

LabChip GX System – Supporting Regulatory Compliance

Revision History

Revision	Date	Description
1.0	3/10/09	Initial draft

Approvals

Name	Signature	Date
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Approved By: <Name or Designee – Dept.Name>		



LabChip | GX/GXII

with LabChip GxP Software

Supporting Regulatory Compliance

Regulatory Compliance

Caliper LabChip GX/GXII suite of instruments provides automated electrophoresis to analyze quality, size, and concentration, of DNA, RNA, and proteins. Caliper LabChip GxP Software enables the users to run the instruments in regulated environments, such as GLP (Good Laboratory Practice), GCP (Good Clinical Practice), or GMP (Good Manufacturing Practice), commonly referred as GxP.

The Importance of Qualification of Analytical Instruments and Validation of Computerized Systems

In the regulated environments, users are required to qualify analytical instruments for their intended use, to maintain the instruments on a regular basis to ensure the performance, and to keep the maintenance records. If the instruments are computerized, the users are subject to 21 CFR Part 11 requirements, which include validation of systems, audit trails, copies of records, record retention, and other provisions.

Among several models of qualification of analytical instruments and validation of computerized systems, the following 4Q approach has been commonly used:

- Design Qualification (DQ)
- Installation Qualification (IQ)
- Operation Qualification (OQ)
- Performance Qualification (PQ)

In 2008, the United States Pharmacopeia (USP) incorporated this 4Q approach and published USP Chapter <1085> titled “Analytical Instrument Qualification”, the compendial procedure for pharmaceutical industries.

Caliper is fully aware of our customer requirements in terms of DQ, IQ, OQ, PQ, and 21 CFR Part 11 compliance. This white paper describes how our services and our products are able to address your needs using our systems in regulated environments.

Design Qualification

Caliper Life Sciences, Inc. is ISO 9001 - 2000 certified (Figure 1). Caliper product development is based on ISO 9001 – 2000 Design Control Process. Our instruments and software systems have been thoroughly tested before release to ensure that the products conform to their design specification. Caliper has well established customer support and service programs to assure that our customers get adequate support using our systems.

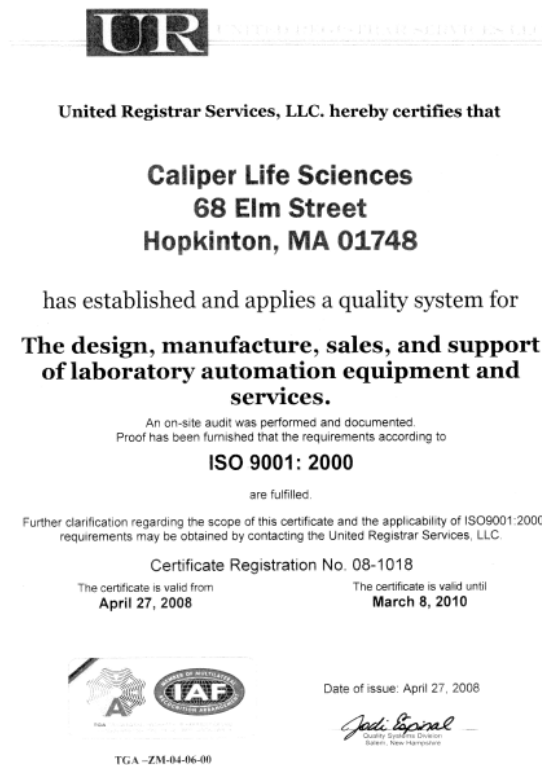
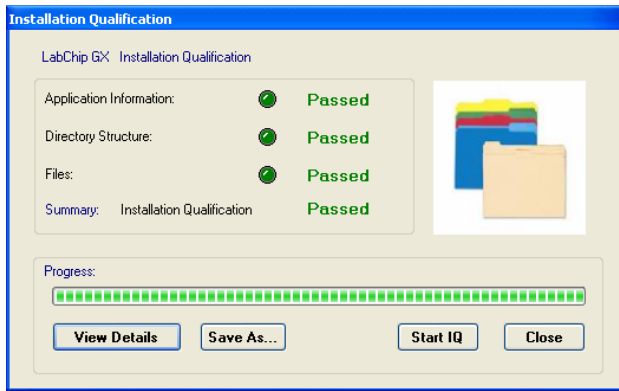


Figure 1. ISO 9001-2000 Certificate

Installation Qualification

Caliper provides full services for on-site installation qualification. In addition to that, our



checklist and step-by-step instructions for installation qualification allow our customers to perform installation qualification themselves on an 'as needed' basis. Moreover, the LabChip GxP Software has a built-in IQ tool to automate the software installation qualification (Figure 2). Users have options to save the IQ results to a file for future reference or to review the details of IQ results and to print out the results for documentation purpose.

Figure 2. Software Installation Qualification Tool

The IQ tool comes in handy for checking software installation qualification after each computer system maintenance or service routine, such as disk cleanup, installing antivirus software, or installing Microsoft service packs. This IQ tool checks LabChip GxP Software registry settings, the directory structure, and the integrity of each file specified for the software application.

Operation Qualification

The Caliper LabChip GxP Software contains OQ tool specifically designed to automate the operation qualification process. As shown in Figure 3, the left pane of the Instrument Diagnostics graphical user interface (GUI) lists each instrument component subject to OQ testing. Users have options to select or deselect items for testing to tailor their needs.

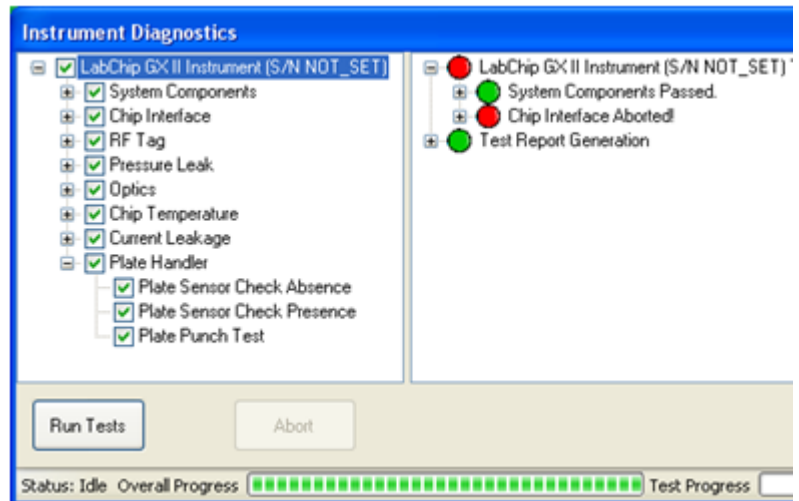


Figure 3. Automated OQ Tool

The user works interactively with the GxP OQ tool. Once the testing gets started by clicking the “Run Tests” button, the software guides the user through the process by providing detailed instructions for the user to follow and the options that the user can choose. For example, in the step of checking the chip cartridge interlock, a dialog box pops up asking the user to unload the chip in order to proceed (see Figure 4.)

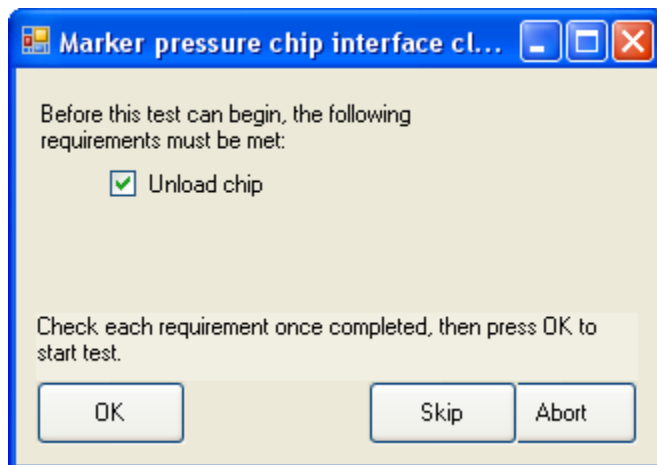


Figure 4. User Friendly OQ Testing

Guide

Once each test item is completed, the test result is listed on the right pane of the OQ GUI. At the end of the OQ process, the test report is generated and saved to a file for review, printing, and documentation purpose.

Performance Qualification

Caliper field services are available to customers for their performance qualification needs. This service will be variable by customer need, and will be quoted on an individual basis. Depending on the type of application, for example, quality control (QC) testing for RNA, DNA or protein, users may want to establish application specific performance qualification and monitoring procedures. Caliper application scientists and consultants are available to assist the design of performance qualification procedures that are specific to the user applications.

21 CFR Part 11 Compliance

Caliper LabChip GX/GXII instruments with LabChip GxP Software are computerized systems designed to automate the analysis of DNA, RNA or proteins using Caliper Sipper Chip technologies. The systems allow the users to create, modify, and maintain the records in electronic form and allow the users to perform electronic signatures on the records generated from the system. It takes a combination of administrative controls, procedural controls, and technical controls for the users of a computerized system to comply with 21 CFR Part 11 regulations. The LabChip GxP Software contains built-in technical controls and features specifically designed to support the users for 21 CFR Part 11 compliance. These technical controls and features include user account management and access controls, device check, enforcing permitted sequencing of steps, audit trails, record copying, record retention, system documentation, and electronic signature controls.

User account management and access controls

A Caliper LabChip GX/GXII instrument with LabChip GxP Software is a 'closed system' (21 CFR 11.10). The system can be located in a designated laboratory room to limit system access to authorized individuals (21 CFR 11.10(d)). The software contains an application security module for user account management and for access of controls to meet the requirement of 21 CFR 11.10(g). As shown in Figure 5, the system administrator can do the following:

- Manage user accounts
- Define access
- Set policies

The screenshot shows the 'LabChip GX - User Administration' window. On the left, under 'Select Task:', there are buttons for 'Create New User', 'Edit Users', 'Show User Info', 'De/Activate User', 'Define Access', 'Set Policies', and 'Close'. The 'Create New User' form on the right includes fields for Username, First Name, Middle Name, Last Name, Position (set to 'Unknown'), Access Level (set to 'Restricted User'), Password, and Confirm Password. There is also a section for 'User Can Perform Signature' with a checked checkbox and its own Password and Confirm Password fields. A 'Save' button is at the bottom right.

Figure 5. User Administration

Only valid users are permitted to log on the system. Depending on the role of each user, a user can be assigned to one of the following four user groups:

- Restricted User
- Operator
- Supervisor
- Administrator

The screenshot shows the 'LabChip GX - User Administration' window with the 'Assign Access Levels' section active. It features a table with 11 rows of access rights and 4 columns for user groups: Administrator, Supervisor, Operator, and Restricted User. Each cell contains a dropdown menu with 'Enabled' or 'Disabled' options. Buttons for 'Save', 'Print Preview...', and 'Print' are at the bottom.

	Access Right	Administrator	Supervisor	Operator	Restricted User
1	User Administration	Enabled	Disabled	Disabled	Disabled
2	Run Assay	Enabled	Disabled	Disabled	Disabled
3	Save Existing Data File	Enabled	Enabled	Enabled	Disabled
4	Save Workspace	Enabled	Disabled	Disabled	Disabled
5	Plate Editor	Enabled	Disabled	Disabled	Disabled
6	Archive or Restore CDR	Enabled	Disabled	Enabled	Disabled
7	Manage CDR Folders	Enabled	Disabled	Disabled	Disabled
8	Perform IQ/OQ/ PQ Diagnostics	Enabled	Disabled	Enabled	Disabled
9	Print/Export Analysis Results	Enabled	Disabled	Disabled	Disabled
10	Audit Trail Access	Enabled	Disabled	Enabled	Enabled
11	Assay Editor	Enabled	Disabled	Disabled	Disabled

The system has a set of predefined permissions allowing the system administrator to enable or disable for each group as shown in Figure 6. The access settings can be printed out for documentation purpose.

Figure 6. Role Access Control

LabChip GxP Software uses a user authentication and role-based access control mechanism for authority checks to ensure that only authorized individuals can use the system, perform the operation at hand, electronically sign a record, or alter a record (21 CFR 11.10(g)). Each user ID (identification) is unique (21 CFR 11.300(a)).

As shown in Figure 7, the system administrator can set the password and login policies to prevent password aging (21 CFR 11.300(b)), and to limit the attempts of unauthorized use of the system (21 CFR 11.300(d)). After the limited number of failed login attempts, the account is locked out and only the administrator can unlock the account.

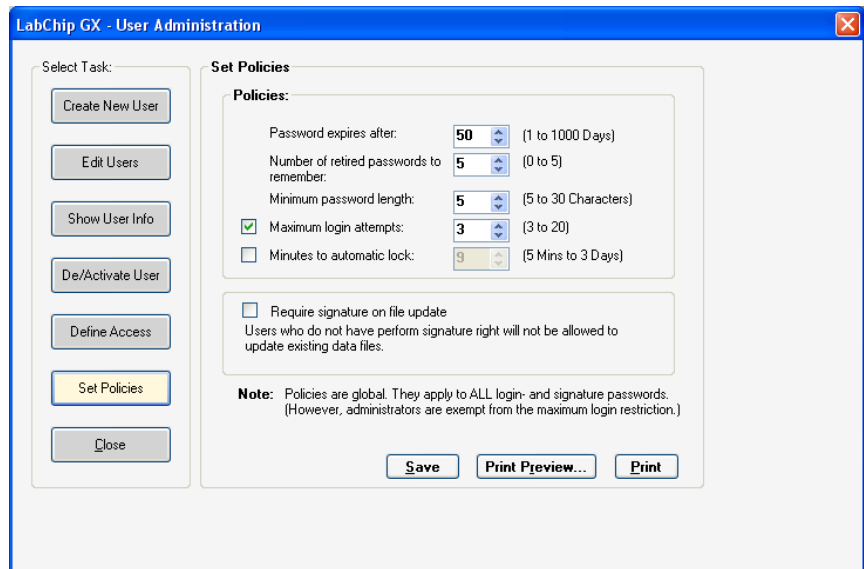


Figure 7. Policies Setting

The system has automatic lock feature to prevent the unauthorized access to the unattended system that is running. Similar to password protected screen saver application, after logging on and idle for specified time limit, the system allows the jobs to continue running in the background while it does not allow users access any functions without logging again on with valid password.

Device Check

Each Caliper LabChip GX/GXII instrument has a unique serial number to identify the specific instrument. After the system is validated and approved for GxP use, the user can enter the serial number into the system to enforce the device check (21 CFR 11.10(h)). Before starting each run, the system software automatically checks the device serial number to ensure the validity of the source of the data input. The device serial number is tied to the result of each run as part of the records.

Enforcing Permitted Sequencing of Steps

LabChip GX/GXII Systems allow users to run DNA, RNA, or protein assays. Each assay has its own sequencing of steps by design, which is automatically enforced by the system software (21 CFR 11.10(f)).

Audit Trails

LabChip GXP Software uses secured, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create,

Event Category	Event Detail	Username	Application Access Level	Date/Time	Comment
1	Login Version: 2.0.229.0 User: administrator Login: Login succeeded.	administrator	Administrator	Monday, March 09, 2009 9:17:16 PM	
2	Login Version: 2.0.229.0 User: administrator Exit: Exit succeeded.	administrator	Administrator	Monday, March 09, 2009 9:11:26 PM	
3	Login Version: 2.0.229.0 User: administrator Login: Login succeeded.	administrator	Administrator	Monday, March 09, 2009 4:43:58 PM	
4	Login Version: 2.0.229.0 User: administrator Login: Login succeeded.	administrator	Administrator	Monday, March 09, 2009 4:17:09 PM	
5	Login Version: 2.0.229.0 User: administrator Exit: Exit succeeded.	administrator	Administrator	Monday, March 09, 2009 3:48:03 PM	
6	Login Version: 2.0.229.0 User: administrator Login: Login succeeded.	administrator	Administrator	Monday, March 09, 2009 3:30:54 PM	
7	Login Version: 2.0.229.0	administrator	Administrator	Thursday, March 05,	

modify, or delete electronic records as shown in Figure 9. The audit trails can be printed out for documentation purpose. The audit trail documents can be made available for agency review and copying (21 CFR 11.10(e)).

Figure 9. Audit Trails

The system uses versioning mechanism so that record changes do not obscure previously recorded information. The users can always retrieve the previously recorded information by selecting a corresponding version of the records.

To facilitate the review of audit trails, the user can customize the audit trails view and can search the audit trails based on date range, username, or file name (see Figure 10).

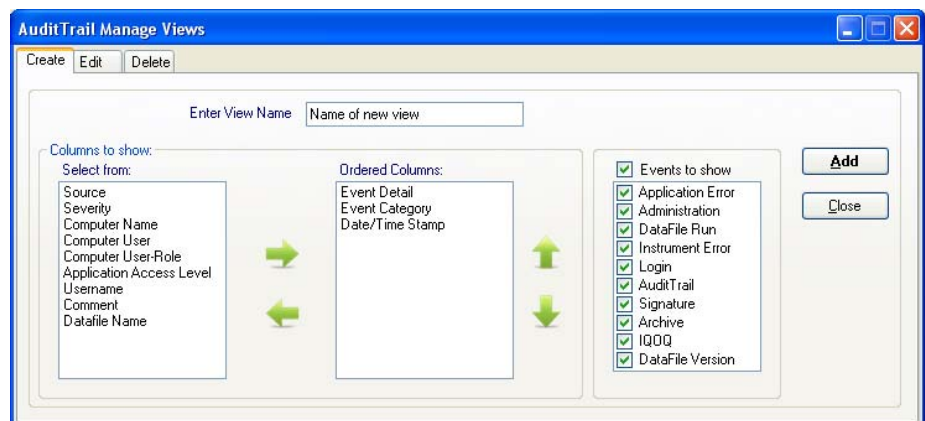


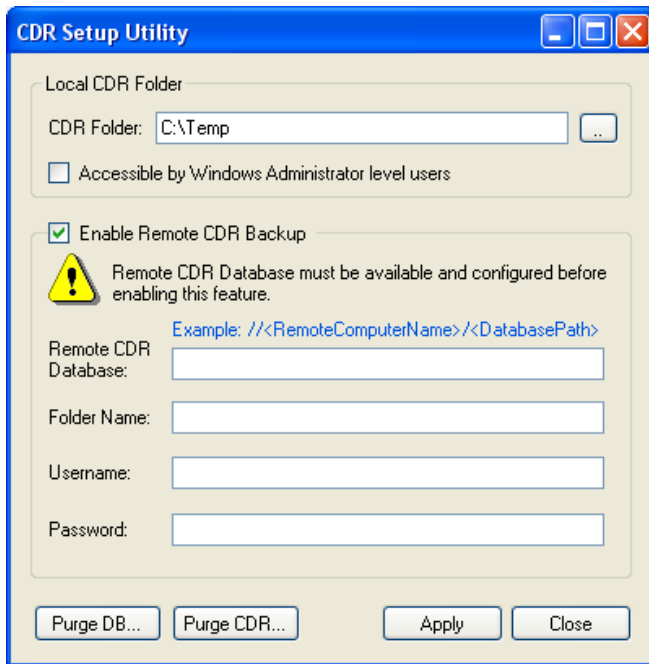
Figure 10. Audit Trail Manage Views

Copies of Records

LabChip GxP Software has the ability to generate accurate and complete copies of records in both human readable (electronic display or printout) and electronic form suitable for inspection, review, and copying by regulatory inspector. These records include run results, assay settings, signatures, and audit trails. These records can be printed on paper or exported to ASCII files. The exported records are clearly marked as uncontrolled records.

Record Retention

In addition to record printing function to support users meeting record retention requirements set forth in *21 CFR 11.10(c)* in paper form, LabChip GxP Software allows user to store and retrieve the records in electronic form via backup/restore mechanism.



During the installation of the LabChip GxP Software, the user has options to select CDR (Caliper Data Repository) on a network drive for backup purpose. The CDR Setup Utility enables the user to manage the CDR as shown in Figure 11.

Figure 11. CDR Setup Utility

System Documentation

Caliper provides version controlled documentation for system operation and maintenance that is consistent with the released system. The built-in IQ tool automatically checks if the correct version of online document is installed.

Electronic Signature

LabChip GxP Software uses unique combination of user ID and password for users to sign records electronically (21 CFR 11.100(a)). As shown in Figure 12, each signature contains the following information (21 CFR 11.50(a)):

- The printed name of the signer;
- The date and time when the signature was executed; and
- The meaning associated with the signature.



Figure 12. Perform Signature

The signature is linked to the record undersigned (21 CFR 11.70), is subject to the same controls as for electronic records, and is included as part of electronic display or printout of the electronic record (21 CFR 11.50(b)).