Technical Information

EZ2® Connect IT and 21 CFR Part 11 Regulations

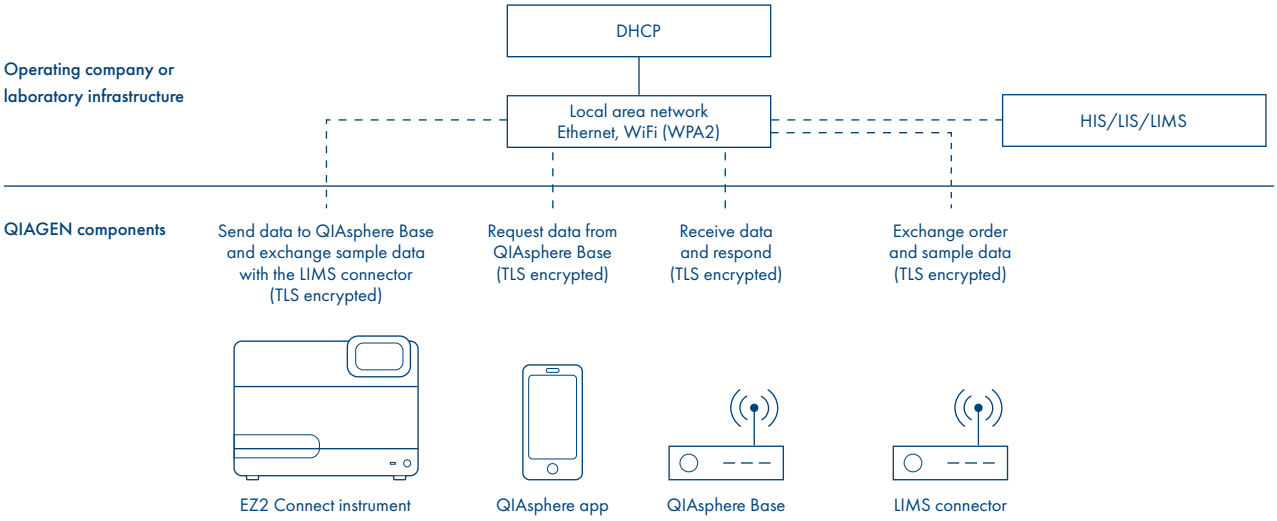
The EZ2 Connect instrument is designed to automate nucleic acid purification with the help of QIAGEN kits indicated for use with the EZ2 Connect. The EZ2 Connect system includes the instrument, the LIMS connector, the QIAsphere® Base and the QIAsphere app. The QIAsphere Base and the QIAsphere app allow users to remotely access their instrument, so they can manage their EZ2 Connect and monitor their runs even from outside the laboratory.

An increasing number of laboratories are using electronic records and electronic signatures for exchanging and storing data.

Electronic documentation offers many benefits, including increased efficiency and productivity when storing data, as well as easier information sharing and data mining.

Compliance with 21 CFR Part 11 involves both technical (i.e., hardware and software) and procedural requirements. This Technical Information explains how the EZ2 Connect system, referred to as "the system" in the following, contributes to fulfilling the technical requirements of FDA regulation 21 CFR Part 11.10: *Controls for closed systems*.

The EZ2 Connect is a closed system – access is controlled by users who are responsible for the content of the electronic records on that system. The software forms part of the electronic record system by which electronic records are created, modified, stored and secured against further modification. The EZ2 Connect does not provide electronic signature functionality.



DHCP: dynamic host configuration protocol; EAP: extensible authentication protocol; HIS: hospital information system; LAN: local area network; LIMS: laboratory information management system; LIS: laboratory information system; TLS: transport layer security; WiFi: wireless fidelity; WPA: WiFi protected access.

Figure 1. EZ2 Connect architecture diagram. The communication from the instrument to the app is supported unidirectionally via the QIAsphere Base gateway. With the help of the LIMS connector, order and samples information can be exchanged with the corresponding company infrastructure.

Controls for Closed Systems – 21 CFR Part 11.10

The sections of 21 CFR Part 11.10, as well as their subjects, requirements, how the subjects are implemented in the system and the compliance status, are summarized in Table 1.

Table 1. Sections of 21 CFR Part 11.10 and their implementation in the EZ2 Connect system

Section	Subject	Requirement	System implementation	Status
11.10 (a)	System validation	Validation of systems to ensure accuracy, reliability, consistent intended performance and the ability to discern invalid or altered records.	The EZ2 Connect operating software is validated by QIAGEN to ensure accurate, reliable and intended performance of the EZ2 Connect system. IQ/OQ procedures for the proper function of the instrument can be put in place.	compliant
11.10 (b)	Record generation	The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency. Persons should contact the agency if there are any questions regarding the ability of the agency to perform such review and copying of the electronic records.	The EZ2 Connect operating software generates run specific report files in PDF format. An additional output file is provided in XML format for electronic data processing.	compliant

Section	Subject	Requirement	System implementation	Status
11.10 (c)	Record protection	Protection of records to enable their accurate and ready retrieval throughout the records retention period.	The EZ2 Connect system generates electronic records that do not expire and are stored until downloaded by the user, for storage in an external electronic archive. The log file has a retention time of 52 workdays, and the audit trail file has a retention time of up to six months. After this time period, old data will be overwritten. Security measures for report storage outside of the system lies within the responsibility of the operating company or laboratory.	compliant
11.10 (d)	Access limitation	Limiting system access to authorized individuals.	Access to the system is controlled by user login. User management of the EZ2 Connect system enables creation of user accounts based on roles. Users with Operator access can run protocol files, perform assay setup, download reports and execute instrument maintenance protocols. In addition to that, users with Administrator access can change time, date and network settings, update the set of protocol files, update the operating software, manage user accounts and access the audit trail. Service users can do everything an Administrator can do; they can also log in with a keyfile and password and can perform special maintenance runs, performance tests and setup tasks. All changes to the user database are logged in the audit trail.	compliant
11.10 (e)	Audit trails	Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.	A time-stamped audit trail records the type of action, the user identification and any action that creates or modifies the system configuration or the execution of maintenance tasks. The logged data is stored for up to six months. After that time, it will be overwritten without warning. The audit trail data is stored in separate files with a checksum and cannot be modified by the user.	compliant
11.10 (f)	Operational system checks	Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate.	The EZ2 Connect user interface provides a guided step-by-step run setup with user confirmation. Instrument versions equipped with the optional camera perform a final worktable loadcheck before executing a protocol run. Only protocols provided by QIAGEN can be run on the system.	compliant
11.10 (g)	Authority checks	Use of authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand.	Access to software functions is based on the assigned user role (Operator or Administrator). It is the responsibility of the company or laboratory to assign the appropriate user role to each individual user depending on the desired level of authorization.	compliant

Section	Subject	Requirement	System implementation	Status
11.10 (h)	Device checks	Use of device (e.g., terminal) checks to determine, as appropriate, the validity of the source of data input or operational instruction.	The validity of the data source for configuration data and protocol files, including the labware data, is ensured by validation during the installation. The protocol files cannot be modified by users. This ensures that all input data of an experiment (except sample ID definition and necessary parametrization) were generated by QIAGEN personnel or software and that the data have not been altered after generation.	compliant
11.10 (i)	Education and Training	Determination that persons who develop, maintain, or use electronic record/ electronic signature systems have the education, training, and experience to perform their assigned tasks.	QIAGEN developers and service personnel are fully and continually trained. QIAGEN offers optional training on the EZ2 Connect instrument. In addition, user manuals and documentation are provided by QIAGEN. Establishing and maintaining the appropriate training level for EZ2 Connect users is the responsibility of the company or laboratory. The EZ2 Connect system supports fulfillment of this requirement by applying a role-based user management. The EZ2 Connect system does not provide electronic signature functionality.	compliant
11.10 (j)	Written policies	The establishment of, and adherence to, written policies that hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification.	Responsibility of the operating company or laboratory.	compliant
11.10 (k)	System documentation	Use of appropriate controls over systems documentation including: (1) Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance. (2) Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.	The EZ2 Connect system is delivered together with electronic user documentation that is associated with the specific version of the software. The manuals are provided in PDF and cannot be changed by the user.	compliant

Summary

The sections of 21 CFR Part 11.10, their subjects, and how and by whom the subjects are handled are summarized in Table 2.

Table 2. Responsibilities of the operating company or laboratory and QIAGEN

Section	Subject	Company/Laboratory	QIAGEN	Responsibility handling
11.10 (a)	System validation	x		Policies of the company or laboratory operating the EZ2 Connect system.
11.10 (b)	Record generation		x	Existence of electronic records in human-readable form and exportation to PDF standard.
11.10 (c)	Record protection	x	x	All electronic records are kept on the file system until the user transfers them to an external electronic archive.
11.10 (d)	Access limitation	x	x	Controlled access to the EZ2 Connect system through user authentication.
11.10 (e)	Audit trails	x	x	System tracks changes in an audit trail that does not expire. The creation of backups is under the responsibility and control of the company or laboratory.
11.10 (f)	Operational system checks	x	x	Guided run setup with user confirmation and load check of the instrument. Only QIAGEN protocols can be run.
11.10 (g)	Authority checks	x	x	Controlled access to the system by user authentication. User cannot modify electronic records or protocols. Operating company or laboratory has to ensure that each username can be traced to a real individual and that roles are correctly assigned.
11.10 (h)	Device checks	x	x	Checksum validation for configuration and protocols by the system during the installation. The sample ID and kit information input, as well as worktable setup, is under the responsibility and control of the company or laboratory.
11.10 (i)	Education and training	x	x	Manuals and documentation are provided by QIAGEN. Establishing and maintaining the appropriate training level is the responsibility of the company or laboratory.
11.10 (j)	Written policies	x		Establishing and maintaining procedures to comply with this regulation is the responsibility of the company or laboratory.
11.10 (k)	System documentation	x	x	EZ2 Connect system documentation cannot be changed by the user. The distribution of documentation to the users and version control of the documentation is the responsibility of the company or laboratory.

The EZ2 Connect is designed to perform fully automated purification of nucleic acids and proteins in molecular biology applications. The system is intended for use by professional users trained in molecular biological techniques and the operation of the EZ2 Connect. This product is not intended for the diagnosis, prevention, or treatment of a disease.

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit instructions for use or user operator manual. QIAGEN instructions for use and user manuals are available at **www.qiagen.com** or can be requested from QIAGEN Technical Services (or your local distributor).

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