December 2016

QIAGEN GeneReader® User Manual

For use with Advanced Process Flow (APF) Instrument Configuration

For Research Use Only. Not for use in diagnostic procedures.

Sample to Insight

QIAGEN

Contents

Instrument Configuration History

Document title	Document number	Date	Description of changes and specifications	Compatible software and sequencing kits
QIAGEN GeneReader User Manual for use with APF Instrument Configuration	HB-2325-001	December 2016	Supports Advanced Process Flow (APF) workflow compatible with: 1. GeneRead™ QIAact Actionable Insights Tumor Panel, cat. no. 181910 2. GeneRead QIAact Lung DNA Panel, cat. no. 181930 3. GeneRead QIAact BRCA 1/2 DNA Panel Updated the following specifications: 1. Higher read length, >30% 2. Higher data output, >50% 3. Higher sample multiplexing capacity per flow cell for the GeneRead QIAact Actionable Insights Tumor Panel (ATP) 4. Approximately 20% less reagent consumption per cycle 5. Equal or less sequencing time 6. Parallel or staggered processing of up to 3 flow cells GeneReader instruments released prior to the Advanced Process Flow instrument configuration can be upgraded to the APF instrument configuration	GeneReader™ Software version 1.4.0 QIAGEN GeneRead® Advanced Sequencing Q Kit (3), cat. no. 185231 GeneRead Sequencing Buffer Q Kit (16), cat. no. 185901 **IMPORTANT**: When used in combination with the QIAGEN GeneRead Advanced Sequencing Q Kit, the GeneRead Sequencing Buffer Q Kit (16) will allow the user to process 6 flow cells.
GeneReader User Manual	HB-2023-001	December 2015	Specifications: 1. Compatible with GeneRead QIAact Panels, Powered by QCI™, cat. no. 181910 2. Approximately 45 hours sequencing time 3. Parallel or staggered processing of up to 4 flow cells	GeneReader Software up to version 1.1.3 GeneRead Sequencing Q Kit (1), cat. no. 185200 GeneRead Sequencing Q Kit (4), cat. no. 185201 GeneRead Sequencing Buffer Q Kit, (16) cat. no. 185901

1 Introduction

Thank you for choosing the GeneReader. We are confident it will become an integral part of your laboratory.

Before using the GeneReader, it is essential that you read this user manual carefully and pay particular attention to the safety information. The instructions and safety information in the user manual must be followed to ensure safe operation of the instrument and to maintain the instrument in a safe condition.

1.1 About this user manual

This user manual provides information about the GeneReader in the following sections:

- User Manual History
- Introduction
- Safety Information
- General Description
- Installation Procedures
- Operating Procedures
- Maintenance
- Troubleshooting
- Technical Data
- Appendices
- Index

The appendices contain the following information:

- Declaration of Conformity
- License Terms
- Waste Electrical and Electronic Equipment (WEEE)
- FCC Declaration
- Liability Clause
- GeneReader accessories

1.2 General information

1.2.1 Technical assistance

At QIAGEN, we pride ourselves on the quality and availability of our technical support. Our Technical Services Departments are staffed by experienced scientists with extensive practical and theoretical expertise in molecular biology and the use of QIAGEN products. If you have any questions or experience any difficulties regarding the GeneReader or QIAGEN products in general, do not hesitate to contact us.

QIAGEN customers are a major source of information regarding advanced or specialized uses of our products. This information is helpful to other scientists as well as to the researchers at QIAGEN. We therefore encourage you to contact us if you have any suggestions about product performance or new applications and techniques.

For technical assistance, contact QIAGEN Technical Services.

1.2.2 Policy statement

It is the policy of QIAGEN to improve products as new techniques and components become available. QIAGEN reserves the right to change specifications at any time. In an effort to produce useful and appropriate documentation, we appreciate your comments on this user manual. Please contact QIAGEN Technical Services.

1.3 Intended use of the GeneReader

The GeneReader is designed to perform next-generation sequencing (NGS) applications by integrating highly parallel fluorescence-based sequencing chemistry with detection of the corresponding fluorescent signals from templates that have been clonally amplified using the GeneRead QIAcube®.

GeneReader software provides a wizard for setting up the sequencing, data storage management, and the functionality for base calling and generation of FASTQ files.

The GeneReader is intended to be used only in combination with QIAGEN kits indicated for use with the GeneReader for applications described in the respective QIAGEN kit product sheets or handbooks.

The GeneReader is intended for Research Use Only. Not for use in diagnostic procedures.

The GeneReader is intended for use by professional users trained in molecular biological techniques and in the operation of the GeneReader.

1.4 Requirements for GeneReader users

The table below covers the general level of competence and training necessary for transportation, installation, use, maintenance and servicing of the GeneReader.

Task	Personnel	Training and experience
Transportation	No special requirements	No special requirements
Installation	**QIAGEN Field Service Specialists only**	
System relocation	**QIAGEN Field Service Specialists only**	Special training required
Routine use (running protocols)	Laboratory technicians or equivalent	Appropriately trained and experienced personnel familiar with use of computers and automation in general
Regular and weekly maintenance	Laboratory technicians or equivalent	Appropriately trained and experienced personnel familiar with use of computers and automation in general
Annual preventative maintenance and servicing	**QIAGEN Field Service Specialists only**	No special requirements

2 Safety Information

Before using the GeneReader, it is essential that you read this user manual carefully and pay particular attention to the safety information. The instructions and safety information in the user manual must be followed to ensure safe operation of the instrument and to maintain the instrument in a safe condition.

The following types of safety information appear throughout the *QIAGEN GeneReader User Manual for Advanced Process Flow (APF) Instrument Configuration*.

WARNING ⚠	The term WARNING is used to inform you about situations that could result in **personal injury** to you or others. Details about these circumstances are given in a box like this one.

CAUTION ⚠	The term CAUTION is used to inform you about situations that could result in **damage to an instrument** or other equipment. Details about these circumstances are given in a box like this one.

The guidance provided in this manual is intended to supplement, not supersede, the normal safety requirements prevailing in the user's country.

2.1 Proper use

WARNING ⚠	**Risk of personal injury and material damage** Improper use of the GeneReader may cause personal injuries or damage to the instrument. The GeneReader must only be operated by qualified personnel who have been appropriately trained. Servicing of the GeneReader instrument must only be performed by a QIAGEN Field Service Specialist.

Perform the maintenance as described in Section 6. QIAGEN charges for repairs that are required due to incorrect maintenance.

WARNING ⚠	**Risk of personal injury and material damage** The GeneReader is too heavy to be lifted by one person. To avoid personal injury or damage to the instrument, do not lift the instrument alone. Contact QIAGEN Technical Services to relocate the instrument.

WARNING ⚠	**Risk of personal injury and material damage** Do not attempt to move the GeneReader during operation.

WARNING ⚠	**Risk of personal injury and material damage** Load flow cell only in accordance with step-by-step instructions provided by GeneReader software. Beware of moveable parts.

WARNING ⚠	**Risk of personal injury and material damage** Do not stare into the beam of the flow cell bar code reader.

CAUTION ⚠	**Risk of material damage** Avoid moving the workbench and causing vibrations to the GeneReader during operation to prevent disturbing sensitive optical measurements.

CAUTION ⚠	**Damage to the instrument** Avoid spilling water or chemicals onto the GeneReader. Damage caused by water or chemical spillage will void your warranty.

CAUTION ⚠	**Risk of material damage** Do not place any items on top of the instrument.

In case of emergency, power OFF the GeneReader using the power switch at the right, rear panel of the instrument and unplug the power cord from the power outlet.

CAUTION ⚠	**Damage to the instrument** Only use QIAGEN consumables with the GeneReader. Damage caused by use of other types of consumables will void your warranty.

CAUTION ⚠	**Damage to the instrument** Make sure that the flow cell is inserted in the correct position. Incorrect insertion of the flow cell can damage the instrument.

WARNING ⚠	**Fire hazard** Empty the liquid waste bottle before each run and make sure to place it in the correct orientation back in the GeneReader instrument. Spilling of liquid-waste may cause an electrical short-circuit and fire.

2.2 Electrical safety

Disconnect the line power cord from the power outlet before servicing.

WARNING ⚠	**Electrical hazard** Any interruption of the protective conductor (earth/ground lead) inside or outside the instrument or disconnection of the protective conductor terminal is likely to make the instrument dangerous. Intentional interruption is prohibited. **Lethal voltages inside the instrument** When the instrument is connected to line power, terminals may be live and opening covers or removing parts is likely to expose live parts.

WARNING ⚠	**Damage to electronics** Before powering ON the instrument make sure that the correct supply voltage is used. Incorrect use of supply voltage may cause damage to electronics. See specifications indicated on the type plate of the instrument.

WARNING ⚠	**Risk of electric shock** Do not open any panels on the GeneReader. **Risk of personal injury and material damage** Only perform maintenance that is specifically described in this user manual.

To ensure satisfactory and safe operation of the GeneReader, follow the advice below:

- The line power cord must be connected to a line power outlet that has a protective conductor (earth/ground).

- Place instrument in a location so that the power cord is accessible and can be connected/disconnected.
- Use only the power cord delivered by QIAGEN.
- Do not adjust or replace internal parts of the instrument.
- Do not operate the instrument with any covers or parts removed.
- If liquid has spilled inside the instrument, switch off the instrument, disconnect it from the power outlet and contact QIAGEN Technical Services.

If the instrument becomes electrically unsafe, prevent other personnel from operating it and contact QIAGEN Technical Services.

The instrument may be electrically unsafe when:

- It or the line power cord appears to be damaged.
- It has been stored under unfavorable conditions for a prolonged period.
- It has been subjected to severe transport stresses.

2.3 Environment

2.3.1 Operating conditions

WARNING ⚠	**Explosive atmosphere** The GeneReader is not designed for use in an explosive atmosphere.

WARNING ⚠	**Risk of explosion** The GeneReader is intended for use with reagents and substances supplied with QIAGEN kits. Use of other reagents and substances may lead to fire or explosion.

CAUTION	**Damage to the instrument** Direct sunlight may bleach parts of the instrument and cause damage to plastic parts. The GeneReader must be located out of direct sunlight.

2.4 Chemicals

WARNING	**Hazardous chemicals** Some chemicals used with this instrument may be hazardous or may become hazardous after completion of the protocol run. Always wear safety glasses, gloves, and a lab coat. The responsible body (e.g., laboratory manager) must take the necessary precautions to ensure that the surrounding workplace is safe and that the instrument operators are not exposed to hazardous levels of toxic substances (chemical or biological) as defined in the applicable Safety Data Sheets (SDSs) or OSHA,[*] ACGIH[†] or COSHH[‡] documents. Venting for fumes and disposal of wastes must be in accordance with all national, state, and local health and safety regulations and laws.

[*] OSHA: Occupational Safety and Health Administration (United States of America).

[†] ACGIH: American Conference of Government Industrial Hygienists (United States of America).

[‡] COSHH: Control of Substances Hazardous to Health (United Kingdom).

2.5 Waste disposal

Used labware may contain hazardous chemicals. Such wastes must be collected and disposed of properly according to local safety regulations.

For more information about how to dispose of the GeneReader, see "Waste Electrical and Electronic Equipment (WEEE)", page 70.

WARNING ⚠	**Hazardous chemicals and infectious agents** The waste contains samples and reagents. This waste may contain toxic or infectious material and must be disposed of properly. Refer to your local safety regulations for proper disposal procedures.

2.6 Mechanical hazards

The door of the GeneReader must remain closed during operation of the instrument. Only handle the flow cell loading station when the flow cell door has been released by the software.

Note: Only power OFF the instrument if the process has been properly terminated by the software and the flow cell door is closed.

WARNING ⚠	**Moving parts** To avoid contact with moving parts during operation of the GeneReader, the instrument must be operated with the flow cell door closed. If the door sensor is not functioning correctly, contact QIAGEN Technical Services.

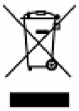
WARNING ⚠	**Risk of overheating** To ensure proper ventilation, maintain a minimum clearance of 10 cm at the sides and rear of the GeneReader. Slits and openings that ensure the ventilation of the GeneReader must not be covered.

2.7 Maintenance safety

WARNING ⚠	**Risk of personal injury and material damage** Only perform maintenance that is specifically described in this user manual.

CAUTION ⚠	**Damage to the instrument** Do not use bleach, solvents, or reagents containing acids, alkalis, or abrasives to clean the GeneReader.

2.8 Symbols on the GeneReader

Symbol	Location	Language	Description
	Inside instrument	–	Heat hazard – do not perform maintenance before the system has cooled down.
	On the instrument	–	Mechanical hazard – avoid contact with moving parts.
	On front of the instrument, open door	–	Mechanical hazard – avoid contact with moving parts.
	Inside instrument	–	Electric shock hazard
	On the instrument, right side panel	EN	This product contains a class 2 laser. Do not stare into the beam.
	On the instrument, right side panel	FR	This product contains a class 2 laser. Do not stare into the beam.
	On front of the instrument, open door	–	This product contains a class 2 laser. Do not stare into the beam.
	Type plate on the right side panel	–	WEEE about the disposal of waste electrical and electronic equipment for Europe and rest of the world.
	Type plate on the right side panel	–	Legal manufacturer.
	On the instrument, right side panel	–	Consult instructions for use.
	On the instrument, right side panel	EN	Disconnect power supply before servicing.
	Inside instrument	–	Earth (Ground)

Symbol	Location	Language	Description
CE	Type plate on the back of the instrument	–	CE mark for Europe
FC	Type plate on the back of the instrument	–	FCC mark of the United States Federal Communications Commission
✓	Type plate on the back of the instrument	–	RCM (former C-Tick) for Australia (supplier identification N17965)
25	Type plate on the back of the instrument	–	RoHS mark for China (the restriction of the use of certain hazardous substances in electrical and electronic equipment)
SN	Type plate on the back of the instrument	–	Instrument serial number
CSA C US	Type plate on the back of the instrument	–	Certification mark Indicates that the product was tested and has met the certification requirements for electrical, plumbing and/or mechanical products
APF instrument configuration ETI-00000056	Sticker on the instrument, right side panel	–	Sticker indicating GeneReader with Advanced Process Flow (APF) instrument configuration

3 General Description

The QIAGEN GeneReader performs fully automated next-generation sequencing (NGS) by integrating highly parallel fluorescence-based sequencing chemistry with detection of the corresponding fluorescent signals on templates that have been clonally amplified using the GeneRead QIAcube.

The GeneReader sequencer consists of the GeneReader, the workstation, the GeneReader software and a handheld bar code scanner that connects to the workstation for scanning bar codes of kits and buffers, which are then automatically entered into the GeneReader software. The initial software installation is performed by a QIAGEN Field Service Specialist. There are two USB connections between the GeneReader instrument and workstation. The GeneReader sequencer includes several additional components, which are listed in Section 4.1.

The GeneReader software provides a FASTQ file of sequence information for each analyzed sample that is ready for QCI Analyze or GeneRead Link. QCI Analyze automatically runs an optimized workflow for GeneReader panels and generates a VCF result file that is ready for upload to QCI Interpret.

3.1 QIAGEN GeneReader Sample to Insight® NGS workflow

The QIAGEN GeneReader Sample to Insight workflow provides a streamlined and standardized approach to next-generation sequencing, from sample preparation to the biological interpretation of sequencing data.

The majority of the workflow is automated, ensuring greater standardization and more accurate results.

QIAGEN Clinical Insight combines analytical tools and integrated human disease content, providing access to current and advanced interpretations of genomic data. QCI Analyze or GeneRead Link automatically sends samples through predefined workflows and provides a web-based result viewer. Afterwards, QCI Interpret (another web-based viewer) provides a biological interpretation.

3.2 GeneReader principle

The workflow includes the following 6 processes: sequencing primer hybridization, flow cell preparation, reagents preparation, experiment set-up, flow cell loading and run start, and post-run maintenance wash. These procedures are described in detail starting on page 35 and the principle behind a sequencing run on the GeneReader is shown below in Figure 1.

The GeneReader sequencing-by-synthesis technology consists of the incorporation of unique, reversible terminated and fluorescent-labeled dNTPs ("labeled nucleotides") first, followed by unlabeled reversible terminated dNTPs ("dark nucleotides"). The GeneReader sequencing chemistry uses four dye colors for labeling with each color indicating a different base (A, C, G or T) that is incorporated onto the DNA fragment. Furthermore, the reversible terminators facilitate the addition of only one engineered nucleotide at a time to the growing strand of all DNA templates. Upon signal detection from each bead the fluorescent labeling as well as the terminators are removed allowing for a new cycle of incorporation, ensuring highly accurate and cost-effective next-generation sequencing.

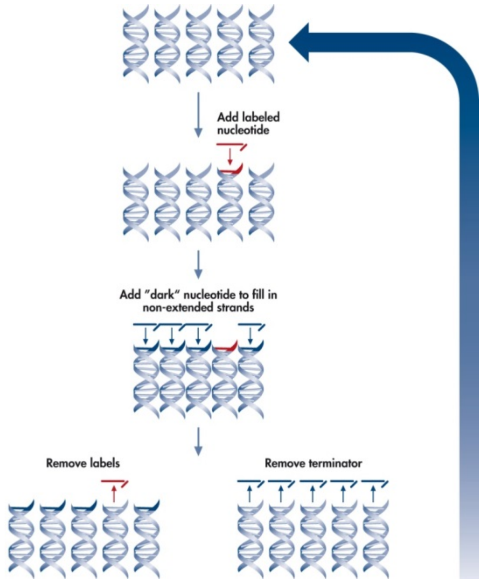


Figure 1. Principle behind sequencing-by-synthesis technology on the GeneReader.

DNA libraries are clonally amplified on beads using the GeneRead QIAcube® to serve as a sequencing template. After hybridization of a sequencing primer, the primer-template carrying beads are immobilized via direct bead-glass interaction to produce a high-density array on a GeneReader Flow Cell. To read out the content of templates on each bead, the array of fragments is first subjected to reagents containing uniquely engineered dNTPs, as described above. These bases are incorporated by a modified DNA polymerase to the end of the growing strand of DNA in accordance with the base on the complementary strand (as shown in Figure 1). The array is subsequently scanned by a high-resolution digital camera and the fluorescent output of each of the four dye colors at each array position is measured and recorded. Finally, the array is exposed to cleavage chemistry to break off the fluorescent dyes and reversible terminators that will then allow additional bases to be incorporated. This cycle is then repeated on the GeneReader.

3.3 External features of the GeneReader

Front view **Side view (right side panel)**

1 Status lights
2 Flow cell door
3 Hood
4 Fluidic drawer
5 USB port (GeneReader connection)
6 USB port (camera connection)
7 Power switch
8 Power cord socket
9 Cooling air outlet (back of instrument)
10 Main Hood (QIAGEN service only)
11 Instrument configuration sticker (right side panel)

3.3.1 Status lights

The status lights illuminate in the following pattern:

- When the instrument is not running the status lights are off.
- When a protocol is running normally, the green light is on.
- When a protocol is running, but a pause has been requested, or when a protocol is paused, the green light blinks.
- When all protocols have been stopped, canceled or an error has occurred, the red light is on.
- When the protocol has finished successfully, the green light blinks.

3.3.2 Flow cell door

Opening the flow cell door

Flow cells are inserted through the flow cell door. Opening the flow cell door is controlled by software.

Note: The flow cell door cannot be opened manually.

Closing the flow cell door

Push the flow cell door manually until the fastener snaps in place to lock the door.

Note: The GeneReader will not work if the flow cell door is not locked.

3.3.3 Hood

Opening the hood

Opening the hood is controlled by software. The hood must be opened prior to opening the fluidic drawer.

Note: The hood can be manually released if the GeneReader loses power. Insert your hand, palm facing upward, and feel for the hole located approximately where the Main Hood meets the fluidic drawer. When your fingers are in the hole you will feel a lever on the right and by pulling slightly towards the front the hood will open.

Manually opening the hood

Closing the hood

The fluidic drawer must be closed (pushed all the way in until a clicking sound is heard) prior to manually pulling down the hood.

Note: The Main Hood on the left side of the instrument must only be opened by QIAGEN Field Service Specialists.

3.3.4 Fluidic drawer

Open the fluidic drawer to:

- Load or unload 1 liter wash bottles.
- Load or unload 50 ml tubes.
- Insert or remove the liquid waste bottle.
- Clean the cooling block, remove excessive condensation
- Clean the drawer
- Clean the dip sticks
- Clean the waste level sensor surface

The fluidic drawer remains locked during a run.

Note: If the hood is closed, the fluidic drawer cannot be opened.

3.3.5 USB ports

The 2 USB ports are used to connect the GeneReader with the workstation. They are located on the right side panel of the instrument.

3.3.6 Power switch

The power switch is located on the right side panel of the GeneReader.

3.3.7 Power cord socket

The power cord socket is located on the right side panel of the GeneReader. It allows connection of the GeneReader to a power outlet via the supplied power cord.

3.3.8 Cooling air outlet

Cooling air outlets are on the right side and back of the GeneReader. They allow cooling of the internal components. The instrument should not be positioned in close proximity to a wall that could block airflow.

3.3.9 Workstation equipment

The GeneReader system is operated with a workstation.

The workstation specifications are listed in Section 8.3.

3.4 Internal features of the GeneReader

Internal view of the fluidic drawer

1	50 ml conical tubes in cooling compartment	**3**	Liquid waste bottle
2	One liter bottles for sequencing wash buffer or maintenance wash buffer		

3.4.1 GeneReader Flow Cell

Sequencing beads carrying single strand DNA templates with sequencing primers annealed are deposited into the GeneReader Flow Cell according to the *QIAGEN GeneRead Advanced Sequencing Q Handbook*. The flow cell should be loaded into the GeneReader through the flow cell door with the bar code towards the left side of the GeneReader.

Loading the flow cell

View inside the flow cell door

Flow cell bar code reader

Upon loading of a flow cell, the flow cell bar code reader scans the bar code on the flow cell and provides the information to the GeneReader software. If the flow cell has been inserted in the wrong orientation an error message is displayed.

4 Installation Procedures

4.1 System delivery and installation

The unpacking and installation of the GeneReader is performed by a certified QIAGEN Field Service Specialist. A person who is familiar with your laboratory and computer equipment should be present during the installation.

The following items are delivered:

- GeneReader instrument
- *GeneReader User Manual for Advanced Process Flow (APF) Instrument Configuration*
- Workstation
- GeneReader software (will be installed by QIAGEN Field Service during initial set up)
- Additional components: 1 international power cable set, 2 USB cables, 1 handheld bar code scanner, 1 waste container and 4 one liter bottles

Note: The computer required for data analysis is optionally provided by QIAGEN. Refer to the *QIAGEN Clinical Insight Analyze 1.2 User Manual* for the required powerstation specifications.

4.2 Site requirements

The GeneReader must be located out of direct sunlight, away from heat sources, and away from sources of vibration and electrical interference. Refer to Appendix A for the operating conditions (temperature and humidity). The site of installation should be free of excessive drafts, excessive moisture and dust, and not be subject to large temperature fluctuations.

Refer to Section 8 for the weight and dimensions of the instrument.

Use an appropriate workbench to accommodate the GeneReader. Ensure that the workbench is dry and clean, and has additional space for accessories. To accommodate the GeneReader instrument with the hood open, 125 cm (49.3 in.) minimum clearance above the workbench is required. Allow at least 10 cm (4 in.) of free space behind the instrument for cables and cooling of the instrument.

The GeneReader must be placed within approximately 1.5 m (59 in.) of a properly grounded (earthed) AC power outlet. The power line to the GeneReader should be voltage regulated and surge protected, and an uninterruptable power supply (UPS) is optional.

Note: Do not place the GeneReader instrument on a vibrating surface or near vibrating objects.

WARNING ⚠	**Risk of overheating** To ensure proper ventilation, maintain a minimum clearance of 10 cm at the sides and rear of the GeneReader. Slits and openings that ensure the ventilation of the GeneReader must not be covered.

WARNING ⚠	**Risk of personal injury and material damage** The GeneReader is too heavy to be lifted by one person. To avoid personal injury or damage to the instrument, do not lift the instrument alone.

4.3 AC Power and USB cable connections

4.3.1 Power requirements

The GeneReader operates at:

- 100–240 V AC, 50/60 Hz, max. 600 VA

The workstation operates at:

- 100–240 V AC, 50/60 Hz, max. 400 VA

Make sure that the voltage rating of the GeneReader and workstation are compatible with the AC voltage available at the installation site.

WARNING ⚠	**Damage to electronics** Incorrect use of supply voltage may cause damage to electronics. See specifications indicated on the type plate of the instrument.

4.3.2 Grounding requirements

To protect operating personnel, the National Electrical Manufacturers' Association (NEMA) recommends that the GeneReader be correctly grounded (earthed). The instrument is equipped with a 3-conductor AC power cord that, when connected to an appropriate AC power outlet, grounds (earths) the instrument. To preserve this protection feature, do not operate the instrument from an AC power outlet that does not have a ground (earth) connection.

4.3.3 Installation of AC power cords, USB cables and workstation

IMPORTANT: Make sure that the GeneReader and workstation power switches are set to the OFF position.

Connect the power cords and USB cables as shown in the diagram below.

Note: It is recommended to plug the instrument and workstation directly into a shared line power outlet because the instrument and workstation are connected with 2 USB cables. This configuration results in less interference caused by ground loops.

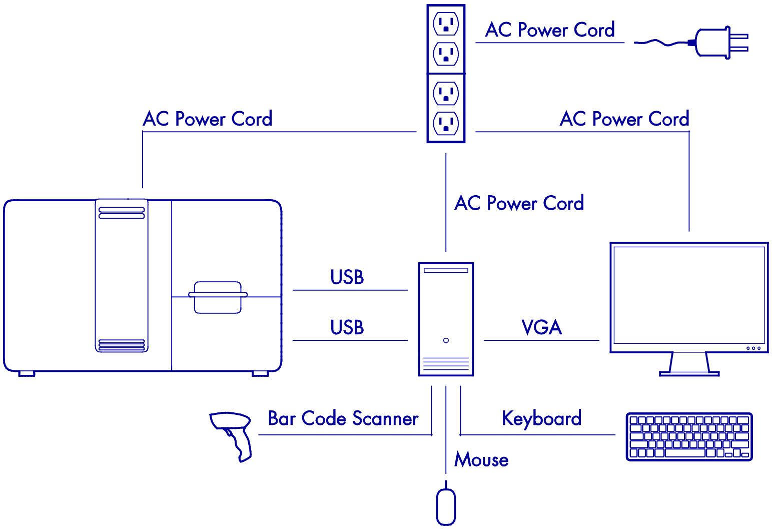


Diagram of cable connections

4.3.4 Installation of AC power cords, USB cables and workstation using an optional UPS

IMPORTANT: Make sure that the GeneReader and workstation power switches are set to the OFF position.

Connect the GeneReader and workstation to the UPS as shown in the diagram below. The UPS should be configured in such a way that a Windows® shutdown command is issued shortly before backup power is lost. The UPS should be able to supply the GeneReader and workstation with a maximum 1000 VA for the desired time.

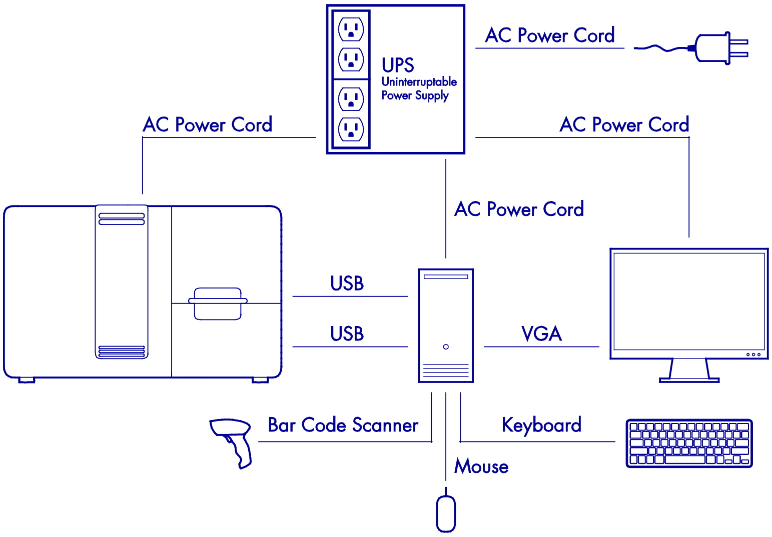


Diagram of cable connections using an optional UPS

4.4 Workstation requirements

The workstation, supplied with the GeneReader instrument, fulfills the requirements of the GeneReader software as detailed in the following table.

Workstation system requirements

Description	Minimum requirement
Operating system	Microsoft® Windows 7 Professional 64-bit (D/F/E/I)
Processor	Intel® Xeon® E5–1650 v3 (3.50 GHz 6 Core)
Main memory	32GB (4x8 GB) DDR4-2133 ECC (max. 128 GB)
Hard disk space	1 x 256 GB SATA SE SSD 3 x 2.0 TB SATA 7200 rpm HDD
Graphic card	NVIDIA Quadro K2200 4 GB Graphics
Monitor	Resolution at least 1920 x 1080 pixels
Ports	1x VGA: Monitor 2x USB: GeneReader 2x USB: Mouse, keyboard 1x USB: Bar code scanner

Adobe® Reader® software is preinstalled on the computer to view reports generated in PDF format.

IMPORTANT: Microsoft Windows 7 Professional comes preinstalled on the GeneReader workstation. By default, the following Microsoft background activities are disabled and any change to the Microsoft Windows configuration by an operator may affect sequencing performance:

- Automatic Windows update
- Background indexing
- Automatic background defragmentation
- Automatic backup
- Energy saver mode

4.5 Getting started

4.5.1 Powering ON the GeneReader and workstation

1. Power ON the GeneReader using the power switch located on the right side panel of the GeneReader.
2. Power ON the workstation and monitor.

3. Log in to the system using your password.
4. Start the GeneReader software.

When the GeneReader software has been started, the following window will appear:

IMPORTANT: If virus scan software is installed on the GeneReader workstation, make sure that active scanning or anti-virus software updates are not performed during a sequencing run.

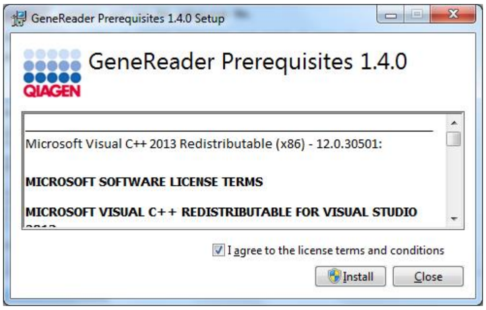
Note: After the instrument is powered ON and the software is running, the temperature regulation of the GeneReader starts. The specified temperature will be reached in 30 minutes.

4.5.2 Software upgrade

The GeneReader software is not preinstalled. QIAGEN Field Service will perform the installation. To upgrade software, follow the steps below:

1. Confirm that the following requirements are met before you begin the upgrade process:
   a. A run is not being performed
   b. There are no loaded flow cells on the instrument
   c. The GeneReader software is closed
2. Create a folder named “Upgrade” on the desktop. Copy the **GeneReaderInstaller** zip file that is provided by QIAGEN to the newly created “Upgrade” folder.
3. Extract the **GeneReaderInstaller** zip file into the “Upgrade” folder by right-clicking the file and selecting **Extract all...** from the content menu.
4. Go to the “Upgrade” folder.
5. Go to the “GeneReaderInstaller” subfolder and run the **setup.exe** file.

6. Follow the on-screen instructions to confirm all license agreements and install all parts of the software. The sequence of this process may differ depending on the existing and new software version.



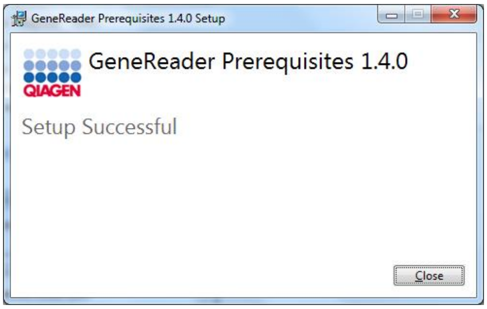
GeneReader Prerequisites 1.4.0

Microsoft Visual C++ 2013 Redistributable (x86) - 12.0.30501:

MICROSOFT SOFTWARE LICENSE TERMS

MICROSOFT VISUAL C++ REDISTRIBUTABLE FOR VISUAL STUDIO

☑ I agree to the license terms and conditions



GeneReader Prerequisites 1.4.0

Setup Successful

7. The computer may require a restart after the installation is complete. Follow the on-screen instructions and restart the computer.
8. The installer places a shortcut icon for starting the GeneReader software on the desktop. Other shortcut icons are created to start the software in service mode, but they are intended for service purpose only.
9. Start the GeneReader software by clicking the **GeneReader** shortcut icon. If necessary, the GeneReader firmware updater appears. If this occurs click **OK** to perform a firmware update. This may take several minutes to finish.

   Note: Make sure that a required firmware update is performed successfully.
10. After the firmware update is complete, wait until the software has finished the initialization and homing processes. The GeneReader software will re-start automatically.
11. Delete the “Upgrade” folder that was created on the desktop in step 2. The software is now ready for use.

   Note: To uninstall, run the **setup.exe** file in the “GeneReaderInstaller” subfolder.

5 Operating Procedures

Before proceeding, we recommend that you familiarize yourself with the features of the instrument by referring to the Section 3.

CAUTION ⚠	**Damage to the instrument** Only use QIAGEN flow cells and consumables with the GeneReader. Damage caused by use of other types of flow cell or consumable will void your warranty.

CAUTION ⚠	**Risk of material damage** Avoid moving the workbench and causing vibrations to the GeneReader during operation to prevent disturbing sensitive optical measurements.

5.1 Use of the GeneReader software

5.1.1 Start-up

During start-up, the software will perform a self-test and take an inventory of its own configuration files and any loaded flow cells and reagents. If flow cells are still loaded, you will be asked to unload them. Should a configuration file be missing, or any failure occur during the start-up procedure, contact QIAGEN Technical Services.

5.1.2 Software workflow

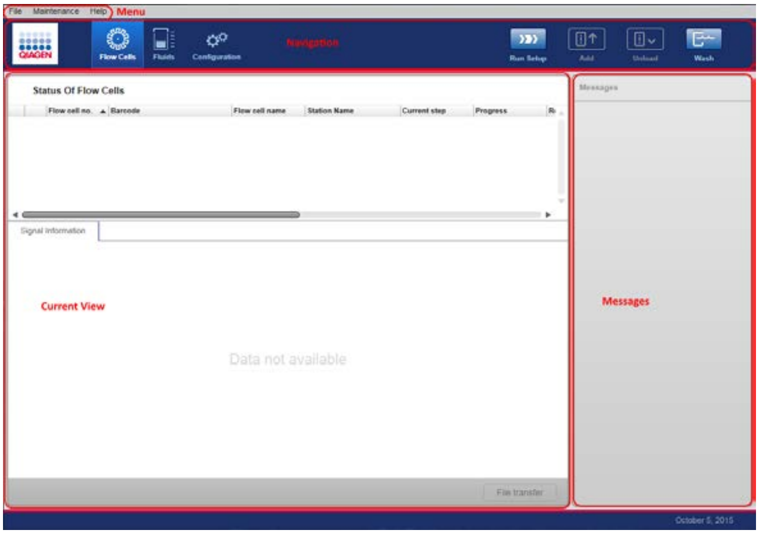
The GeneReader software provides a sample-to-result workflow, which includes the following stages:

- Definition of flow cell parameters, including multiplexing information
- Step-by-step loading instructions
- Sequence detection
- Generation of FASTQ data file

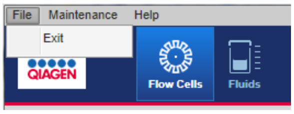
The software also provides step-by-step instructions for the maintenance wash that is part of routine GeneReader maintenance (see Section 6).

5.1.3 User interface

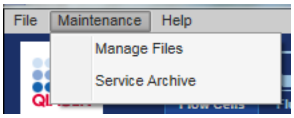
The GeneReader software is divided into four distinct areas (see image below). At the top, the menu offers access to general functionalities. Below the menu bar, the navigation area contains quick links to the commonly used views and workflows. The main portion of the screen is dedicated to the work area, which displays the current setup of flow cells and status of a protocol run, and on the right side the message area displays messages relating to protocol function, setup and errors.



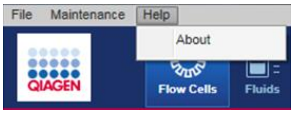
Menu and navigation



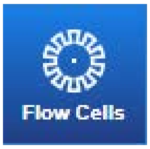
Select **File** and **Exit** in the menu to close the GeneReader software. This cannot be done while a protocol is running or if any flow cells are still loaded.



Select **Maintenance** and the **Manage Files** command to start the Manage Files wizard, which can be used to clear space on the hard drive prior to starting a run. Any selected data for clearing will be permanently deleted. If data is still needed, make sure to create a proper backup on an external drive. Select **Maintenance** and the **Service Archive** command to create a service archive if requested by QIAGEN Technical Services.



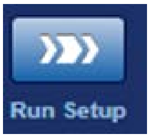
Use the **Help** menu to access version and copyright information in the **About** dialog.



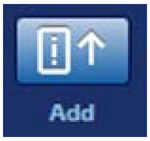
The **Flow Cells** button displays the status of all flow cells inside the GeneReader. Refer to Section 5.1.4 for more information

The **Fluids** button displays the status of all fluids in the main work area. Refer to Section 5.1.5 for more information.

The **Configuration** button opens the view for editing several configuration values. Refer to Section 5.1.6 for more information



Use the **Run Setup** command to open the workflow and to setup and start a run. Refer to Sections 5.2.1 and 5.2.2 for more information.



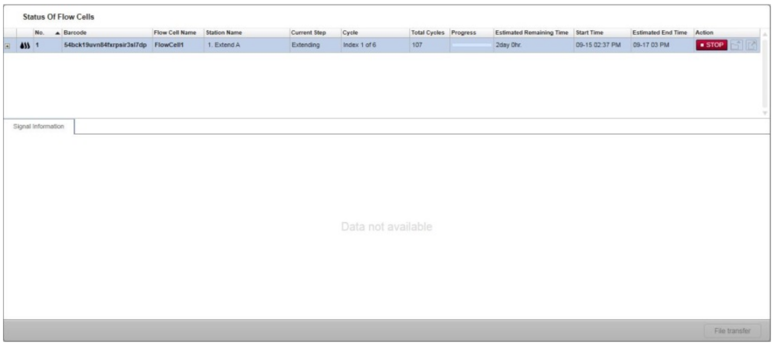
Use the **Add** command to load flow cells during a run in staggered mode once the first cycle of sequencing is complete, and prior to 24 hours after the run has started. Refer to Section 5.2.3 for more information.

Use the **Unload** command to unload flow cells from the device. Refer to Section 5.2.4 for more information.

Use the **Wash** command to open the maintenance workflow. Refer to Section 6 for more information.

5.1.4 Status of Flow Cells view

Status of Flow Cells is displayed in the main work area and displays an overview of all flow cells loaded inside the instrument.



Status Of Flow Cells

		No.	Barcode	Flow Cell Name	Station Name	Current Step	Cycle	Total Cycles	Progress	Estimated Remaining Time	Start Time	Estimated End Time	Action
+		1	54bck19uvn84fxrpsir3sl7dp	FlowCell1	1. Extend A	Extending	Index 1 of 6	107		2day 0hr.	09-15 02:37 PM	09-17 03 PM	■ STOP

The current statuses of all loaded flow cells are shown, as well as estimations for remaining run times. In the **Action** column on the right-hand side of the screen, there are icons for performing specific actions regarding the particular flow cell. The icons may not be enabled if the action is not available for the current status of the flow cell.

■ STOP

The run can be interrupted by pressing the **Stop** icon. Be aware that the protocol does not stop immediately. The protocol will stop after the currently running process step is complete. This button is available if the flow cell is running, after first cycle of sequencing is complete.

The **Open Flow Cell Data Folder** icon opens the run folder of the corresponding flow cell. This button is available if the flow cell is either finished or stopped, and the analysis is not currently running.

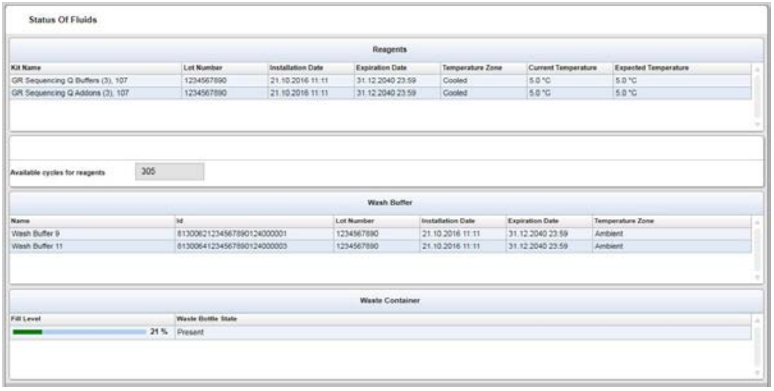
The **Flow Cells Results** icon opens the folder button that contains the analysis result data of the corresponding flow cell. This button is available if the flow cell is finished and the analysis is not currently running, but not if the flow cell was stopped.

Note: The number of cycles for a loaded flow cell will be slightly higher than the amount of cycles selected for sequencing. This is due to an extra cycle being required for lead/lag correction and to the additional cycles required to sequence the sample index.

To view flow cell details, press the **(+)** icon at the beginning of each row to display the current quality information for a run. By expanding the row of a flow cell, you can also view the multiplexing details.

5.1.5 Status of Fluids view

The Status of Fluids view is displayed in the main work area and provides an overview of all fluids currently loaded on the GeneReader.



Status Of Fluids

Reagents

Kit Name	Lot Number	Installation Date	Expiration Date	Temperature Zone	Current Temperature	Expected Temperature
GR Sequencing Q Buffers (3), 107	1234567890	21.10.2016 11:11	31.12.2040 23:59	Cooled	5.0 °C	5.0 °C
GR Sequencing Q Addons (3), 107	1234567890	21.10.2016 11:11	31.12.2040 23:59	Cooled	5.0 °C	5.0 °C

Available cycles for reagents: 305

Wash Buffer

Name	Id	Lot Number	Installation Date	Expiration Date	Temperature Zone
Wash Buffer 9	81300621234567890124000001	1234567890	21.10.2016 11:11	31.12.2040 23:59	Ambient
Wash Buffer 11	81300641234567890124000003	1234567890	21.10.2016 11:11	31.12.2040 23:59	Ambient

Waste Container

Fill Level	Waste Bottle State
21 %	Present

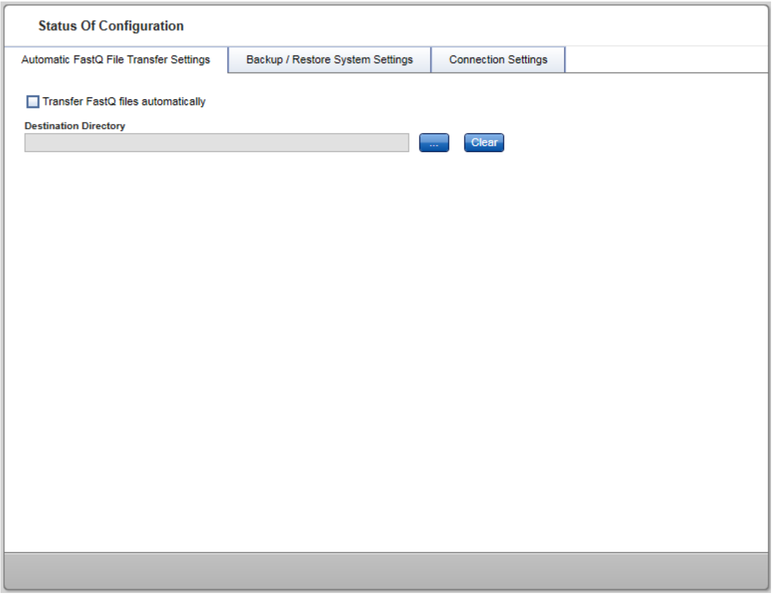
The screen is partitioned into three areas and provides information on the levels of reagents (top), wash bottles (middle) and the waste bottle (bottom). This view provides information only and does not allow the user to perform any actions.

5.1.6 Status of Configuration view

The Status of Configuration view provides the ability to edit several configuration settings. The view is divided into three areas (**Automatic FastQ File Transfer Settings**, **Backup/Restore System Settings** and **Connection Settings**) that are selected by tabs.

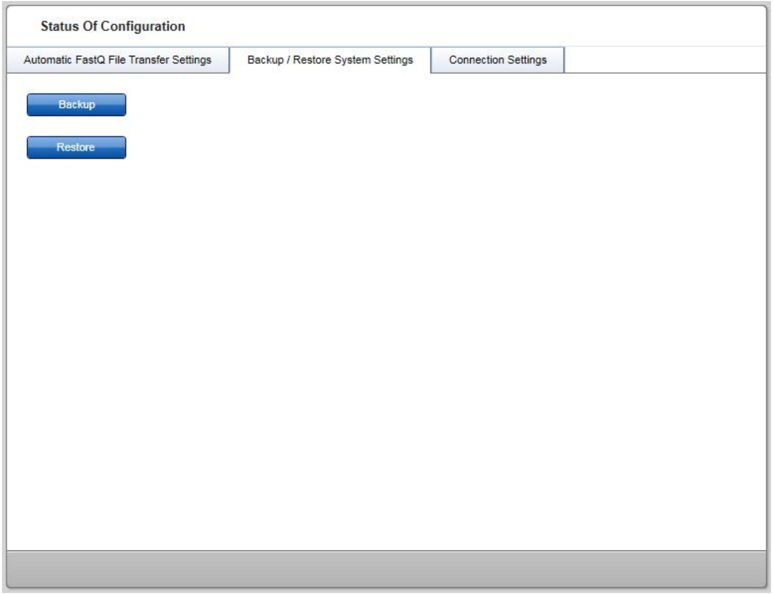
Automatic FastQ File Transfer Settings

The **Automatic FastQ File Transfer Settings** tab displays a checkbox to enable the automatic FASTQ file transfer. The destination folder for the FASTQ files can be specified using the “Destination Directory” field. Depending on the connections entered on the **Connection Settings** tab, these settings may not be editable.



Backup/Restore System Settings

The **Backup/Restore Systems Settings** tab displays two buttons: one to save all GeneReader instrument settings to a **Backup** file and one to **Restore** the settings by loading a backup file that was previously saved. **Backup** and **Restore** may be disabled depending on the current state of the GeneReader instrument and software.



Connection Settings

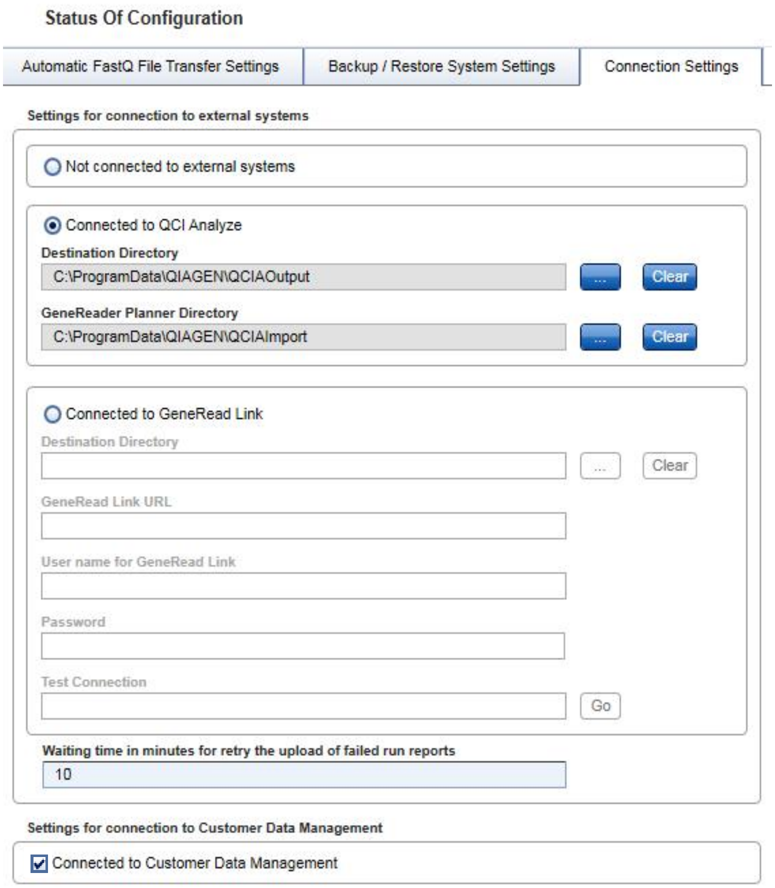
The **Connection Settings** tab allows the setup of connections to external systems for experiment planning and analyses. Depending on the system used, there are three possibilities to select by marking the corresponding radio button

- **Not connected to external system**: Select this if there is no external experiment planning system available.
- **Connected to QCI Analyze**: Select this if QCI Analyze is used as the experiment planning system. The user must provide the network share directory that the QCI Analyze experiment planner files will be stored, and the directory that the result data files will be saved to. For more information refer to the *QIAGEN Clinical Insight Analyze 1.2 User Manual.*
- **Connected to GeneRead Link**: Select this if GeneRead Link is used as the experiment planning system. The user must provide several configuration values: First, the network share directory that the result data files will be saved must be entered. Second, the URL, user name and password of the GeneRead Link server must be provided. By clicking the **Go** button it is possible to confirm that the connection to GeneRead Link is working. Third, the user must provide the time (in minutes) to wait for a retry if the data upload failed. For more information refer to the *GeneRead Link v1.2 User Manual*.

  Note: Previous settings for the connection of the GeneReader software to an external experiment planner system are not saved after connection settings are changed. Make sure that connection settings are recorded (i.e., written down) to re-store a connection after configuration is changed.

The **Connection Settings** tab also allows the setup of a connection to GeneRead Databank as an external data management tool. If GeneRead Databank is used to manage files, select the **Connected to Customer Data Management** check box:

- **Connected to Customer Data Management**: If GeneRead Databank is used as external system, the **Manage Files** command in the **Maintenance** menu is deactivated. For more information about GeneRead Databank (Customer Data Management) refer to the *GeneRead Databank v1.0 User Manual*.



Settings for connection to external systems

○ Not connected to external systems

● Connected to QCI Analyze

Destination Directory: C:\ProgramData\QIAGEN\QCIAOutput

GeneReader Planner Directory: C:\ProgramData\QIAGEN\QCIAImport

○ Connected to GeneRead Link

Destination Directory

GeneRead Link URL

User name for GeneRead Link

Password

Test Connection

Waiting time in minutes for retry the upload of failed run reports: 10

Settings for connection to Customer Data Management

☑ Connected to Customer Data Management

5.1.7 File handling

Required files

The GeneReader software performs an inventory of its own files and configuration upon start-up. If a message is shown about missing files, please contact QIAGEN Technical Services.

5.2 Workflow procedures

5.2.1 Flow cell setup

There are 3 options for generating a flow cell setup in the GeneReader NGS System:

- QCI Analyze for importing flow cells
- GeneRead Link for importing flow cells
- GeneReader software for adding flow cells manually

QCI Analyze (web interface)

QCI Analyze is a browser-based system for analyzing NGS data. Underneath QCI Analyze, a CLC Genomics Server is running the analyses, storing data and handling various processes such as queuing. QCI Analyze can import NGS data, analyze it, display results for inspection and export result data in VCF format. In addition, it can connect directly to QCI Interpret for interpretation and reporting. For more information on how to generate a flow cell setup using QCI Analyze refer to the *QIAGEN Clinical Insight Analyze 1.2 User Manual*.

See "Protocol: Loading and Running the GeneReader" in the *QIAGEN GeneRead Advanced Sequencing Q Handbook* for information on how to import a flow cell setup from QCI Analyze.

GeneRead Link (web interface)

GeneRead Link is QIAGEN middleware software that is intended for planning and executing the GeneReader NGS System workflow for samples. It provides bidirectional connectivity with a Laboratory Information Management System (LIMS), the work instructions for laboratory users and automatically interfaces to specific QIAGEN instruments. For more information on how to generate a flow cell setup refer to the *GeneRead Link v1.2 User Manual*.

See "Protocol: Loading and Running the GeneReader" in the *QIAGEN GeneRead Advanced Sequencing Q Handbook* for information on how to import a flow cell setup from GeneRead Link.

GeneReader software

GeneReader software can be directly used for a flow cell setup. See "Protocol: Loading and Running the GeneReader" in the *QIAGEN GeneRead Advanced Sequencing Q Handbook* for a step-by-step guide on how to add a flow cell manually using the GeneReader software user interface.

IMPORTANT: If GeneReader software is used for flow cell setup there will be no automatic data analysis of FASTQ files generated by the sequencer through QCI Analyze. In order to integrate data analysis in QCI Analyze use the QCI Analyze or the GeneRead Link web interfaces for flow cell setup.

Note: If GeneReader software is used for flow cell setup with staggered loading, ensure that sufficient reagents are loaded for all planned flow cells of the run.

5.2.2 Loading and running the GeneReader

See “Protocol: Loading and Running the GeneReader” in the *QIAGEN GeneRead Advanced Sequencing Q Handbook* for a step-by-step guide on how to load one or more flow cells using the GeneReader software user interface.

5.2.3 Staggered loading of flow cells

See “Protocol: Staggered Loading of Flow Cells” in the *QIAGEN GeneRead Advanced Sequencing Q Handbook* for a step-by-step guide on how to load one or more flow cells in staggered mode after a sequencing run has been started in the GeneReader software.

5.2.4 Unloading reagents and flow cells

See “Protocol: Unloading Reagents and Flow Cells” in the *QIAGEN GeneRead Advanced Sequencing Q Handbook* for a step-by-step guide on how to unload reagents and flow cells in the GeneReader software.

5.2.5 Run finished

When the sequencing and analysis of all flow cells is completed, the Run Finished wizard will allow:

- Transfer of FASTQ and report files to another local or network directory by clicking **Transfer**.
- Viewing of result directory
- Unloading of flow cells and fluids
- A deionized (DI) water or maintenance wash to be performed
- Running the “Manage Files” wizard

A run report is generated automatically after the analysis of the flow cells. A separate report is created for every flow cell in the run and it is saved to the flow cell directory within the run directory. The report contains sections on the run setup, the quality score distribution, data on bead quality and the sequence quality score, as well as multiplex data. Additionally, run reports contain any errors or warnings that may have been logged/reported during the course of the sequencing and analysis processes.

Log files

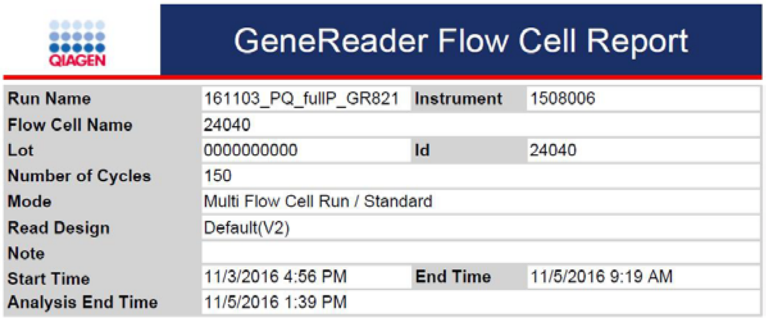
- The GeneReader software writes an EventLog.txt file to the folder: C:\ProgramData\QIAGEN\GeneReader\GeneReader. This log file contains warnings and errors and is intended to provide information in case of an issue. To prevent this log file from getting too large, a new log file is created once a month.
- During a run, a run-specific event log file is created within the run folder. Refer to this file for any issues that occurred during the execution of a sequencing protocol.

Final report

- When the analysis software is completed, a flow cell report is generated as a PDF file and written to the path:
  \<timestamp>_<run_name>\FC<flow_cell_name>_<barcode>\Analyze\<timestamp>_<flow_cell_name>_FinalReport.pdf.
  An example file is:
  D:\QIAGEN\GRSData\2016_10_06_133222_SampleRun\FC_FC1_2c0sbgi977zjkqbktbg1vuj71\Analyze\1610061332_ FC1_FinalReport.pdf

The **FinalReport.pdf** file contains important run information such as:

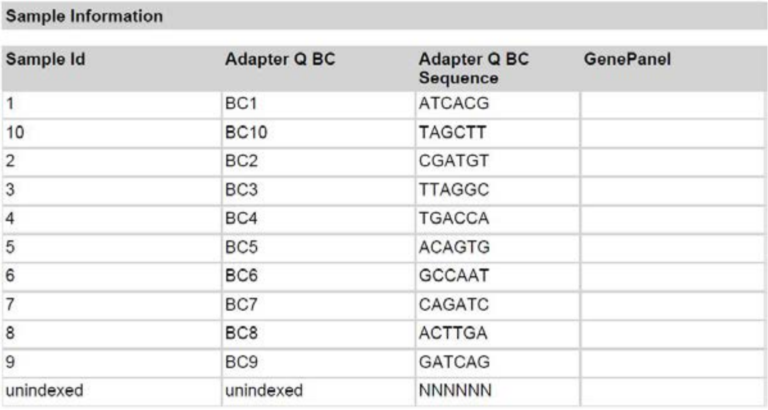
- General information about the run



GeneReader Flow Cell Report

Run Name	161103_PQ_fullP_GR821	**Instrument**	1508006
Flow Cell Name	24040		
Lot	0000000000	**Id**	24040
Number of Cycles	150		
Mode	Multi Flow Cell Run / Standard		
Read Design	Default(V2)		
Note			
Start Time	11/3/2016 4:56 PM	**End Time**	11/5/2016 9:19 AM
Analysis End Time	11/5/2016 1:39 PM		

- Sample information



Sample Information

Sample Id	Adapter Q BC	Adapter Q BC Sequence	GenePanel
1	BC1	ATCACG	
10	BC10	TAGCTT	
2	BC2	CGATGT	
3	BC3	TTAGGC	
4	BC4	TGACCA	
5	BC5	ACAGTG	
6	BC6	GCCAAT	
7	BC7	CAGATC	
8	BC8	ACTTGA	
9	BC9	GATCAG	
unindexed	unindexed	NNNNNN	

- Reagent kits

Reagent Kits

Sequencing Kit	Lot	Material	Exp date
GR Sequencing Q Buffers (3), 157	0154015256	9803301	12/31/2060
GR Sequencing Q Addons (3), 157	0154015256	9803401	12/31/2016

- Wash kits

Wash Kits

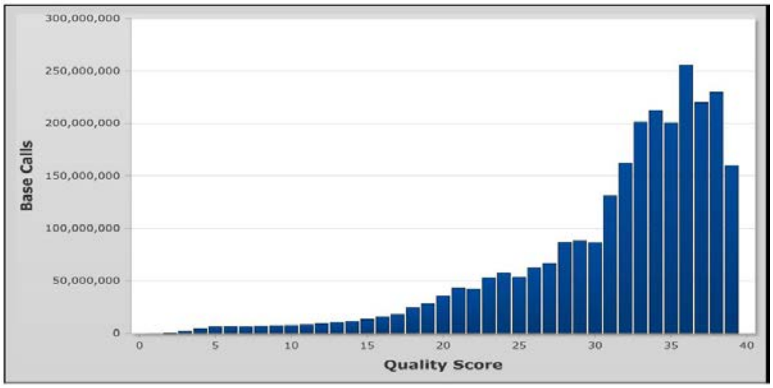
Wash Kit	Lot	Material	Exp date
Wash Buffer 9	0154030898	8130062	4/30/2018
Wash Buffer 11	0154022874	8130064	4/30/2018

- Software version

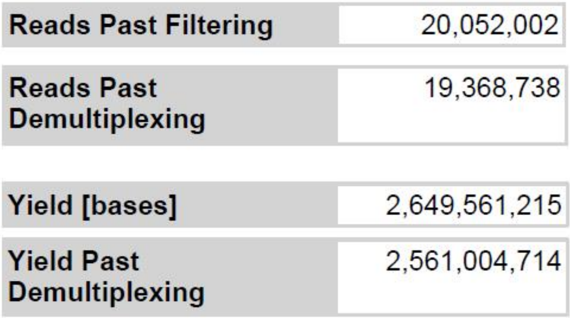
Software Version	GeneReader Software 1.4.0

- Quality score distribution

Quality Score Distribution



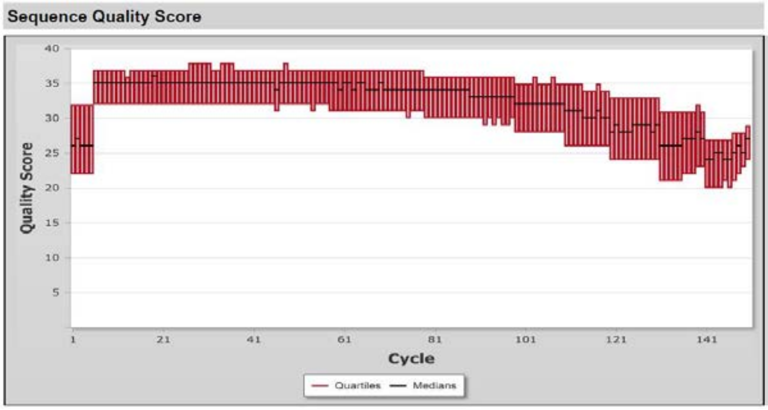
- Run metrics



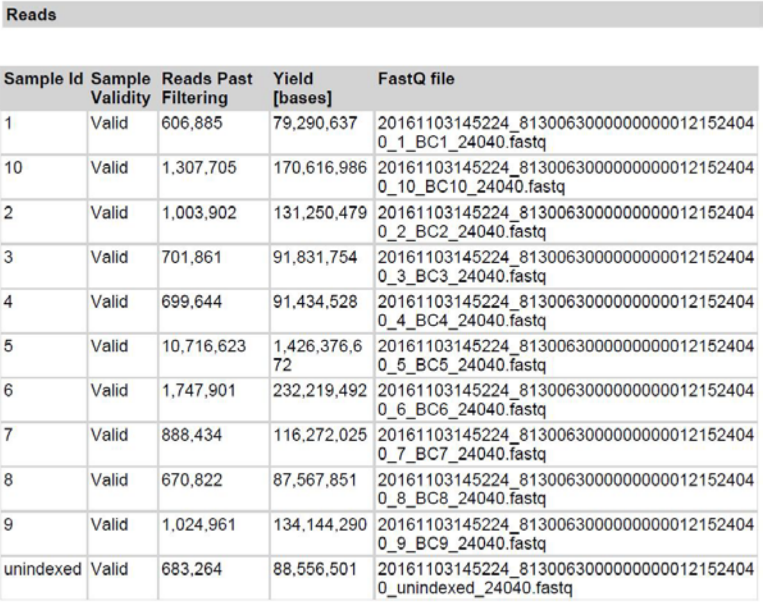
Reads Past Filtering	20,052,002
Reads Past Demultiplexing	19,368,738
Yield [bases]	2,649,561,215
Yield Past Demultiplexing	2,561,004,714

Reads Past Filtering reports the count of reads that passed Q-score-based quality filtering before demultiplexing (i.e., the count of reads as written in the FASTQ file).
Reads Past Demultiplexing reports the count of reads for which a sample bar code could be identified.
Yield [bases] reports the total number of base calls before demultiplexing.
Yield Past Demultiplexing reports the total number of base calls for which a sample bar code could be identified.

- Sequence quality score



- Reads information



Reads

Sample Id	Sample Validity	Reads Past Filtering	Yield [bases]	FastQ file
1	Valid	606,885	79,290,637	20161103145224_8130063000000000121524040_1_BC1_24040.fastq
10	Valid	1,307,705	170,616,986	20161103145224_8130063000000000121524040_10_BC10_24040.fastq
2	Valid	1,003,902	131,250,479	20161103145224_8130063000000000121524040_2_BC2_24040.fastq
3	Valid	701,861	91,831,754	20161103145224_8130063000000000121524040_3_BC3_24040.fastq
4	Valid	699,644	91,434,528	20161103145224_8130063000000000121524040_4_BC4_24040.fastq
5	Valid	10,716,623	1,426,376,672	20161103145224_8130063000000000121524040_5_BC5_24040.fastq
6	Valid	1,747,901	232,219,492	20161103145224_8130063000000000121524040_6_BC6_24040.fastq
7	Valid	888,434	116,272,025	20161103145224_8130063000000000121524040_7_BC7_24040.fastq
8	Valid	670,822	87,567,851	20161103145224_8130063000000000121524040_8_BC8_24040.fastq
9	Valid	1,024,961	134,144,290	20161103145224_8130063000000000121524040_9_BC9_24040.fastq
unindexed	Valid	683,264	88,556,501	20161103145224_8130063000000000121524040_unindexed_24040.fastq

6 Maintenance

This section describes routine and weekly maintenance procedures.

6.1 Equipment and reagents to be supplied by user

When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. For more information, please consult the appropriate safety data sheets (SDSs) available from the product supplier.

The following material is required to perform maintenance of the GeneReader instrument:

- Deionized water or laboratory grade pure water (referred to as DI water)

6.2 Maintenance wash

The following maintenance procedures must be performed to ensure reliable operation of the GeneReader:

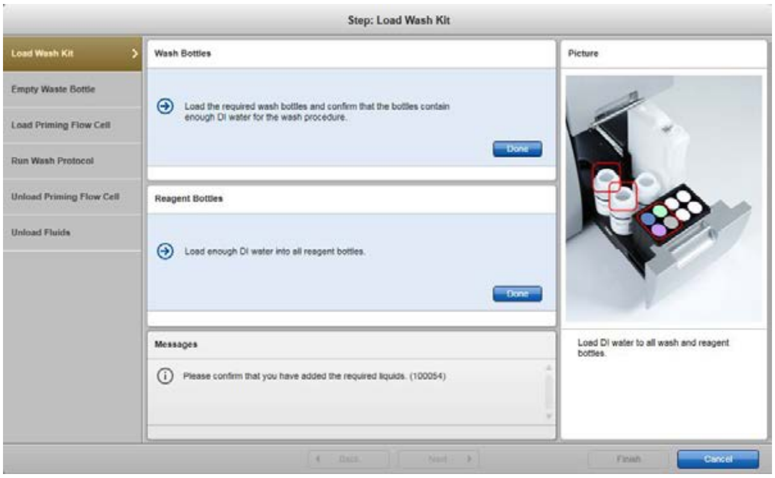
- Routine maintenance – A DI water wash must be performed if the GeneReader will be idle and/or a run has completed, and there are no additional runs immediately following
- Weekly maintenance – The maintenance wash must be performed once a week or every 4 runs

Following these procedures ensures that the GeneReader is free of dust and helps prevent clogging of the fluidics system.

6.2.1 Routine maintenance

After a sequencing run has finished and the GeneReader will be idle, or no other sequencing run is planned, a DI water wash will prevent the formation of air pockets and the drying of reagent lines.

1. Open the GeneReader software. Click **Wash** in the navigation panel.
2. Select **DI Water Wash** and click **Next**.
3. The hood will open. Load 2 wash bottles containing ≥200 ml DI water in positions 9 and 11.
4. Load 50 ml conical tubes containing at least 46 ml (6 ml dead volume) DI water into the cooling compartment in positions 1, 2, 5, and 6. Click **Done** twice and then **Next**.



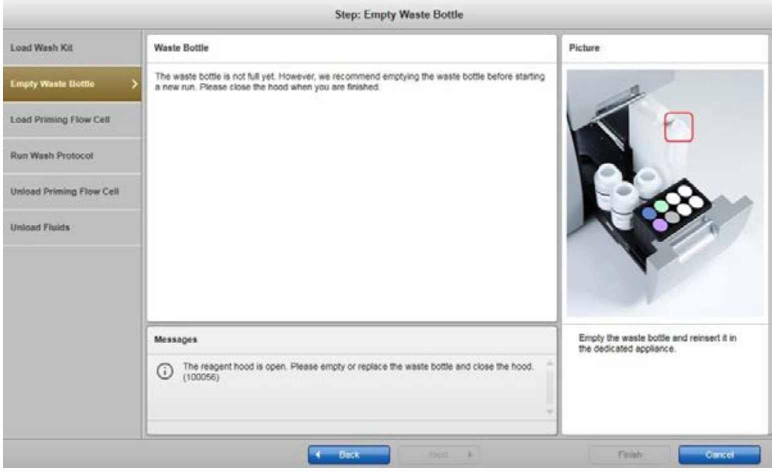
Load the required wash bottles and confirm that the bottles contain enough DI water for the wash procedure.

Load enough DI water into all reagent bottles.

Please confirm that you have added the required liquids. (100054)

Load DI water to all wash and reagent bottles.

5. Empty the waste bottle and dispose of the contents according to local safety regulations. Reload the empty waste bottle into the instrument. Close the hood and click **Next**.

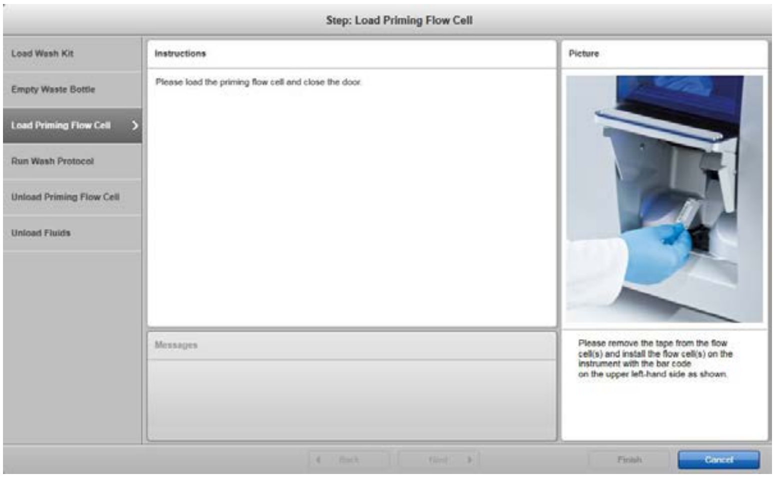


The waste bottle is not full yet. However, we recommend emptying the waste bottle before starting a new run. Please close the hood when you are finished.

The reagent hood is open. Please empty or replace the waste bottle and close the hood. (100056)

Empty the waste bottle and reinsert it in the dedicated appliance.

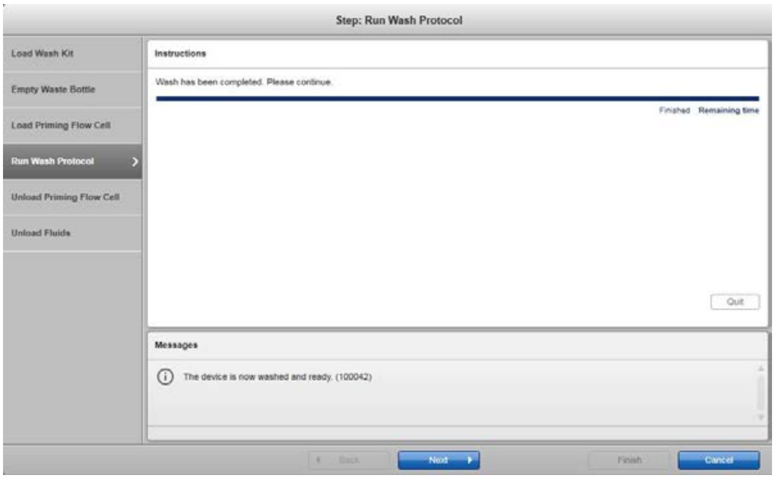
6. The flow cell door will open. Load an empty or used flow cell (priming flow cell) in order to allow liquid flow. Close the flow cell door and click **Next**.



Please load the priming flow cell and close the door.

Please remove the tape from the flow cell(s) and install the flow cell(s) on the instrument with the bar code on the upper left-hand side as shown.

7. Instrument will now prime with DI water. Once complete, click **Next**.



Step: Run Wash Protocol

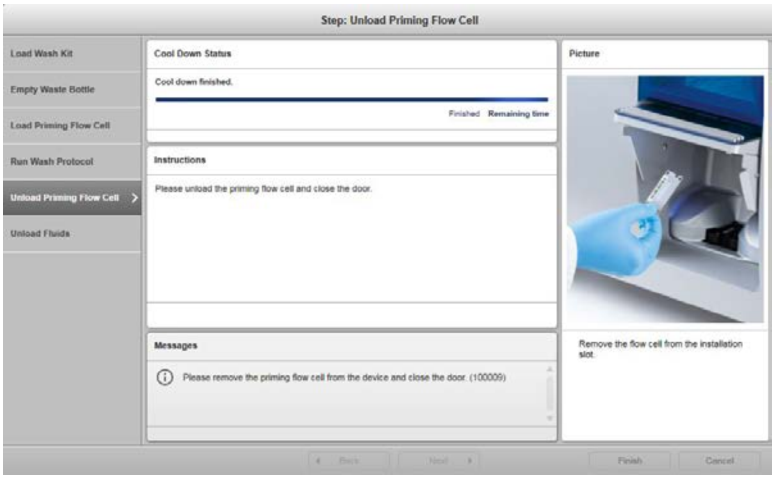
Instructions

Wash has been completed. Please continue.

Messages

The device is now washed and ready. (100042)

8. The flow cell door will open. Unload the priming flow cell. Close the flow cell door and click **Next**.



Step: Unload Priming Flow Cell

Cool Down Status

Cool down finished.

Instructions

Please unload the priming flow cell and close the door.

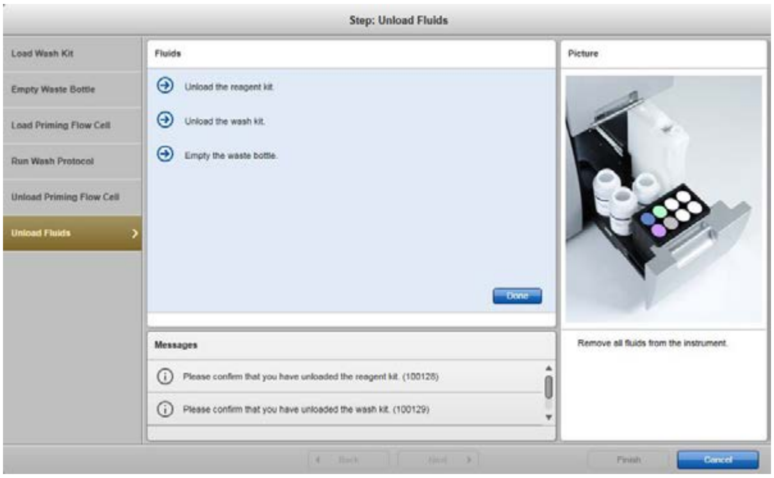
Messages

Please remove the priming flow cell from the device and close the door. (100009)

Picture

Remove the flow cell from the installation slot.

9. The hood will open. Unload the reagent and wash kit. Empty the waste bottle. Close the hood and click **Done**.



Unload the reagent kit.

Unload the wash kit.

Empty the waste bottle.

Remove all fluids from the instrument.

Please confirm that you have unloaded the reagent kit. (100128)

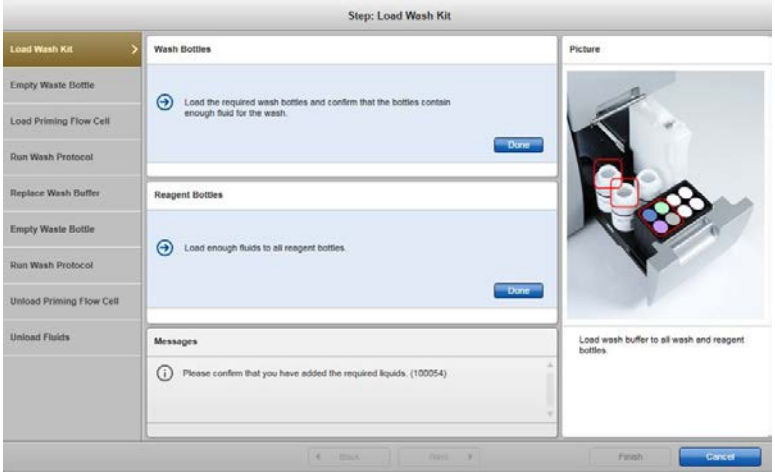
Please confirm that you have unloaded the wash kit. (100129)

10. Click **Finish** to close the wizard.

6.2.2 Weekly maintenance

To make sure reagent lines remain clear and to prevent buildup of material that could potentially clog the lines, a maintenance wash must be performed every 4 runs or once per week (whichever occurs first). The maintenance wash utilizes the maintenance wash buffer provided in the GeneRead Sequencing Buffer Q Kit (16) (cat. no. 185901). The steps below describe the maintenance wash procedure.

1. If sequencing run has just completed, make sure that all flow cells are removed, reagents have been removed from the cooling compartment and discarded, and wash buffers are removed and stored at room temperature.
2. If software is not open, click the GeneReader software icon to open. GeneReader will scan for flow cells upon opening software. Remove if present.
3. Click **Wash** in the navigation panel.
4. Select **Maintenance Wash** and click **Next**.
5. The hood will open. Load 1 liter bottles containing ≥200 ml of DI water into position 11 in the fluidic drawer.
6. Load 1 liter bottle containing 50 ml of Maintenance Wash Buffer into position 9 of the fluidic drawer.
7. Load 50 ml conical tubes containing at least 46 ml (6 ml dead volume) DI water into the cooling compartment in positions 1, 2, 5, and 6.



Load the required wash bottles and confirm that the bottles contain enough fluid for the wash.

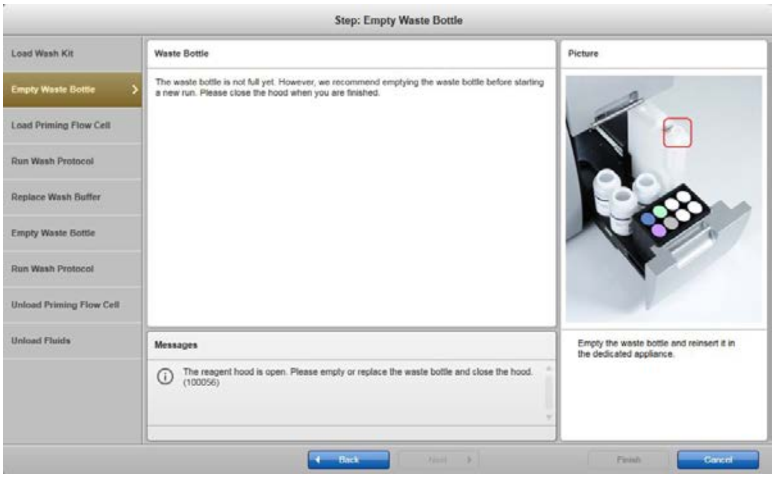
Load enough fluids to all reagent bottles.

Please confirm that you have added the required liquids. (100054)

Load wash buffer to all wash and reagent bottles.

8. Click **Done** twice when finished.
9. Click **Next**.
10. Empty the waste bottle and dispose of the contents according to local safety regulations. Reload the empty waste bottle into the instrument. Close the hood and click **Next**.

    IMPORTANT: Make sure to reload the waste bottle into the instrument in the correct orientation. An incorrect orientation may damage the instrument. Do not use force to close the hood. If blocked, check the waste bottle orientation and correct if necessary before retrying to close the hood.

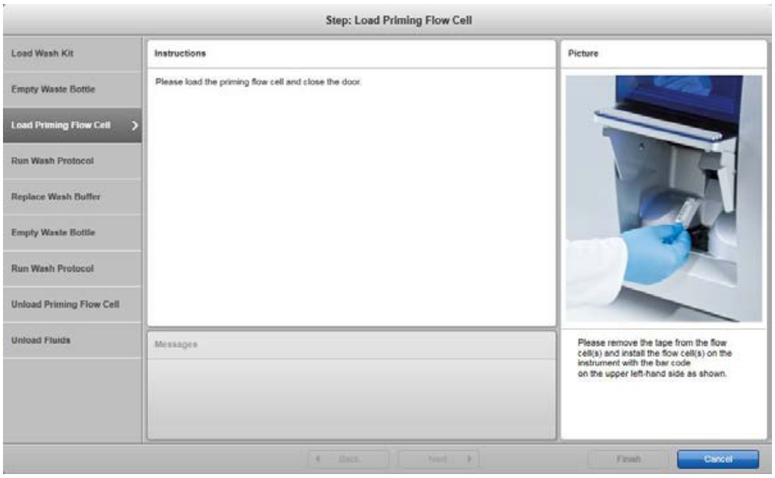


The waste bottle is not full yet. However, we recommend emptying the waste bottle before starting a new run. Please close the hood when you are finished.

The reagent hood is open. Please empty or replace the waste bottle and close the hood. (100056)

Empty the waste bottle and reinsert it in the dedicated appliance.

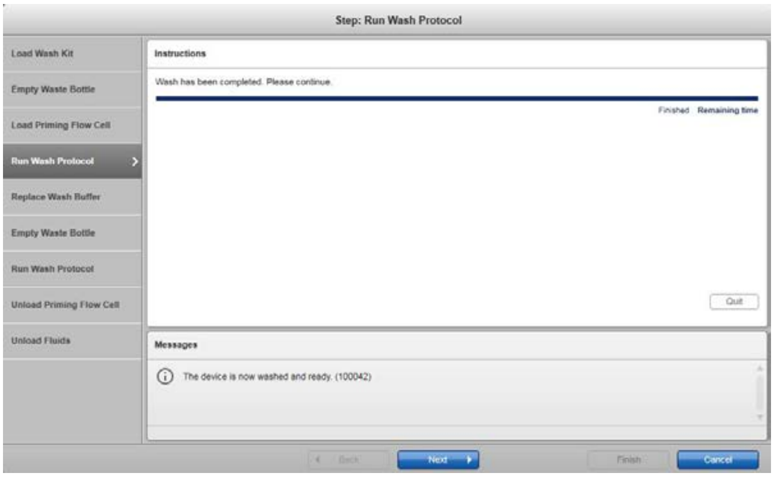
11. Load an empty or used flow cell (priming flow cell) in order to allow liquid flow, close the flow cell door and click **Next**.



Please load the priming flow cell and close the door.

Please remove the tape from the flow cell(s) and install the flow cell(s) on the instrument with the bar code on the upper left-hand side as shown.

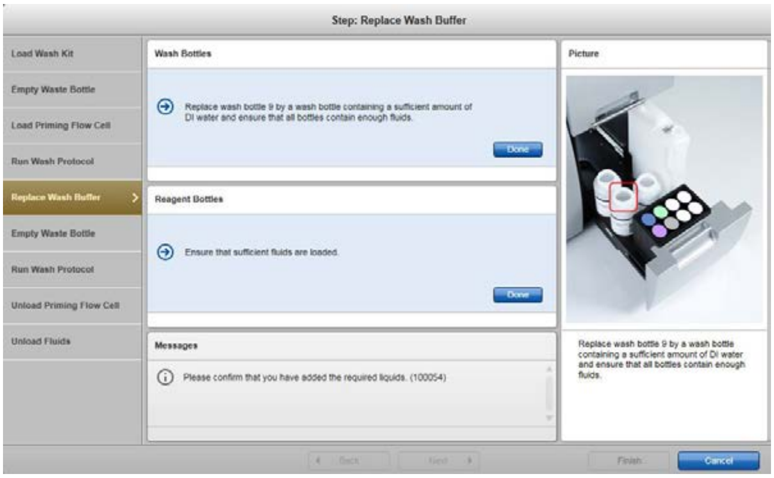
12. When the wash is complete, click **Next**.



Wash has been completed. Please continue.

The device is now washed and ready. (100042)

13. The hood will open. Replace Maintenance Wash Buffer in position 9 with 200 ml DI water.



Replace wash bottle 9 by a wash bottle containing a sufficient amount of DI water and ensure that all bottles contain enough fluids.

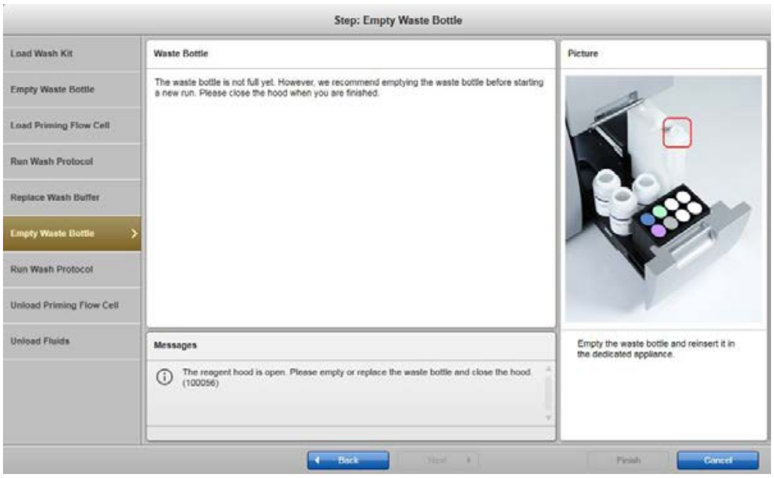
Ensure that sufficient fluids are loaded.

Please confirm that you have added the required liquids. (100054)

Replace wash bottle 9 by a wash bottle containing a sufficient amount of DI water and ensure that all bottles contain enough fluids.

14. Click **Done** twice when finished.
15. Click **Next**.
16. Empty the waste bottle and dispose of the contents according to local safety regulations. Reload the empty waste bottle into the instrument. Close the hood and click **Next**.

    IMPORTANT: Make sure to reload the waste bottle into the instrument in the correct orientation. An incorrect orientation may damage the instrument. Do not use force to close the hood. If blocked, check the waste bottle orientation and correct if necessary before trying to close the hood again.

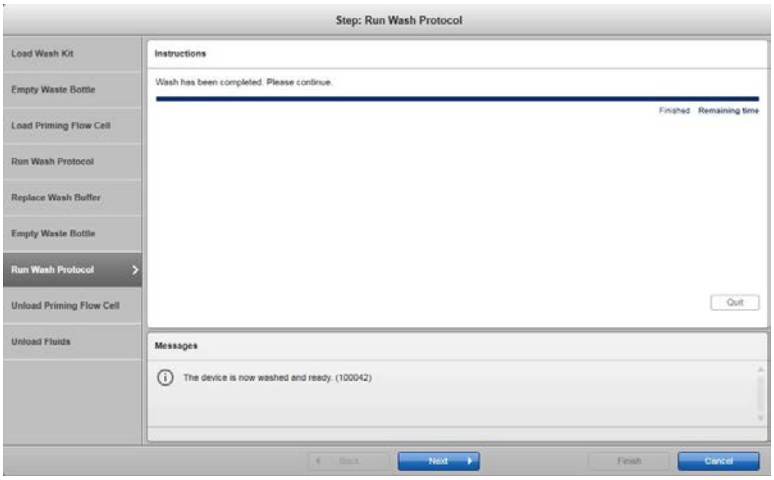


The waste bottle is not full yet. However, we recommend emptying the waste bottle before starting a new run. Please close the hood when you are finished.

The reagent hood is open. Please empty or replace the waste bottle and close the hood (100056)

Empty the waste bottle and reinsert it in the dedicated appliance.

17. After the final wash is complete, click **Next**.



Step: Run Wash Protocol

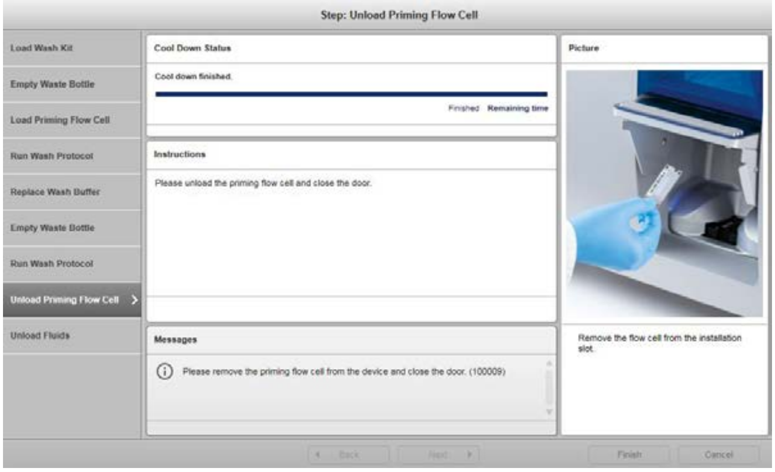
Instructions

Wash has been completed. Please continue.

Messages

ⓘ The device is now washed and ready. (100042)

18. The flow cell door will open. Unload the priming flow cell. Close the flow cell door and click **Next**.



Step: Unload Priming Flow Cell

Cool Down Status

Cool down finished.

Instructions

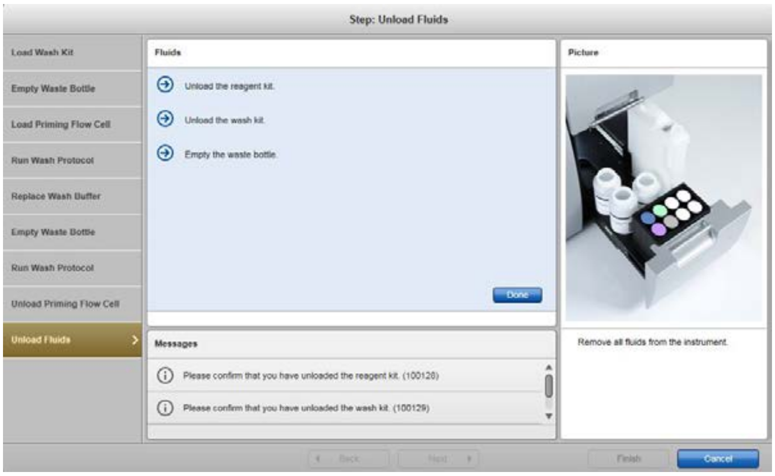
Please unload the priming flow cell and close the door.

Messages

ⓘ Please remove the priming flow cell from the device and close the door. (100009)

Remove the flow cell from the installation slot.

19. The hood will open. Unload the reagent and wash kit. Empty the waste bottle. Close the hood and click **Done**.



Unload the reagent kit.

Unload the wash kit.

Empty the waste bottle.

Remove all fluids from the instrument.

Please confirm that you have unloaded the reagent kit. (100128)

Please confirm that you have unloaded the wash kit. (100129)

20. Click **Finish** to close the wizard.

6.2.3 Preparing the GeneReader fluidics lines for long-term storage

If the GeneReader instrument will be stored for a prolonged period of time, the fluidics lines must be emptied.

1. Fill all reagent containers and buffer bottles with ultra-pure water.
2. Perform a maintenance wash and wait until the run has finished.
3. Remove all buffer bottles and reagent containers from the instrument.
4. Run the maintenance wash protocol again (with no bottles or reagent containers) and wait until the run has finished.

   The instrument will be free of liquids and can be stored in this state.

6.2.4 Monthly cleaning procedure

Thoroughly wipe the inside and outside of the GeneReader using the cleaning agents described in Section 6.3.1.

IMPORTANT: Do not use alcohol or alcohol-based disinfectants or detergents to decontaminate the GeneReader hood.

6.3 General cleaning procedures

6.3.1 Cleaning agents

The following disinfectants and detergents are recommended for cleaning the GeneReader instrument:

Mikrozid® Wipes (Schülke & Mayr GmbH; **www.schuelke-mayr.com**) – moistened with ethanol-based disinfectant for wiping alcohol-insensitive surfaces of the GeneReader instrument.

Mikrozid Sensitive Liquid (Schülke & Mayr GmbH; **www.schuelke-mayr.com**) – quaternary ammonium salt-based disinfectant for alcohol-sensitive surfaces (consists of 0.26 g quaternary ammonium compounds, benzyl-C12-C16-alkyldimethyl, chlorides; 0.26 g Didecyldimethyl-ammonium chloride and 0.26 g quaternary ammonium compounds, benzyl-C12-C14-alkyl[(ethylphenyl)methyl]dimethyl, chlorides per 100 g Mikrozid Sensitive Liquid).

IMPORTANT: Do not use alcohol or alcohol-based disinfectants to clean the GeneReader instrument hood. Exposure of the GeneReader hood to alcohol or alcohol-based disinfectants will cause surface cracking. Clean the GeneReader hood with distilled water or Mikrozid Sensitive Liquid only.

Note: If you would like to use different disinfectants from those recommended, ensure that their compositions are similar to those described above. A suitable alternative to Mikrozid Liquid is Incidin® Liquid (Ecolab; **www.ecolab.com**).

6.3.2 General instructions

- Do not use spray bottles to spray cleaning liquids onto surfaces of the GeneReader instrument.
- If solvents or saline, acidic or alkaline solutions are spilled on the GeneReader, or if QIAGEN buffers splash the instrument door, wipe the spilled liquid away immediately.
- Follow manufacturer's safety instruction for handling cleaning agents.
- Follow manufacturer's instruction for concentration of the cleaning agents.
- Do not use alcohol or alcohol-based disinfectants to clean the GeneReader hood. Exposing the GeneReader hood, Main Hood, and flow cell door to alcohol or alcohol-based disinfectants will cause surface cracking. Clean the GeneReader hood with distilled water or Mikrozid Sensitive Liquid only.

WARNING ⚠	**Risk of electric shock** Do not open any panels on the GeneReader. **Risk of personal injury and material damage** Only perform maintenance that is specifically described in this user manual.

WARNING ⚠	**Hazardous chemicals and infectious agents** The waste contains samples and reagents. This waste may contain toxic or infectious material and must be disposed of properly. Refer to your local safety regulations for proper disposal procedures.

WARNING ⚠	**Risk of personal injury and material damage** Improper use of the GeneReader may cause personal injuries or damage to the instrument. The GeneReader must only be operated by qualified personnel who have been appropriately trained. Servicing of the GeneReader instrument must only be performed by a QIAGEN Field Service Specialist.

6.3.3 Servicing

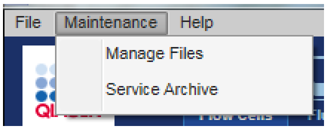
Contact QIAGEN Technical Services or your local distributor for more information about flexible Service Support Agreements from QIAGEN.

6.4 Cleaning the workstation hard disk

A sequencing run requires a large amount of hard disk space. Therefore, the GeneReader software provides a “Manage Files” Wizard to assist with backup tasks in case GeneRead Databank is not used as an external data management tool. To perform the “manage files” process, additional free disk space for the backup is required, such as an external hard drive or network drive.

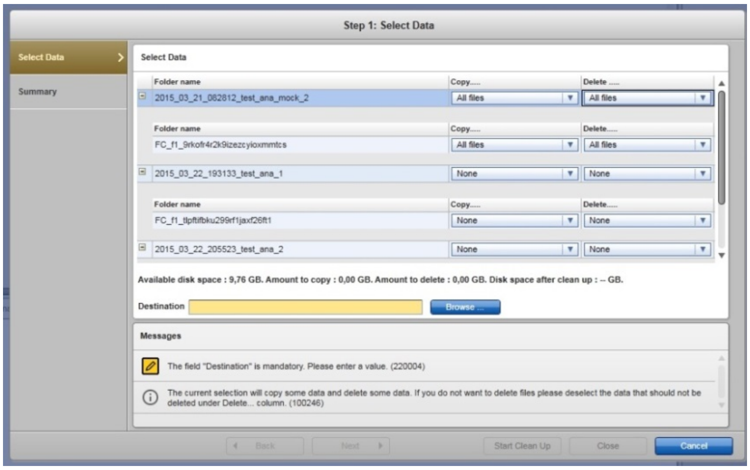
6.4.1 Procedure

1. Click **Manage Files** in the **Maintenance** menu to open the wizard. The wizard will display all previously run directories.



2. Select the folders you wish to backup by setting the respective action in the **Copy …** column. If any folder is chosen for backup, the destination drive needs to be set. Select the folders to be cleaned up by setting the respective action in the **Delete …** column.

   IMPORTANT: It is possible to select folders for clean up without adding them to the list of files which will be backed up. Loss of data may occur if a manual backup has not been performed first!



Folder name	Copy.....	Delete .....
2015_03_21_082812_test_ana_mock_2	All files	All files
FC_f1_9rkofr4r2k9izezcyioxmmtcs	All files	All files
2015_03_22_193133_test_ana_1	None	None
FC_f1_tlpftifbku299rf1jaxf26ft1	None	None
2015_03_22_205523_test_ana_2	None	None

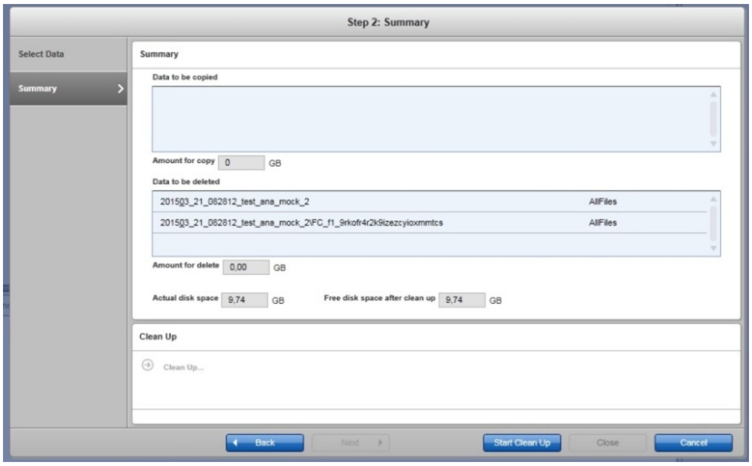
Available disk space : 9,76 GB. Amount to copy : 0,00 GB. Amount to delete : 0,00 GB. Disk space after clean up : -- GB.

Destination

The field "Destination" is mandatory. Please enter a value. (220004)

The current selection will copy some data and delete some data. If you do not want to delete files please deselect the data that should not be deleted under Delete... column. (100246)

3. The wizard will then display a summary of all copy and delete tasks as shown below. Check the estimated free disk space. You may return to the previous screen to change your settings by clicking **Back**.



Data to be copied

Amount for copy: 0 GB

Data to be deleted

201503_21_082812_test_ana_mock_2	AllFiles
201503_21_082812_test_ana_mock_2\FC_f1_9rkofr4r2k9izezcyioxmmtcs	AllFiles

Amount for delete: 0,00 GB

Actual disk space: 9,74 GB

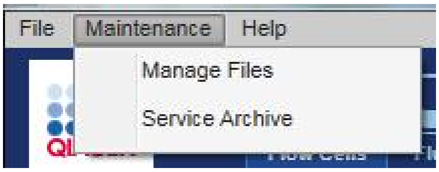
Free disk space after clean up: 9,74 GB

Note: "Manage Files" is deactivated in the **Maintenance** menu if GeneRead Databank is used as an external data management tool.

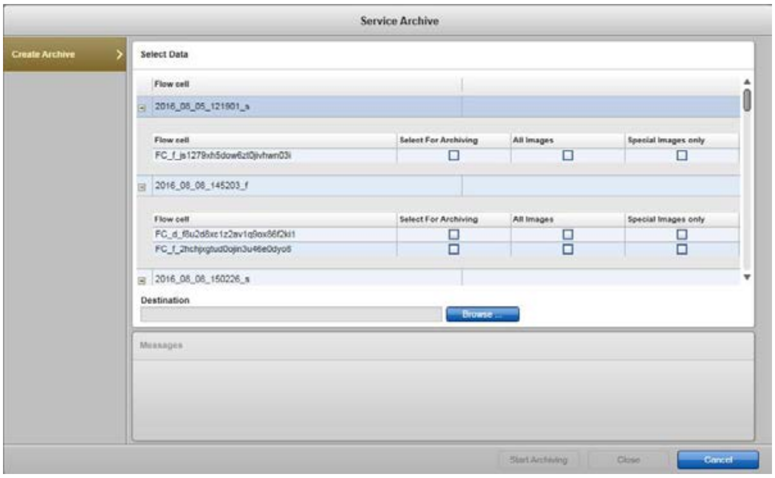
6.5 Creating a service archive folder for troubleshooting

6.5.1 Procedure

1. Click **Service Archive** in the **Maintenance** menu to open the wizard for creating a service archive. The wizard will display all flow cells for which a service archive can be created.



2. Select **Select For Archiving** for each flow cell for which a service archive will be created. All mandatory files for troubleshooting, except images, will be archived. To include images in the service archive, select either **All Images** to archive all images or **Special Images only** to archive only specific images of interest for troubleshooting.



Flow cell	
2016_08_05_121901_s	

Flow cell	Select For Archiving	All Images	Special Images only
FC_f_js1279xh5dow6zt0jivhwn03i	☐	☐	☐

Flow cell	
2016_08_08_145203_f	

Flow cell	Select For Archiving	All Images	Special Images only
FC_d_f6u2d8xc1z2av1q9ox86f2ki1	☐	☐	☐
FC_f_2hchjxgtud0ojin3u46e0dyo8	☐	☐	☐

Flow cell	
2016_08_08_150226_s	

Destination

3. Select a destination folder for the service archive by clicking the **Browse…** button.
4. Start the service archive creation by clicking the **Start Archiving** button.
5. Click **Close** to close the wizard.

7 Troubleshooting

This section provides information about what to do if an error occurs when using the GeneReader system.

If you need to contact QIAGEN Technical Services about an error, note the steps leading to the error and the information from any dialog boxes. This will help the QIAGEN Technical Service Specialist to resolve the error.

QIAGEN Technical Services may request a service archive folder. The service archive wizard can be started by selecting **Maintenance** and **Service Archive** (see Section 6.5).

7.1 Hardware and software errors

7.1.1 Application module

Error message	Comments and suggestions
The application cannot be closed because a run is ongoing.	Stop the run and unload all flow cells.
The application cannot be closed, because there are still flow cells in the instrument.	Unload all flow cells.

7.1.2 Manage Files module

Error message	Comments and suggestions
An error occurred while performing the operation.	Verify that the destination path is still available and that you are running the software with the required permissions to write data there.
Not all files that are selected for deletion are selected for backing up.	Verify that you wish to delete files without creating a backup.
The destination drive is too small to copy the data.	Choose a destination drive with sufficient available space or copy less data.
The disk drive for the source and the destination is the same.	If the source and destination drives are identical, this wizard will not be able to release disk space.
The field "Destination" cannot contain any of the following characters: \ / : * ? " < > |	Correct the path name so that it does not include these characters.
The selected destination path does not exist.	Create the specified directories.
The selected destination path is too long to copy the selected files.	Choose a less nested destination path or rename the folders. The path may not exceed 255 characters in length.

Error message	Comments and suggestions
The selected destination path is write protected.	Verify that you are running the software with the required permissions to write data to the selected path.

7.1.3 Fill fluids

Error message	Comments and suggestions
The data was not successfully saved to Configuration DynamicSettings.ini.	Verify that you are running the software with the required permissions to write data to the selected path.

7.1.4 Flow cells

Error message	Comments and suggestions
Cannot start a run because a maintenance wash has to be performed first.	Perform a maintenance wash.
Cannot start a run because there is not enough space on the hard drive to store run data.	Run the Manage Files Wizard or use GeneRead Databank to free up disk space.
The wash cannot be started during a run.	Complete the run and unload process.
There are still flow cells on the carousel. Please unload these before starting a wash.	Unload all flow cells.
Validation of flow cell failed. Load the flow cell and ensure that the flow cell is placed correctly. Close the door to continue.	Verify that the flow cell orientation is correct and that the bar code is clean and undamaged. The bar code should be face up and to the left. Refer to the relevant QIAGEN kit handbook for more information.

7.1.5 Run module

Error message	Comments and suggestions
There must be at least one flow cell loaded to run a protocol.	Use the Start Run Wizard to load flow cells and fluids before starting a run.
Flow cell door is open.	Close flow cell door.
No flow cell detected at the loader but flow cell <barcode> was expected to be there.	Select **Yes** if this flow cell is at the loader. Select **No** to remove this flow cell from the inventory. Contact QIAGEN Technical Services if this message persists.

7.1.6 Start Run module

Error message	Comments and suggestions
This is not a known reagent kit and may not be used for a sequencing run.	Verify that you are using a GeneRead Advanced Sequencing Q Kit and contact QIAGEN Technical Services.
This is not a valid barcode. Please re-scan the proper barcode from the reagent kit.	Verify that you are using a GeneRead Advanced Sequencing Q Kit and contact QIAGEN Technical Services.
This is not a valid barcode. Please re-scan the proper bottle from the wash kit.	Verify that you are using GeneRead Sequencing Wash Buffer and contact QIAGEN Technical Services.

8 Technical Data

8.1 Environmental conditions – operating conditions

Power	100–240 V AC (±10%), 50/60 Hz Max. 600 VA (GeneReader) Max. 400 VA (workstation)
Overvoltage category	II
Air temperature	18 to 25°C (64 to 77°F)
Relative humidity	10–75% (noncondensing)
Altitude	Up to 2000 m (6500 ft.)
Place of operation	For indoor use only
Pollution level	2
Environmental class	3K2 (IEC 60721-3-3)

8.2 Mechanical data and hardware features

Dimensions (hoods closed)	Width:	93 cm (36.6 in.)
	Height:	61 cm (24.0 in.)
	Depth:	59 cm (23.2 in.)
Dimensions (hood open)	Width:	93 cm (36.6 in.)
	Height:	112 cm (44.1 in.)
	Depth:	59 cm (23.2 in.)
Dimensions (Main Hood open)	Width:	93 cm (36.6 in.)
	Height:	125 cm (49.3 in.)
	Depth:	59 cm (23.2 in.)
Weight	102 kg (224.9 lb.)	
Capacity	Up to 3 flow cells simultaneously	

8.3 Workstation specifications (hardware and software)

8.3.1 Workstation

- Intel Xeon E5–1650 v3 (3.50 GHz 6 Core)
- 32GB (4x8 GB) DDR4-2133 ECC (max. 128 GB)
- 1 x 256 GB SATA SE SSD
- 3 x 2.0 TB SATA 7200 rpm HDD
- NVIDIA Quadro K2200 4 GB Graphics
- Display resolution of 1920 x 1080 pixels
- 4 x USB 3.0 (front), 2 x USB 2.0 (rear), and 4 x USB 3.0 (rear)
- DVD drive
- Keyboard and mouse

- Monitor
- Handheld bar code scanner

8.3.2 Software

- Microsoft Windows 7 Professional 64-bit (D/F/E/I)
- GeneReader software v1.4.0

Adobe Reader software is preinstalled on the computer to view reports generated in PDF format.

Appendix A

Declaration of Conformity

Name and address of the legal manufacturer

QIAGEN GmbH
QIAGEN Strasse 1
40724 Hilden
Germany

An up-to-date Declaration of Conformity can be requested from QIAGEN Technical Services.

License Terms

The license terms for all software used with GeneReader, including QIAGEN software components, commercial software components and open source software components, are provided in the files **licenses.rtf** and **Prerequisite.LicenseAgreements.rtf** located on the GeneReader workstation under the following paths:

C:\ProgramData\QIAGEN\GeneReader\licenses.rtf

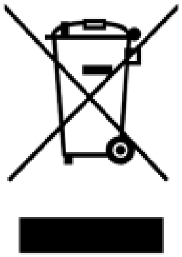
C:\ProgramData\QIAGEN\GeneReader\Prerequisite.LicenseAgreements.rtf.

Waste Electrical and Electronic Equipment (WEEE)

This section provides information about disposal of waste electrical and electronic equipment by users.

The crossed-out wheeled bin symbol (see below) indicates that this product must not be disposed of with other waste; it must be taken to an approved treatment facility or to a designated collection point for recycling, according to local laws and regulations.

The separate collection and recycling of waste electronic equipment at the time of disposal helps to conserve natural resources and ensures that the product is recycled in a manner that protects human health and the environment.



Recycling can be provided by QIAGEN upon request at additional cost. In the European Union, in accordance with the specific WEEE recycling requirements and where a replacement product is being supplied by QIAGEN, free recycling of its WEEE-marked electronic equipment is provided.

To recycle electronic equipment, contact your local QIAGEN sales office for the required return form. Once the form is submitted, you will be contacted by QIAGEN either to request follow-up information for scheduling collection of the electronic waste or to provide you with an individual quote.

FCC Declaration

The ''United States Federal Communications Commission'' (USFCC) (in 47 CRF 15. 105) declared that the users of this product must be informed of the following facts and circumstances.

''This device complies with part 15 of the FCC:

Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) this device must accept any interference received, including interference that may cause undesired operation.''

"This Class B digital apparatus complies with Canadian ICES-0003.''

The following statement applies to the products covered in this manual, unless otherwise specified herein. The statement for other products will appear in the accompanying documentation.

NOTE: This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to Part 15 of the FCC Rules and meets all requirements of the Canadian Interference-Causing Equipment Standard ICES-003 for digital apparatus. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that the interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one or more of the following measures:

Reorient or relocate the receiving antenna.

Increase the separation between the equipment and receiver.

Connect the equipment into an outlet on a circuit different from that to which the receiver is connected.

Consult the dealer or an experienced radio/TV technician for help.

QIAGEN GmbH Germany is not responsible for any radio television interference caused by unauthorized modifications of this equipment or the substitution or attachment of connection cables and equipment other than those specified by QIAGEN GmbH, Germany. The correction of interference caused by such unauthorized modification, substitution or attachment will be the responsibility of the user.

Liability Clause

QIAGEN shall be released from all obligations under its warranty in the event repairs or modifications are made by persons other than its own personnel, except in cases where the Company has given its written consent to perform such repairs or modifications.

All materials replaced under this warranty will be warranted only for the duration of the original warranty period, and in no case beyond the original expiration date of original warranty unless authorized in writing by an officer of the Company. Read-out devices, interfacing devices, and associated software will be warranted only for the period offered by the original manufacturer of these products. Representations and warranties made by any person, including representatives of QIAGEN, which are inconsistent or in conflict with the conditions in this warranty shall not be binding upon the Company unless produced in writing and approved by an officer of QIAGEN.

Appendix B

Ordering information

Note: Only use GeneReader products supplied by QIAGEN.

Product	Contents	Cat. no.
GeneReader System	Includes GeneReader instrument, workstation, USB cables, bar code scanner and international power cable set	9002312
Related Products		
GeneRead Advanced Sequencing Q Kit (3)	Includes reagents, add-ons and 3 flow cells for as many as 3 flow cell runs, up to 157 cycles each, on the GeneReader	185231
GeneRead Sequencing Buffer Q Kit (16)	Includes 800 ml each of Wash Buffer 9/10, 1 L of Wash Buffer 11, and 1 x 900 ml of Maintenance Wash Buffer	185901
Additional products		
Handheld Bar Code Scanner NGS System		9022959
Waste Bottle NGS System		9243790
Workstation NGS System		9024359

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