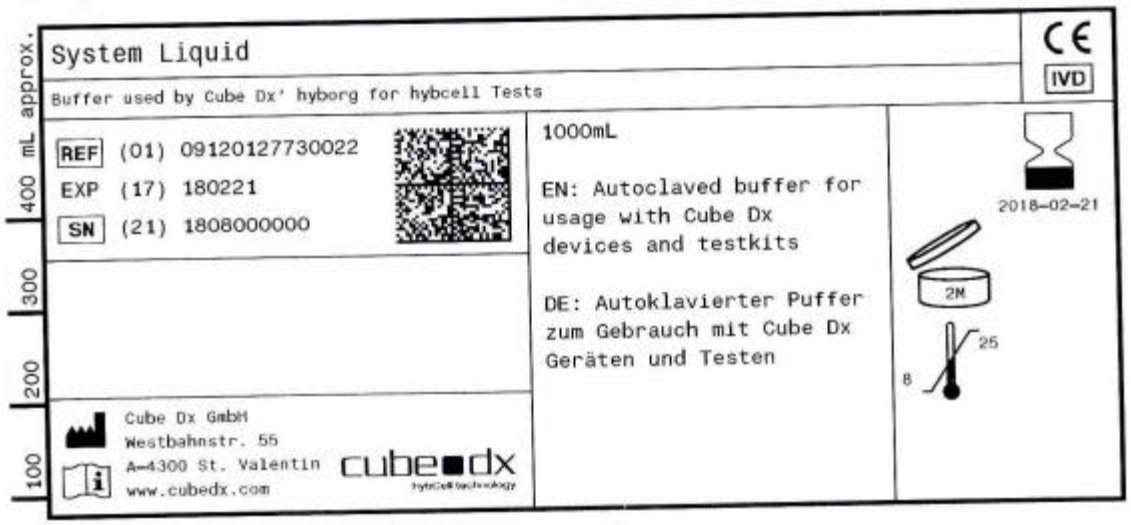


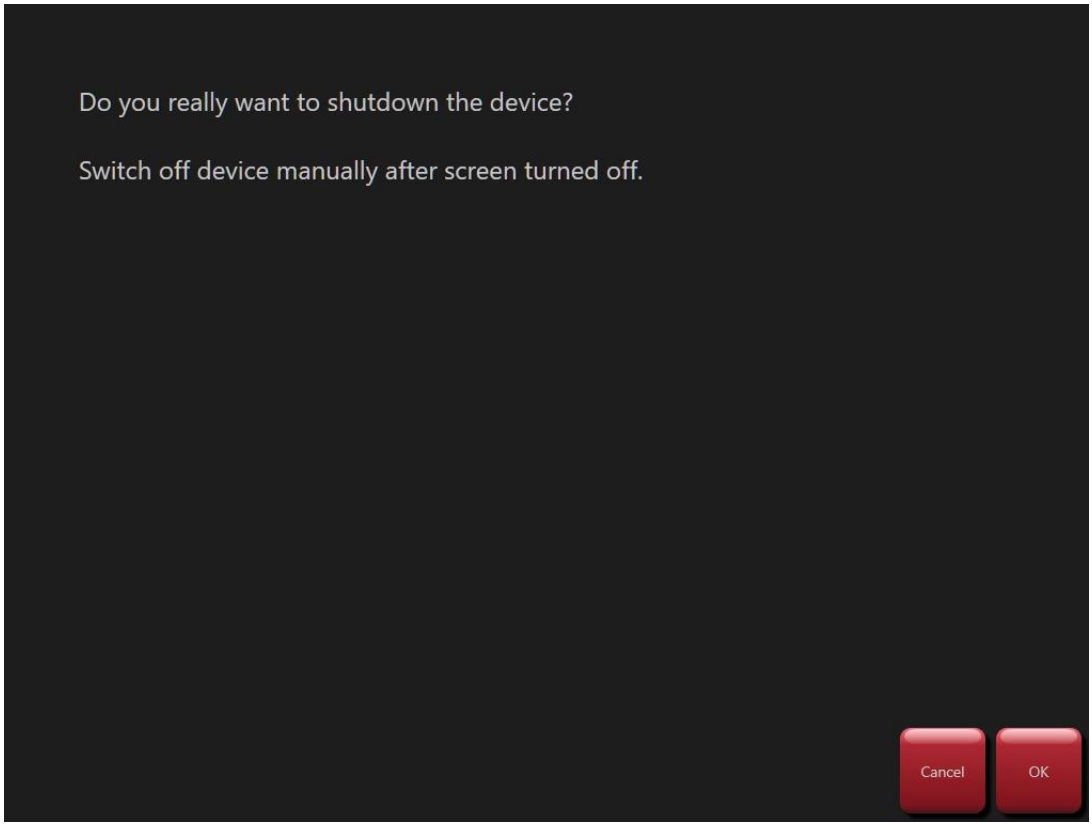
A Label of the System Liquid.

13.5. Check System Pressure

To check the system pressure, click the *Check pressure* button. With this function you can check if the pressure is constant after a change of bottles. If not, the bottle might not be closed tightly enough or there is some leak elsewhere.

13.6. Shutdown

To shut down the hyborg software and the hyborg – for example to pause its operation for some longer period, press the *Shutdown* button. This button is only activated, if the hyborg is not processing a hybcell or cleaning itself. The user will be prompted to confirm the shutdown. Confirm the shutdown by pressing the *OK* button.



Confirming the shutdown of the device.

After shutdown (black screen), turn the main switch off (on the right side of the device).

13.7. Analyze Scan

Previously made scans (as tiff-files) might be analyzed offline or with different protocols (e.g., to examine variations or influence of different variations).

To analyze scans, the scan itself (tiff-file) as well as the protocol (xml-file) have to be loaded from an external source (file system).

Once loaded, this feature creates the same formats as analyzing regular results (compare *Basic hybcell Processing, See Results, Check Plausibility* and *Print report* above).

Similar screens as for *Import New Protocols* (see above) are used to select protocol and scan (tif) for analysis.

13.8. Show Information on Software Versions

Pressing the *Information* button prompts the below screen to pop-up. It contains information on the last execution of the hybcell Control and the installed software versions and copyright information.

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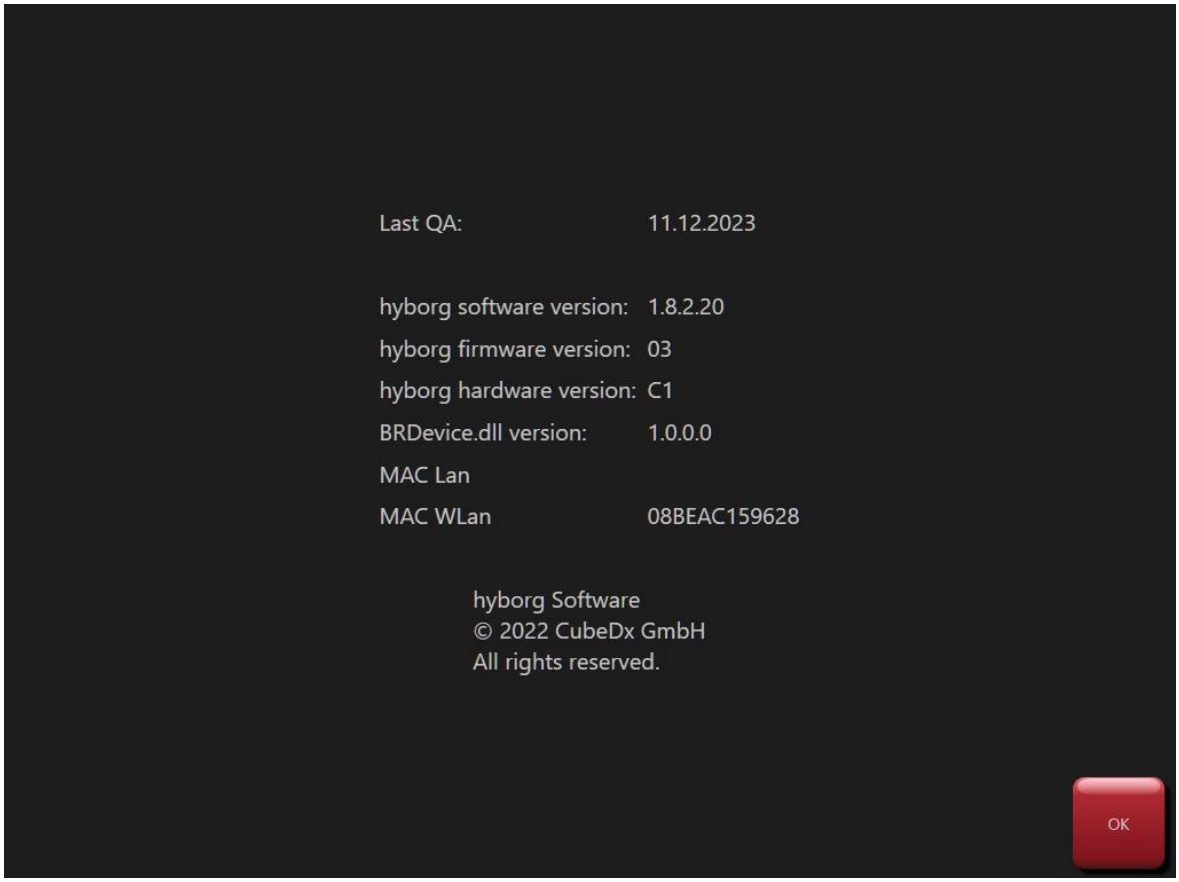

Information on software versions installed.

13.9. Diagnose the Status of Device Hardware / Electronics

Pressing the *Device diagnose* button prompts a screen depicting the status of hardware (electronics). This information should help during trouble shooting and you might be asked by service technicians about that information.

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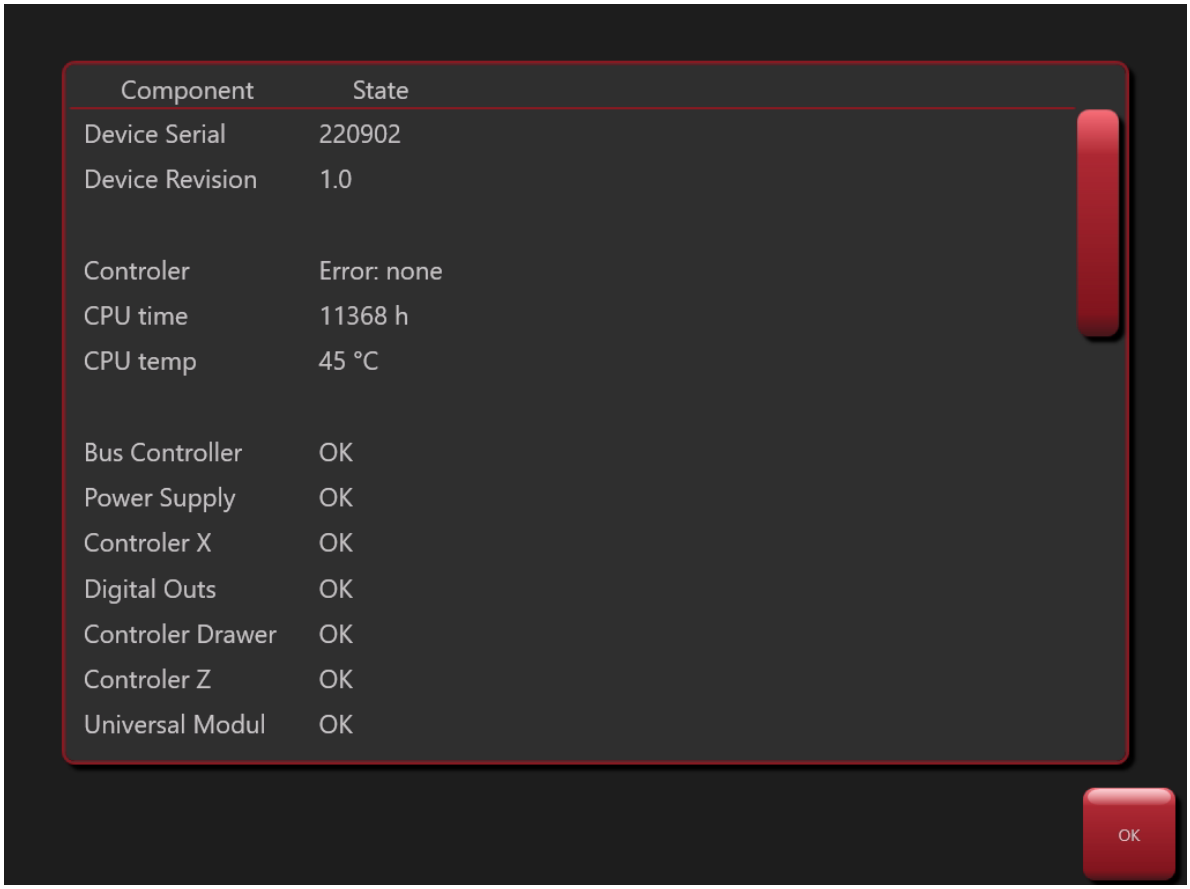

Information on status of hardware components.

13.10. Show Log, Usage and this Manual

By clicking the *Show log* button, the log of the device is shown. The log lists the actions of the device with a time stamp. Actions are for example the start of the device and software, the processing of a hybcell or the exchange of liquids.

By clicking the *Usage overview* button, statistics about the usage of different hybcells (protocols) for a user-defined period of time is presented.

By clicking the *Show manual* button, this manual is shown (in pdf-format).

13.11. Control hybcell and Quality Assurance

The hybcell Control xC (HC0006-12) offers the possibility to control the basic functionalities of hyborg Dx RED2. These functionalities are liquid transport, optics and scanning, temperature control and hybcell handling.

To start the control, the barcode of hybcell Control xC has to be scanned at the position *Control barcode*.

After a valid barcode was scanned the procedure is initiated by clicking the *Start control* button.

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The result of the control is added to the list of previously done controls (at the top of the list). By clicking the result, details of the results are shown.

If the control failed, please contact Cube Dx or respective distribution partners.

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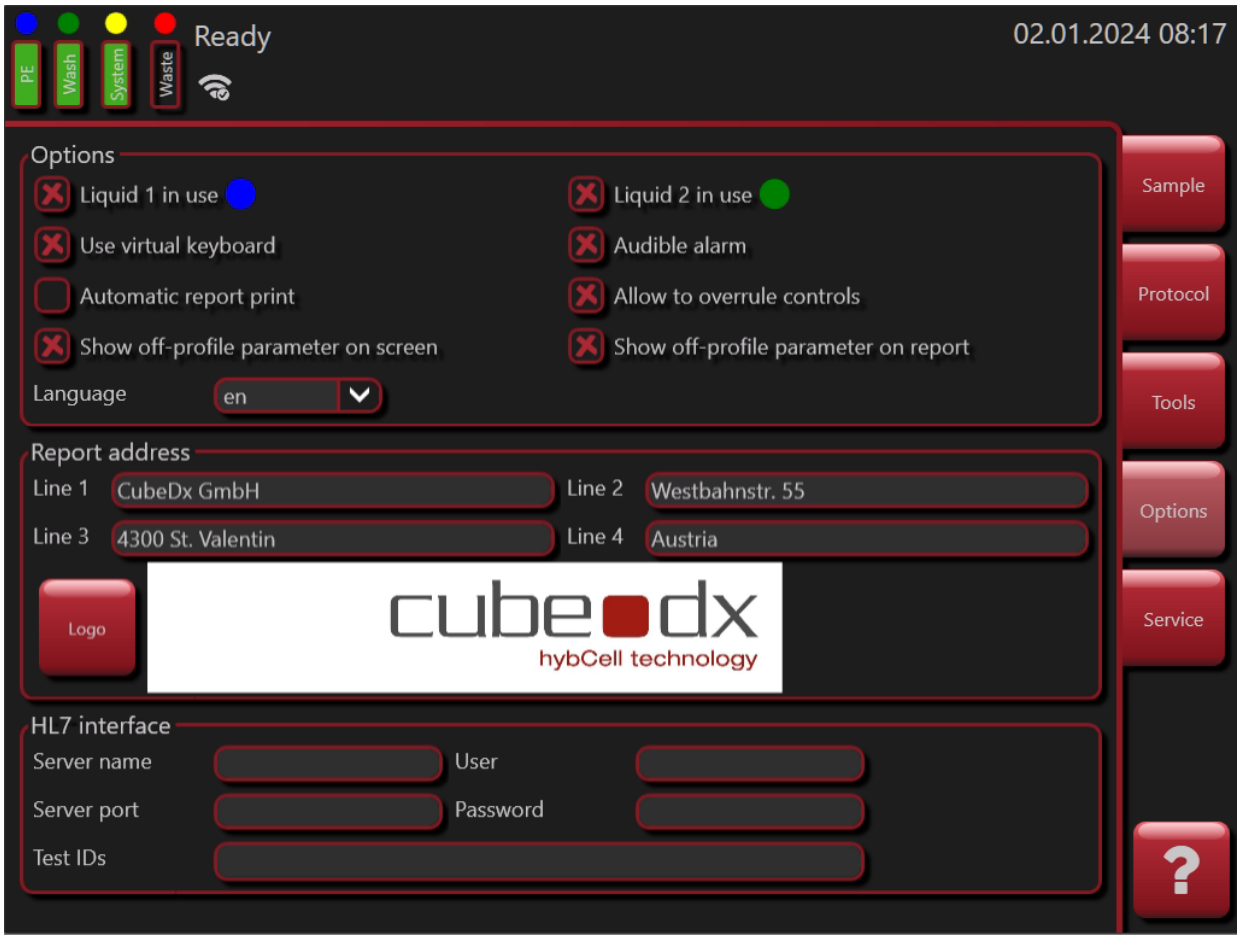
14. Options

The hyborg offers a few options for operation, 4 freely configurable lines to be depicted on the reports as well as an HL7 Interface.



The device and software options.

Several options for operation of the device can be (un)selected by (un)checking a checkbox:

- *Liquid 1 in use/Liquid 2 in use*: Indicate if you want to use liquid 1 and liquid 2. If you use one or both of these liquids, their corresponding level sensors are checked by the software and during start-up the flow-rate is checked.
- *Use virtual keyboards*: if checked, texts and numbers can be entered with help of the touchscreen, as a virtual keyboard is displayed when the user is prompted to input (textual) data.
- *Audible alarm*: In case of an error an audible alarm will be triggered.
- *Automatic report print*: After each processed hybcell the associated report will be automatically printed by the defined standard printer.

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- *Allow to overrule controls*: If this option is selected, it is possible to overrule defined controls and to visualize results despite failed controls during checking results in expert mode. After leaving the expert mode the parameter will be presented which would have been suppressed due to failed controls.
- *Show off-profile parameter on screen/Show off-profile parameter on report*: The screen results / report includes results for parameters that are not defined in the used profile.

The four lines under the section *Report* can be modified by the user. These lines are displayed on each report generated by the hyborg software.

The settings under the section *HL7 Interface* configure a unidirectional HL7 interface (upload). Ask for support, if you want to use the HL7 interface.

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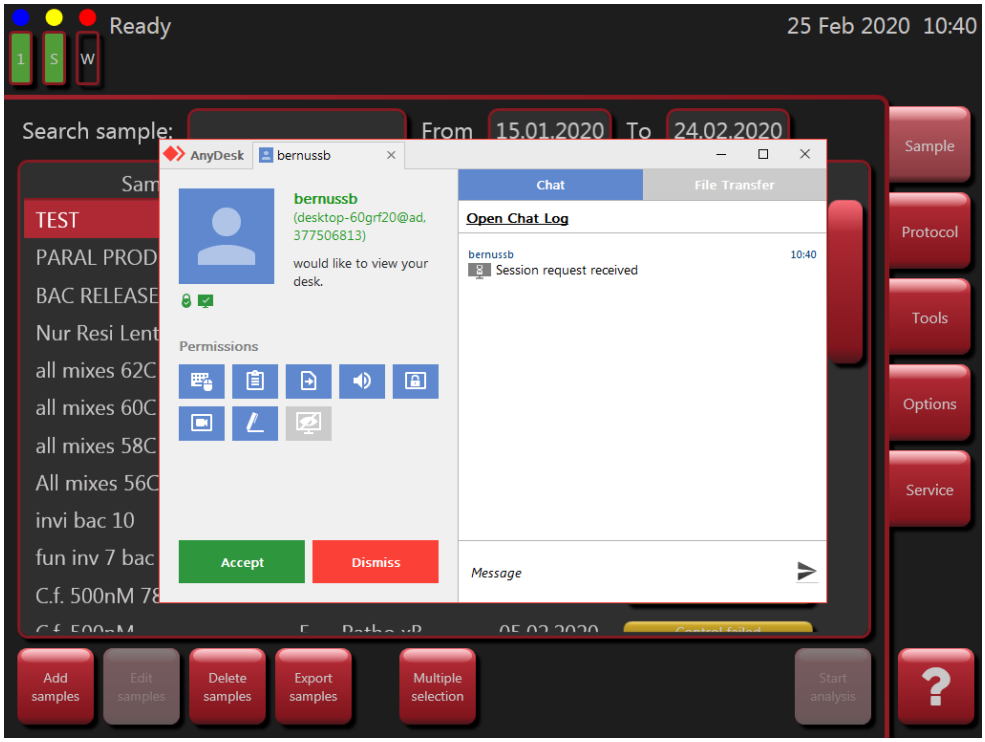
15. Troubleshooting

Make sure to shut down the hyborg and disconnect the power supply cable any time you have remove the cover of the device. (See the *Tools section*, *Shutdown* above).
All trouble shooting might only be done by trained operators (authorized training by Cube Dx or its distributors).

15.1. Granting Access to a Member of the Cube Dx Support Team

If the hyborg is connected to the internet a remote connection to the instrument can be established by a Cube Dx support member. This remote maintenance software explicitly asks for permission to access the device from outside for each remote maintenance session. To do this, you must authorise the support member to access the device.



Remote session.

15.2. Removing hybcell Components from the Inside

If an error occurs that causes a hybcell part to be stuck in the analysis chamber or in another position, the device should remove these parts by itself. These hybcell parts will be moved behind the opening of the drawer. The drawer cover must be opened manually by the user and the hybcell parts must be taken out.

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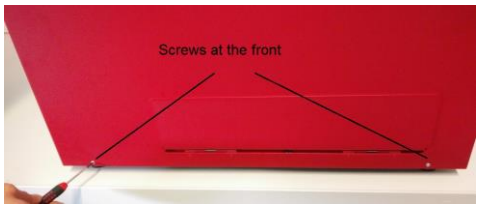
Open the drawer manually.

Remove hybcell parts.

It might be necessary to open the gripper. A popup window asks, if such opening is intended. If you confirm, the gripper opens automatically.

In rare occasions it might be necessary to remove hybcell parts manually from the inside of the device. To do so, you can either access the device via the drawer, or you have to remove the device cover.

To do so, shutdown device and pull out power cable. You have to remove 4 screws (2 at the bottom of the front and 2 at the top of the rear).



Remove two screws at the front.

Remove two screws at the rear.

Take off cover.

Wear protective gloves when you are checking for hybcell parts! Remove the hybcell parts and attach the cover once again.

Do not operate the device without the cover! During the start-up, the device will initialize.

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15.3. Empty Liquids / Full Waste

If the necessary liquids (System Liquid, PE-Buffer, custom solutions…) are detected to be empty by the sensors, you have to exchange the liquids. Open the corresponding bottle by unscrewing the cap, exchange the bottle and attach the cap once again – it must air-tightly seal the bottle. If the waste bottle is full, remove it by detaching it from the cap and attaching a new waste bottle. The bottles, caps and the position in the device are colour-coded:

Waste Bottle:	red.
System Liquid:	yellow.
Custom solution / Wash buffer:	green.
PE-Buffer:	blue.

Use the Manage liquids function under the Tools screen to teach the software the new liquids (Liquid barcodes, compare *Tools, Manage Liquids*)

Make sure to check the technical description of the liquids for safety and disposal information. The waste bottle may contain bio-hazard material. Make sure to wear appropriate protective gear before handling the filled waste bottles.

15.4. Barcodes on liquid bottles not readable

If the barcode on the liquid bottle is not readable by the software and the bottle cannot be replaced, then please check following possible causes:

- Bottles are single use and can only scanned once by the software.
- Use the original barcode reader supplied with the device.
- If the barcode is damaged, please contact your local distributer.
- The barcode reader must be programmed to read the barcodes correctly. You may try to reprogram the reader by scanning following barcodes in this sequence:

ENTER/EXIT PROGRAMMING MODE

French (France)

German

Italian

Spanish

United Kingdom

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15.5. Invalid Controls / Results

Invalid internal controls or suspicious analysis results may be due to incorrectly connected liquids or congested tubing. Check the connection of liquids and execute a *Clean tubing* command (see above). See the test manuals for more details.

15.6. Serious Incidents / Vigilance

Make sure to immediately report serious incidents related with the use of the device to Cube Dx or respective distribution partners and the national competent authority. Please note your national legislation about reporting serious incidents!

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