Validation of a Laser Scanning Cytometer for Use in Regulated Studies

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Introduction

- Objective and unbiased cytometric analysis has an important place in pre-clinical and clinical studies that support investigational new drugs.
- In order to use laser scanning cytometry (LSC) to support key pharmacodynamic endpoints of regulated studies, we performed a computer system validation of an iCyte® cytometer.
- Using Good Laboratory Practice (GLP) guidelines we focused on traceability, reliability, data integrity, and the ability to reconstruct experimental data.
- Abbreviations:
  - LSC – Laser Scanning Cytometer, iCyte® and affiliated software version 3.2.1
  - SOP – Standard Operating Procedure
  - GLP – Good Laboratory Practices
  - CFR – Code of Federal Regulations

Table 1. Team Roles and Responsibilities

Responsibility	Team Members			
	System Expert	Quality Assurance	Project Manager	Management
Validation Plan			X	X
Requirements Specification	X	X	X	X
Qualification Protocol	X		X	
Traceability Matrix	X		X	
Validation Summary Report		X	X	
Document Review		X		X
Timeline Creation and Monitoring			X	

Key Aspects for LSC Validation

- **Change Control:** Prior to executing the Qualification Protocol, the system was placed under change control. Any changes to the system thereafter are validated and documented.

  The configuration tested and documented during the system qualification serves as the reference point at which the system is known to work properly. Therefore, when changes are made to this configuration, only incremental testing is necessary to assess the impact of the change to the system and the performance of any new functionality.
- **Electronic Data:** Because LSC assays produce unusually large amounts of data (>1 GB per assay), unique measures were taken to backup and archive experimental data. Data is transferred from the computer's local hard drive to a dedicated file server via a controlled/validated process. The server is periodically backed up to DVD. At the conclusion of a study, the data is removed from the server and the DVDs are archived per GLP requirements.

Table 2. Components and Deliverables

Task	Purpose	Notes and Description	Examples
Validation Plan	Overall validation strategy which defines the system, the data flow, and the deliverables that will comprise the validation package.	"System" was defined as the cytometer, computer, software, file servers, archive engine, and any other components used to acquire, store and report cytometric data. Assigned roles and deliverables for the validation project (see Table 1), and how test failures and deviations were to be handled.	Here, we trace a successfully tested system requirement through the validation process.
Requirements Specification (1)	Based on intended use of the instrument and federal regulatory codes, this document defines requirements for the configuration, performance, security and maintenance for the system.	Included LSC functionality, data management (acquisition, storage, security), analyst training, environmental (room/power) specifications, hardware, software, GLP, and 21 CFR part 11 requirements.	
Qualification Protocol	Written test cases were designed to challenge each requirement defined in the Requirements Specification	Step-by-step instructions and expected results provide documented evidence that the system meets each requirement. Vendor qualification protocols are included as attachments.	
Requirements Traceability Matrix (2)	Traces each requirement from the Requirements Specification to the corresponding test step(s) in the Qualification Protocol, vendor qualification protocol, or SOP(s).	Essential for auditing the validation package. Document was included as part of the Validation Summary Report and was not finalized until after Qualification testing was complete.	
Execute Qualification Protocol (3)	Establishes and documents the configuration of the system. A vendor Installation Qualification was performed as part of this step.	Defined software versions, hardware manufacturer/model of components and peripherals, actual environment readings, and SOPs with effective dates	
	Documents tested results of system functionality as compared with expected outcomes and requirements defined in Requirements Specification.	Tested LSC functions (e.g. region imaging, statistics, sample loading), user access control, data acquisition, storage, archival, and reporting. Failed tests due to user error were repeated. Failed tests due to system limitations were addressed by implementing additional procedural controls (SOP) governing regulated use of the cytometer	
Validation Summary Report	Summarizes the testing that was performed and deliverables that were generated during the course of the validation.	Described any test failures and/or deviations from the validation plan or test protocols that may have occurred during execution, how they were addressed and their impact on the validation. Includes Requirements Traceability Matrix.	

Here, we trace an unsuccessfully tested system requirement through the validation process.

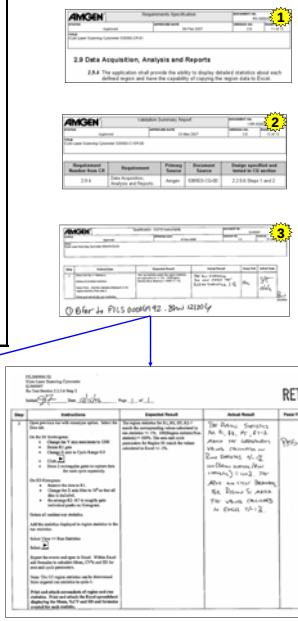
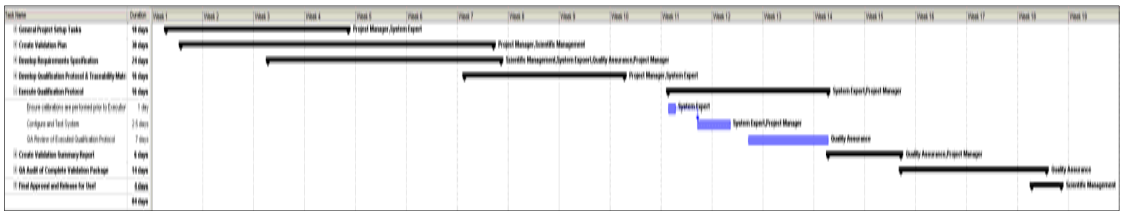


Table 3. Timeline (Test case development ~ 6 weeks; Documentation, reviews and approvals ~ 12 weeks)



Summary

This validated LSC system has been successfully implemented in support of a GLP study, which included several internal compliance audits. The ability to integrate a validated imaging cytometer into a regulated study provides assurance that experimental data is objective, traceable, and of the highest quality before submission to regulatory agencies.

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