A Review of 21 CFR Part 11 Compliant Support Features in Software Solutions for Life Science Applications

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INTRODUCTION

There is widespread agreement that the benefits of electronic record keeping and signatures are significant. The elimination of traditional paper records can increase the speed of information exchange and searching, reduce storage space costs, increase data integration, improve product quality, and reduce vulnerability of signature fraud and report misfiling.

Effective in August, 1997, 21 CFR Part 11 is a result of the efforts of the US Food and Drug Administration (FDA) and members of the pharmaceutical industry to establish a uniform and enforceable standard by which the FDA will consider electronic records equivalent to paper records and electronic signatures equivalent to traditional handwritten signatures. (http://www.fda.gov/ora/compliance_ref/part11/frs/background/11cfr-fr.htm)

This poster is a summary and review of a broad line of software products, provided by Applied Biosystems and Applied Biosystems/MDS Sciex, that support 21 CFR Part 11 compliance for several applications in the life science industry. A summary of features is provided along with a short review of each product based on customer feedback gathered during support activities and customer audits.

The products evaluated here include (1) SQL*LIMS™ software, a laboratory information management system (LIMS) for QA/QC manufacturing, (2) Life Science LIMS software, data collection and analysis software for the operation of genetic analysis and sequence detection systems, and downstream data analysis software used in genomics, (3) Analyst® software for the operation of the API line of triple quadrupole and Q Trap™ mass spectrometers used in proteomics, and (4) Procise® PC software used for the operation of protein sequencing instruments used in proteomics.

MATERIALS AND METHODS

This poster was developed based on SQL*LIMS™ software v4.1, 3730 and 3730xl Data Collection Software v2.0, 3100 and 3100-*Avant* Data Collection Software v2.0, GeneMapper™ Software v3.5, Sequencing Analysis software v5.1, SeqScape® software v2.1, MicroSeq®ID software v1.0, Sequence Detection software v2.2, RQ Manager software v1.1, SNP Manager software v1.1, Analyst® 1.2 software, and Procise® PC software v2.0.

DISCUSSION

Table 1 summarizes the key software features in support of 21 CFR Part 11 requirements. Future updates and/or releases of several of the software applications may include features addressing requirements of 21 CFR Part 11 that are not in the current version of the software.

Addressing 21 CFR Part 11 Requirements in SQL*LIMS Software for QA/QC Manufacturing

SQL*LIMS™ Software. With 20+ years experience in laboratory management systems, Applied Biosystems has built this LIMS system to fully support 21 CFR Part 11 compliance. The system is fully validated and allows controlled access to functions and data. Expanding on the basic Oracle® security model, this LIMS manages centralized user privileges and role-based control of access based on definable business rules and user attributes. (See Figure 1.)

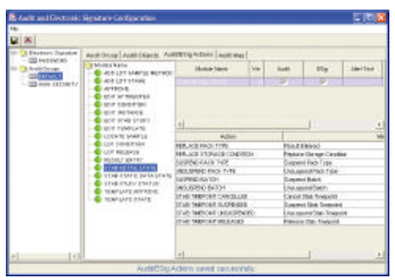
Addressing the requirement for audit trails for access, maintenance and report generation with signature-record linking and signature manifestations, the software includes a comprehensive, independently generated, timestamped audit trail that tracks all record modification, creation, or deletion activity for events that are configured to be auditable. The system provides data reporting and electronic signature history and audit trails in a variety of formats.

To satisfy electronic signature components and controls requirements, the software requires a unique username and a password for electronic signature and allows for periodic checks on identification and password issuance.

Table 1. Summary of 21 CFR Part 11 key requirements for each software type.

	Key features supporting 21 CFR Part 11						
	Electronic Records				Electronic Signatures		
Software Type	Limiting system access to authorized individuals - 11.10 (d)	Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions - 11.10 (e)	Use of authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system, alter a record, or perform the operation at hand - 11.10 (g)	Signed electronic records shall contain information associated with the signing - 11.50 (a)	Signature/record linking. Electronic signatures and handwritten signatures shall be linked to their respective electronic records - 11.70	Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else - 11.100	Electronic signature components and controls - 11.200
LIMS - Laboratory Information Management Systems							
SQL*LIMS v4.1 software	√	√	√	√	√	√	√
Life Science LIMS software	√	√	√	√	√	√	√
Software for genomics							
For data collection and analysis software for Genetic Analysis Systems. (* Features will be added in future revisions.)							
3730 and 3730xl Data Collection v2.0 software	√	√	√	√	— *	—	—
3100 and 3100-*Avant* Data Collection v2.0 software	√	√	√	√	—	—	—
GeneMapper software v3.5	√	√	√	√	—	—	—
Sequencing Analysis v5.1 SeqScape Software v2.1 MicroseqID software v1.0	√	√	√	√	—	—	—
For data collection and analysis software for sequence detection systems							
Sequence Detection v2.2 RQ Manager v1.1 software SNP Manager v1.1 software	√	√	√	√	√	√	√
Software for proteomics							
For mass spectometry							
Analyst v4.1 software	√	√	√	√	√	√	√
For protein sequencing							
Procise PC v2.0 software	√	√	√	√	√	√	√

Figure 1. SQL*LIMS Software – audit and electronic signature configuration view.



Addressing 21 CFR Part 11 Requirements in Software for Genomics

Life Science LIMS software. This software includes all key features mentioned above for the SQL*LIMS system and is designed for discovery applications including gene expression, genotyping, DNA sequencing, and forensics.

Data Collection Software for genetic analysis systems - Applied Biosystems 3730 and 3730xl DNA Analyzers, ABI PRISM® 3100 and 3100-Avant Genetic Analyzers. All the genetic data collection software (3730 and 3730xl Data Collection Software v2.0, 3100 and 3100-*Avant* Data Collection Software v2.0) includes features that limit access to authorized individuals through both a separate login using both username and password. An audit trail of changes is recorded for all users in which reasons for change (free form text only) and old and new values (short strings) are recorded. (See Figure 2.)

Data analysis software for genetic analysis systems. All genetic analysis software (GeneMapper software v3.5, Sequencing Analysis software v5.1, SeqScape software v2.1, and MicroSeq®ID software v1.0) has username and password lockout after an invalid login, and password expiration. In addition, you can specify or pre-configure multiple levels of users, record an audit trail of changes for all users, and generate reports.

Sequence Detection Systems software. Real-time PCR enterprise client software (Sequence Detection software v2.2, RQ Manager software v1.1, and SNP Manager software v1.1) will include many utilities for managing user access and for maintaining the integrity of the sequence detection system, real-time PCR enterprise database. Features such as user access control, audit mapping, and electronic signature enable the user to be 21 CFR Part 11 compliant.

Changes to data in the database will be tracked, and the access to features and functions will be limited. The application will also be tailored to support the regulatory requirements of a specific laboratory by designating which elements of the data are to be audited.

The creation, deletion, and transfer of the data stored by the software can be regulated. The administrator user group will be able to select an electronic signature method for the database, configure the database action groups, and view the history of the electronic signature events.

Addressing 21 CFR Part 11 Requirements in Software for Proteomics

Life Science LIMS software. This software includes all key features mentioned above for the SQL*LIMS system and is designed for discovery applications including proteomics.

Analyst® software. This software is used for the operation of the Applied Biosystems/MDS Sciex API line of triple quadrupole and Q Trap™ mass spectrometers. The software offers a separate login using both username and password. Customizable security allows individuals to be assigned a user type, with specified access to program modules and functions. Analyst provides a secure lab environment by allowing you to close the program and log out of the operating system during acquisition, as well as a configurable screen lock and logout timer for long sessions.

Figure 2. Data Collection Software v2.0 – access control and audit trail features.

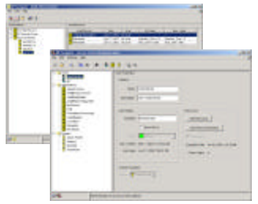
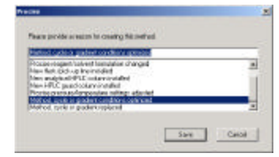


Figure 3. Procise PC Software – reason for change view.



Data files contain a complete record of all acquisition parameters, operator, timestamps, etc., and may be stored with a checksum, to allow automatic validation of the file integrity at a later date. Audit trails track tuning, instrument service, method creation or modification, acquisition, and the generation of results. The searchable audit records are archived with project information. Electronic signatures are recorded in the audit trail for predefined events. For specific audited events, the user is prompted to supply a valid reason and password.

Procise® PC software v2.0. This software is used for the operation of the Applied Biosystems Procise® family of protein sequencing systems. To satisfy the requirements for electronic records, this software offers a user management function that allows an administrator to set user ID, access levels and initial password, and only logged in users have access to the software. The event records all user interactions with users full name, time and date stamp. Further, creating, editing or deleting records requires a user to have editing or administrative rights, and requires submission of user ID, password and reason for the change in order for the change to be executed. The SequencePro™ Software data file contains the raw data from the sample analysis as well as a copy of the Procise software Event Log detailing all user interactions pertinent to that sample as well as a listing of the manufacturing lots of the reagents used for sample analysis. (See Figure 3.)

CONCLUSIONS

- The software products evaluated here will help meet the needs of customers who require the integration of information and instruments across a number of applications, and require support for 21 CFR Part 11 compliance.
- The application of these Applied Biosystems software products will assist users to meet Electronic Signatures for the generation of electronic records, with the exception of the Data analysis software for genetic analysis systems (GeneMapper software v3.5, Sequencing Analysis software v5.1, SeqScape software v2.1, and MicroSeq ID software v1.0), which only address the requirements for electronic records.
- Both laboratory information management systems, SQL*LIMS software and Life Science LIMS software, offer a complete feature set to support 21 CFR Part 11 requirements. Customers, who have been using the software successfully for over 15 years, report to the FDA that they are compliant with the rule based on the current feature set.