

The Guava[®] PCA[™], PCA-96 and PCA-96 AFP Systems

Support for Compliance with
21 CFR Part 11



Table of Contents

Introduction _____	1
How Guava Addresses Compliance _____	2
Referencing Compliance Features by Part 11 Section _____	3
Glossary _____	4

Guava Technologies

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Introduction

21 CFR Part 11, Electronic Records and Electronic Signatures, is the FDA regulation directing the management of electronic records and electronic signatures in open and closed systems. The regulation specifies the criteria under which the agency considers electronic records and electronic signatures to be the equivalent of paper records and handwritten signatures. The regulation became effective in March 1997.

The Guava PCA systems and CytoSoft™ software were designed to facilitate user compliance with 21 CFR Part 11. This white paper provides a summary of how the system addresses the regulatory require-

ments. Under the FDA regulation, the Guava PCA systems and CytoSoft software are closed systems. A closed system is controlled by persons who are responsible for the content of the electronic records generated on the system. In addition to software system technical controls, 21 CFR Part 11 requires that user facilities have established procedural and administrative controls. These include defined and documented lab policies, Standard Operating Procedures, personnel training, notification and management controls. Information in this document applies to the Guava PCA system with CytoSoft software version 2.1 or higher, and the Guava PCA-96 systems with version 2.5 or higher. Previous versions of CytoSoft do not include all the features described.

How Guava Addresses Compliance

Compliance Area	Requirement	Guava Compliance Features and Notes	Relevant Sections of 21 CFR Part 11
1 Data Security	1.1 Limit access to authorized users	<p>1.1.1 Access control in CytoSoft is based on Windows® 2000 User Authentication and Access Control.</p> <p>1.1.2 IT managers can limit access to authorized users.</p> <p>1.1.3 Guava “Administrator”, “Supervisor” and “Operator” user levels control access to data features such as the ability to modify information in files.</p>	11.10(d) (g)
	1.2 Maintain unique User ID and Password codes	<p>1.2.1 Access control in CytoSoft is based on Windows 2000; Windows requires a unique User (login) name and password for each assigned user.</p> <p>1.2.2 Windows 2000 does not allow the creation of two user accounts with the same name.</p>	11.200(a) (b) 11.300(a) (b) (d)
	1.3 Provide authority checks of users	<p>1.3.1 CytoSoft allows assignment of operator levels to authorize or restrict access to flexibility in CytoSoft.</p>	11.10(d)

W H I T E P A P E R

Compliance Area	Requirement	Guava Compliance Features and Notes	Relevant Sections of 21 CFR Part 11
	1.4 Provide accountability policies against falsification of records	<p>1.4.1 Windows 2000 does not allow the creation of two user accounts with the same User name.</p> <p>1.4.2 Within CytoSoft's data files, the user account information is recorded for a) the person creating the data file and b) any person(s) modifying an existing data file.</p> <p>1.4.3 Defined lab policies and procedures must hold personnel accountable for actions initiated under their electronic signature.</p>	11.10(j)
2 Audit Trail	2.1 Ensure the system can detect invalid or altered records; Do not obscure changes to data	<p>2.1.1 If a data file is edited, all changes are recorded to a copy of the original data file; the unaltered original file is retained.</p> <p>2.1.2 Modified data files include the account information of the person making the modifications.</p> <p>2.1.3 A time-stamped Event Log automatically and continuously records status, warnings, and errors; annotations to the Event-Log can be entered and recorded.</p>	11.10(a) (e)
	2.2 Provide a secure, computer-generated, time-stamped audit trail	<p>2.2.1 The Windows 2000 account information is recorded for each data file.</p> <p>2.2.2 Data files are read only and cannot be deleted or modified by ordinary means.</p> <p>2.2.3 IT Managers assign the operational level. Guava "Administrator" and "Supervisor" level user accounts can be configured to grant access to all features of the software, as defined by the Guava Administrator using the Admin Configuration page. "Operator" user accounts can be configured to restrict the ability of the Operator to make changes to instrument settings or analysis markers, gates, etc.</p> <p>2.2.4 A time-stamped Event Log automatically records status, actions, warnings, and errors; manual annotations to the Event Log can be entered and recorded.</p>	11.10(e) (g)
3 System Checks	3.1 Ensure the sequence of steps	<p>3.1.1 Software and analytic sequences are controlled to ensure that required steps are performed in order.</p> <p>3.1.2 "Operator" level access is strictly limited while Guava "Administrator" and "Supervisor" level users have broader access.</p>	11.10(f)
	3.2 Verify the validity of the source of data input	3.2.1 Data files opened for input are validated to be appropriate for the assay in use.	11.10(h)
4 Controls for Electronic Signatures	4.1 Electronic records must include the name, date/ time of signing and the meaning of the signature	<p>4.1.1 User's Full name and date/time stamp are included in data files.</p> <p>4.1.2 The Full name of the user is printed on the printout.</p> <p>4.1.3 Defined lab policies and procedures establish and specify the meaning associated with the signature.</p>	11.50(a) (b)

W H I T E P A P E R

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	4.2 Non-Biometric controls must have ID and password	<p>4.2.1 Windows 2000 requires a unique User name and password for each user.</p> <p>4.2.2 Defined lab policies and procedures establish that codes and passwords are to be used only by authorized individuals.</p>	11.200(a) (b)
5 Signature and Record Linking	5.1 Electronic and handwritten signatures are linked to the e-record.	<p>5.1.1 CytoSoft data files include the name of the user creating the data file.</p> <p>5.1.2 CytoSoft data output files are read only files and cannot be modified by ordinary means.</p>	11.70
6 Data Archiving and Retention	6.1 Generate accurate and complete records in human readable and electronic form	<p>6.1.1 Records are generated in human readable and electronic form. Archived printed records from the FCS and CSV data files provide records in human readable form.</p> <p>6.1.2 Archived FCS and CSV files contain the complete instrument and settings input as well as the raw data and analyzed result outputs.</p>	11.10(b)
	6.2 Enable accurate and easily accessible retrieval of records	<p>6.2.1 FCS and CSV data files are write-protected and cannot be modified by ordinary means.</p> <p>6.2.2 Data files can be maintained in readily retrievable form using file servers and databases.</p>	11.10(c)
7 General Controls For Electronic Signatures	7.1 Electronic signatures are unique; Verify the identity of persons with electronic signatures	<p>7.1.1 Windows 2000 does not allow the creation of two user accounts with the same user name.</p> <p>7.1.2 Defined lab policies establish and verify the identity of individuals with electronic signatures.</p> <p>7.1.3 If appropriate, defined lab policies and procedures certify to FDA that electronic signatures are equivalent to traditional handwritten signatures.</p>	11.100(a) 11.100(b) 11.100(c)
8 System Design and Training	8.1 Provide training for system users, developers and maintenance staff	<p>8.1.1 All Guava developers and test personnel have training and experience in developing software for regulated industries.</p> <p>8.1.2 Guava provides training for users of Guava products.</p> <p>8.1.3 Defined lab policies and procedures document training of personnel.</p>	11.10(i)
	8.2 Control access to and use of system operations and maintenance documentation	8.2.1 Guava documentation is controlled under an Engineering Change Order (ECO) control system. A source code control system and a defect (bug) tracking database are used to maintain source code, specifications, test plans and other project documentation.	11.10(k)(1)
	8.3 Implement change control for documentation changes	<p>8.3.1 Guava documentation is controlled under an ECO system.</p> <p>8.3.2 An audit trail is provided for each item under the system.</p>	11.10(k)(2)

Compliance Area	Requirement	Guava Compliance Features and Notes	Relevant Sections of 21 CFR Part 11
9 System Validation	9.1 Validate the system	<p>9.1.1 For lab-level validation, specific support is provided by the Guava Customer Solutions group.</p> <p>9.1.2 The Guava PCA System was developed and validated under a Product Development process. This process included the use of Marketing requirements, Functional specifications, Test plans, Test cases and reports, high level architectural design documents, Design and code reviews and error tracking and resolution.</p>	11.10(a) 11.10(k)(2)

Referencing Compliance Features by Part 11 Section

Following is a listing of section numbers from the 21 CFR Part 11 regulation with references to the Requirements Sections in the table above ("How Guava Addresses Compliance") which contain information on how Guava products address each Part 11 requirement.

Section of 21 CFR Part 11	Requirement Section(s)
11.10(a)	2.1, 9.1
11.10(b)	6.1
11.10(c)	6.2
11.10(d)	1.1, 1.3
11.10(e)	2.1, 2.2
11.10(f)	3.1
11.10(g)	1.1, 2.2
11.10(h)	3.2
11.10(i)	8.1
11.10(j)	1.4
11.10(k)	8.2, 8.3, 9.1
11.30	not applicable
11.50	4.1
11.70	5.1
11.100	7.1
11.200	1.2, 4.2
11.300	1.2

Glossary

CFR Code of Federal Regulations

CSV Comma Separated Values; a standard format for database files; file name extension normally used for such files. Files of this format are automatically recognized and opened by Microsoft® Excel.

CytoSoft Guava CytoSoft software is used to control the Guava PCA instrument, to manage data acquisition by the Guava PCA system and to analyze this data

ECO process Engineering Change Order; a defined process under which policies, procedures, and documents are controlled, incorporating a process for review and approval of said items

FCS Flow Cytometry Standards; a standardized format for flow cytometry data files, readable by most third party flow cytometry analysis software

Full name (Microsoft Windows term) Specified when creating a Windows user account, usually the actual first and last names of the "owner" of a Windows User account

Guava PCA system System consisting of the Guava PCA instrument, software and reagents for performing cell-based assays

Guava user levels Access to certain features within Guava software are controlled, on a Windows User account basis, by assignment of a Guava user level to

each authorized user of Guava software. There are 3 possible Guava user levels, listed here in order of declining privileges: Guava Administrator, Guava Supervisor, and Guava Operator. See 2.2.3 above for descriptions of privileges for each of these Guava user levels.

Lab level validation Aspects of validation addressed directly by the regulated laboratory (as opposed to aspects addressed primarily by an instrument vendor or other third party)

Login name (Microsoft Windows term) See “User name”

User account (Microsoft Windows term) A record that consists of all the information that defines a user to Windows 2000, including the user name and password required for the user to log on, the groups in which the user account has membership, and the rights and permissions the user has for using the computer and network and accessing their resources

User name (Microsoft Windows term) Primary name used to define a Windows user account; must be entered when logging onto a computer running under the Microsoft Windows 2000 operating system. Also used interchangeably with “Login name”.

Windows 2000 Version of Microsoft Windows on which Guava’s software products are supported by Guava

Product Notes

Products sold by Guava Technologies are intended for in vitro research use only. A technically qualified individual should supervise usage. Individuals receiving this information must exercise independent judgments in determining its appropriateness for a particular purpose. Material Safety Data Sheets are available for each product. Contact Guava Technologies Technical Support for the most up-to-date information.

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