Integrated Biology Solutions

The Agilent 2100 Bioanalyzer System - A Compliant Tool in Life Sciences

IQ OQ/PV 21CFR part 11

Technical Overview

The Agilent 2100 Bioanalyzer is an integrated, inexpensive, compliant solution for the analysis of nucleic acids, proteins, or cells. The new Agilent 2100 expert software (G2946CA) enables users to run the Agilent 2100 Bioanalyzer in regulated lab environments. With IQ (Installation Qualification), OQ/PV (Operational Qualification /Performance Verification) compliant services, and 21CFR part 11 compliance, the system can easily be used for the quality control and analysis of antibodies, protein pharmaceuticals, and other biomolecules such as RNA and DNA.

The Agilent 2100 Bioanalyzer Solution

Since the introduction of the Agilent 2100 Bioanalyzer in 1999, the application portfolio of the 2100 Bioanalyzer has increased steadily. This multi-purpose system is able to analyze DNA, RNA, proteins, and cells on one platform. The Agilent 2100 solution comprises the bioanalyzer instrument, software, as well as application-specific consumables (chip kits). Using the lab-on-a-chip technology, the 2100 Bioanalyzer integrates sample handling, separation, detection, and data analysis on a microfluidic chip. This approach greatly reduces analysis time and sample amount. Depending on the application, up to 12 samples can be automatically analyzed in less than 30 minutes. Data is acquired and archived in digital format. With the introduction of the Agilent 2100 Bioanalyzer expert software (G2946CA) and Agilent 2100 security pack software (G2949CA), the operational area of the 2100 Bioanalyzer is extended further. The software now supports IQ, OQ/PV, and with security pack loaded, 21CFR part 11 compliance, (electronic signatures, and records regulations). This is a prerequisite for use of the Agilent 2100 Bioanalyzer in regulated environments, for example, in pharmaceutical QA/QC labs. A tight quality control of the consumables combined with a lot-specific declaration of conformity to manufacturing specifications ensures the high quality of the LabChip kits and reagents [1]. Agilent Technologies' declaration of conformity for the 2100 Bioanalyzer instrument and the declaration of system validation for the Agilent 2100 expert and security pack software complete the design qualification (DQ) documentation. (See Figure 1.)

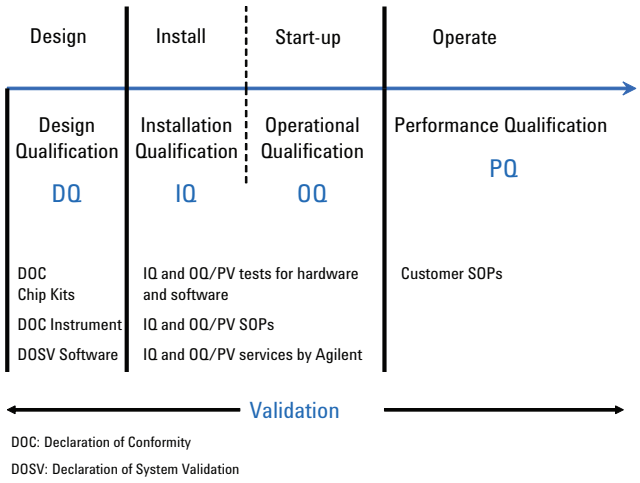

Figure 1. The four 'Q's of compliance, Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ). Agilent provides services for DQ, IQ and OQ. Standard Operating Procedures (SOPs) are developed by the customer for PQ.

The Agilent 2100 Expert Software

The Agilent 2100 expert software (G2946CA) has been upgraded to include a new functionality that will objectively assess the quality of an RNA sample. The proprietary algorithm will independently and automatically provide a RIN score (RNA Integrity Number), determining the integrity of the sample. The RIN algorithm has been "trained" using a neural network to assess the overall quality of the sample by comparing six key areas of the sample's electropherogram. The RIN score provides a valuable tool for all researchers working in the RNA QC field. With the added functionality of 21CFR part 11 compliance and electronic signatures, the bioanalyzer is positioned to be the instrument used for the validation of biomolecules whether the sample is RNA, DNA, cells, or proteins.

The hardware and software requirements for the 2100 expert software are listed below:

PC hardware (minimum requirements):

- CPU: Pentium IV
- RAM: 512 Mbyte
- Ports: 1–2 serial ports
- VGA: Resolution of 1024 × 768
- Hard Disk: 60 Gbyte

The software can control two instruments from one PC using the two RS232 comports to connect to the individual instruments. To operate the instrument, a valid license key for instrument control is required. In addition, separate licenses are required to activate the different modules in the software. There are three modules available in the 2100 expert bioanalyzer software: electrophoresis (G2947CA), cell fluorescence (G2948CA), and security pack (G2949CA). Cell fluorescence and electrophoresis license keys provide access to their respective assays, such as antibody staining, apoptosis, etc. for cell fluorescence, and the electrophoresis license is used for the associated molecular assays, DNA, RNA, and protein. The security pack module allows for operation in a fully secure environment, meaning that no one can acquire or access data without a proper user account and identification. All actions performed within the secured environment are tracked and documented with a clear, traceable audit trail. If no license keys are provided, software functionality is limited to data review and evaluation mode only.

A dedicated 'Declaration of System Validation' ensures that the 2100 expert software was developed according to the quality process and life cycle followed by the 'Life Sciences and Chemical Analysis' division of Agilent Technologies. Life cycle checkpoint details were reviewed and approved by management. The product was found to meet its functional and performance specifications, and release criteria on the release to shipment date.

Compliance Products and Services for the Agilent 2100 Bioanalyzer System

With the 2100 expert software, Agilent offers compliance services for the 2100 Bioanalyzer system. Compliance services can be purchased any time. A certified customer engineer will test and verify the functionality of the hardware and software, thereby qualifying the system. Table 1 summarizes the options that are available for B- and C- Type bioanalyzer instruments (with serial numbers above DE 13701001). For A-type instruments (with serial numbers lower than DE 13701000), the 2100 expert software supports running OQ/PVs based on a SOP developed by the customer.

Table 1. List of Compliant Services Available

Description Option	Service	Product number	
2100 Bioanalyzer system*	IQ	R1015A	–
2100 Bioanalyzer system*	OQ/PV	R1016A	–
2nd cartridge	OQ/PV	R1016A	001
2nd 2100 Bioanalyzer	OQ/PV	R1016A	002
Security pack	OQ/PV	R1016A	003

* System comprises 2100 Bioanalyzer instrument, 2100 expert software, and one cartridge of choice.

Instrument Qualification

IQ ensures upon delivery that the Agilent 2100 Bioanalyzer instrument and the 2100 expert software are installed correctly from the moment the components are unpacked to the point the system is ready for operation – documenting the completeness of shipping, the operating environment, and the components of the system. The IQ includes tests to verify that the software and hardware are installed properly and that all electrical connections are correct. The correct installation of computer software is checked by the verification part (in the verification context) of the 2100 expert software.

IQ should be performed after installation of hardware or software.

The IQ services for the Agilent 2100 Bioanalyzer system include:

Hardware IQ

- Shipment checklist
- Installation according to checklist
- Documentation of instrument details
- System checkout using the autofocus chip to generate a signal
- Certification (document and sign) – audit-ready documentation confirming correct installation of the bioanalyzer

Software IQ

- Software check – IQ tool checks the integrity and revision of the program components
- Certification (document and sign) – audit-ready documentation confirming correct installation of the 2100 expert software

Operational Qualification

The OQ is the process of demonstrating that an instrument will function according to its operational specifications in the selected environment [2]. The OQ does not test to ensure the instrument meets the manufacturer's performance specifications. The Operational Qualification ensures basic accuracy of the system and its ability to function properly. OQ is performed after IQ, to verify and document an Agilent instrument's ability to meet specified performance criteria after it is installed. The OQ involves a comprehensive test of the complete system using established conditions. A key benefit to this procedure is to ensure the basic accuracy and precision of the 2100 Bioanalyzer system and to uncover any potential problems before they occur. (See Figure 2). Agilent recommends that preventive maintenance be performed on the instrument prior to an OQ.

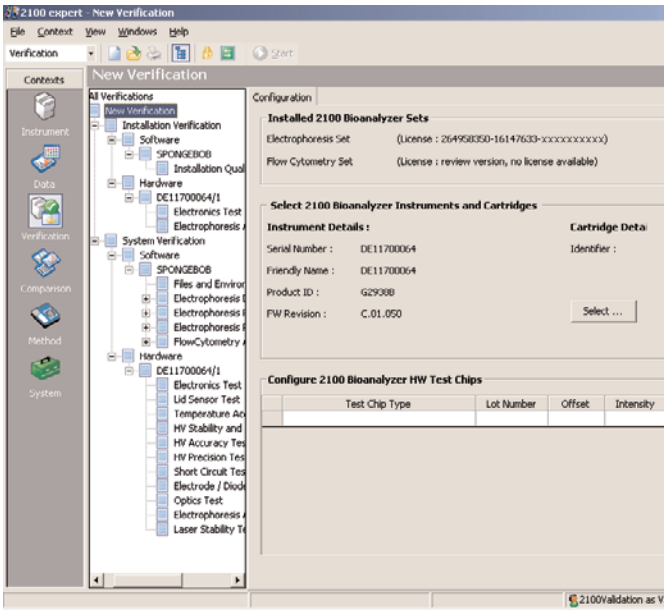

Figure 2. The verification context of the 2100 expert software.

OQ should be performed:

- After installation of hardware or software (after the initial installation)
- After major events, such as repair, upgrades, or relocation
- After any software change that affects system security, data integrity, or administrative controls
- At regular intervals during routine use

The OQ/PV services for the Agilent 2100 bioanalyzer system include:

Hardware OQ/PV

- Instrument validation tests - for example, short circuit test, High Voltage (HV) stability test, HV accuracy test, temperature test, autofocus test, electrode/diode test, laser stability test, etc. using the diagnostic chips provided with the system
- Audit-ready documented evidence confirming that the Agilent 2100 Bioanalyzer is performing according to its operational specifications in the user's lab

Software OQ/PV

- Data calculation engine and software algorithm test
- Test of data files compared with master files
- Audit-ready documented evidence confirming that the Agilent 2100 expert software is performing according to its operational specifications in the user's lab

21CFR part 11 Compliance

Full FDA compliance requires that the software fulfills all rules defined under 21CFR part 11. 21CFR part 11 specifies the requirements of electronic recording, such as data security, data integrity, and audit traceability. With the addition of the security pack module, the 2100 expert software (G2949CA) is now fully compatible with 21CFR part 11. Users are clearly identifiable with distinct user names and passwords. Users are first defined in the operating system and then are set-up with specified roles and functions for use in the 2100 Expert software by the administrator. The different roles available are:

Operator	Permission
Standard Operator	Run Methods
Advanced Operator	Develop and modify methods
2100 Administrator	Setup of users
Backup Operator	Archiving/De-archiving files
Validation Operator	Validation of system
2100 Unlock Operator	Unlock system after timing out
2100 Guest	Review of data (read only)

The expert software limits the functionality of the user as defined by their role, that is, a standard operator cannot act as a validation operator or vice versa. A customer-defined method is developed detailing the instrument and assay type used for the measurement. The method further details the functions of the user for the particular method, that is the number of peer review cycles the data must go through before final approval or rejection of the sample. All adjustments or manipulation of the data is tracked in the secure area and is accompanied by an electronic signature.

Conclusion

With the introduction of the 2100 Expert software (G2946CA), Agilent Technologies addresses the needs of customers in pharmaceutical QA/QC labs and manufacturing departments. By offering IQ and OQ/PV support services, the usage of lab-on-a-chip technology is extended to customers working in regulated environments. The added functionality of the security pack (G2949CA) enables the Agilent 2100 Bioanalyzer to be a fully compliant solution for the analysis of nucleic acids, proteins, or cells.

References

1. T. Preckel, M. Valer, and M. Kratzmeier, "Quality Control for the Agilent 2100 Bioanalyzer Protein 200 Plus LabChip Kits", Agilent Technologies, publication 5989-3336EN
2. P. Bedson, and M. Sargent, (1996), "The development and application of guidance on equipment qualification of analytical instruments", *Accreditation and Quality Assurance*, **1 (6)**, 265–274.

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Printed in the USA
December 27, 2005
5989-4278EN

Agilent Technologies