

# Implementing Electronic Signature Requirements In An Existing LC-MS/MS Data Processing & Reporting System

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## Introduction

FDA has recently published guidance<sup>1,2</sup> that address issues pertaining to computerized systems used to create, modify, maintain, archive, retrieve, or transmit clinical data intended for submission to FDA and provide Guidance and criteria under which FDA will consider electronic records equivalent to paper records and electronic signature equivalent to traditional handwritten signature.

In this poster, we describe our approach to implementing encrypted electronic signatures, electronic audit trails and enhanced system security controls procedures into ALIS98/2000<sup>TM</sup>, an LCMS report writer described previously<sup>3-6</sup> towards satisfying FDA requirements. Much of the design considerations were based on presentations and articles published in the literature and FDA's publications<sup>7,8</sup>.

## 1 Electronic Signatures & Records - Requirements

To be acceptable the data should meet certain fundamental elements of quality whether collected or recorded electronically or on paper. Data should be attributable, original, accurate, contemporaneous, and legible. For example, attributable data can be traced to individuals responsible for observing and recording the data. In an automated system, *attributability could be achieved by a computer system designed to identify individuals responsible for any input.*

The design of a computerized system should ensure that all applicable regulatory requirements for record keeping and record retention in clinical trials are met with the same degree of confidence as is provided with paper systems.

**Electronic Signature** - means a computer data compilation of any symbol or series of symbols, executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature.

**Electronic Record** - means any combination of text, graphics, data, audio, pictorial, or any other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system.

**Computerized System** - means, for the purpose of this guidance, computer hardware, software, and associated documents (e.g., user manual) that create, modify, maintain, archive, retrieve, or transmit in digital form information related to the conduct of a clinical trial.

**Audit Trail** - means a secure, computer generated, time-stamped electronic record that allows reconstruction of the course of events relating to the creation, modification, and deletion of an electronic record.

**Direct Entry** - means recording data where an electronic record is the original capture of the data. Examples are the keying by an individual of original observations into the system, or automatic recording by the system.

**System Security** - Physical and logical security measures ensure that access to the computerized system and to the data is restricted to authorized personnel. Staff should be thoroughly aware of system security measures and the importance of limiting access to authorized personnel. SOPs should be in place for handling and storing the system to prevent unauthorized access. Controls should be in place to prevent, detect, and mitigate effects of computer viruses on study data and software.

**System Dependability & Controls** - System documentation should be readily available at the site. Such documentation should provide an overall description of computerized systems and the relationship of hardware, software, and physical environment.

Validation documentation describing what the software is intended to do and how it is intended to do it; a written test plan based on the design specification, including both structural and functional analysis; and test results and an evaluation of how these results demonstrate that the predetermined design specification has been met. Revalidation should be performed for all changes made to the software.

Change control written procedures should be in place to ensure that changes to the software and modifications are documented. Software Version Control - measures should be in place to ensure that versions of software used to generate, collect, maintain, and transmit data are the versions that are stated in the documentation.

Backup and Recovery of Electronic Records - procedures should be clearly outlined in the SOPs. Records should be backed up regularly in a way that would prevent a catastrophic loss and ensure the quality and integrity of the data. Backup records should be stored at a secure location specified in the SOPs. Storage is typically off-site or in a building separate from the original records.

**Training & Controls** - Each person who enters or processes data should have the education, training, and experience or any combination thereof necessary to perform the assigned functions. Training should be provided to individuals in the specific operations that they are to perform. Training should be conducted by qualified individuals on a continuing basis, as needed, to ensure familiarity with the computerized system. All employee education, training, and experience should be documented.

## 2 LC/MS Work Flow - Implementing Electronic Audit Trails & Electronic Signature

Following user log-in, access is restricted to selected ALIS98 screens based on job function and access privileges. ALIS98 database tables are password protected and can be accessed and modified only under ALIS98 software program only.

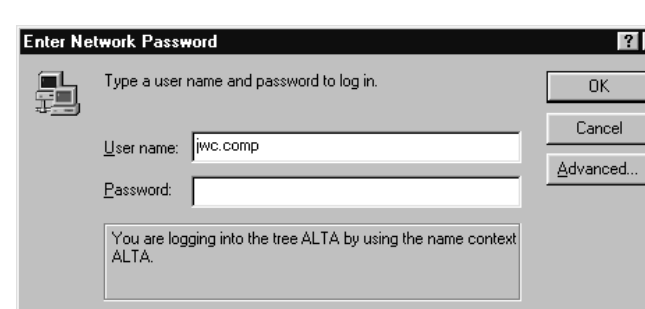
An electronic signature is created by the system automatically based on "User Full Name, User Password and Date and Time Stamp" for every transaction involving modification of existing data in sample log-in, sample preparation and analytical data review modules of ALIS98. The system also creates an electronic signature for data file acquired from the instrument data system based on the unique instrument file id, analyte sequence number and date and time the file was created.

All database transactions involving changes and modifications of existing data are logged to a password protected audit database and linked to the user making these changes via a unique electronic signature. The system incorporates a change control module that requires the users to enter reasons for making modifications to existing data, uploading existing data files or re-calculating existing data sets. All such transactions are logged to audit database.

Upon completion of a project / study, all raw instrument data files (time intensity data), all ALIS98 databases, query reports and analytical reports are preserved on a CD-ROM for archival purposes.

### SYSTEM ACCESS CONTROL

#### LAN (Novell) Access

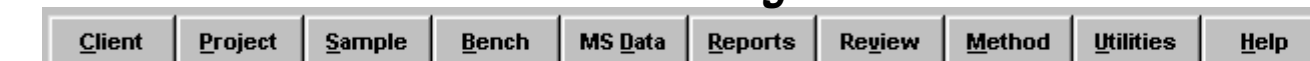


#### ALIS98 Log-In



- Sets User Screen Level Access Rights
- Creates Electronic Signature Using UserID and Password

#### ALIS98 Screen Level Access Rights

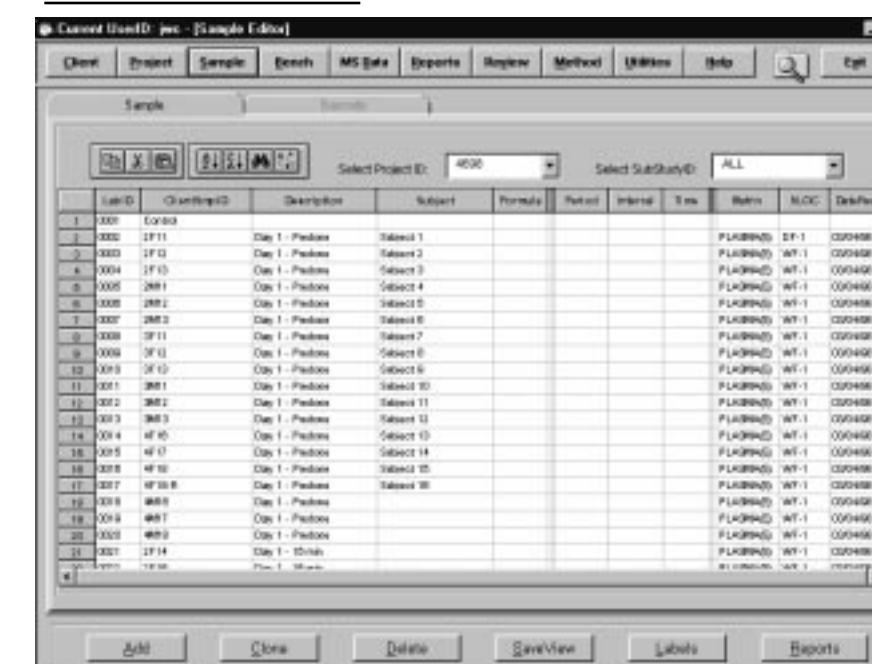


#### E-Signature = UserID + Encrypted Password + Date-Time

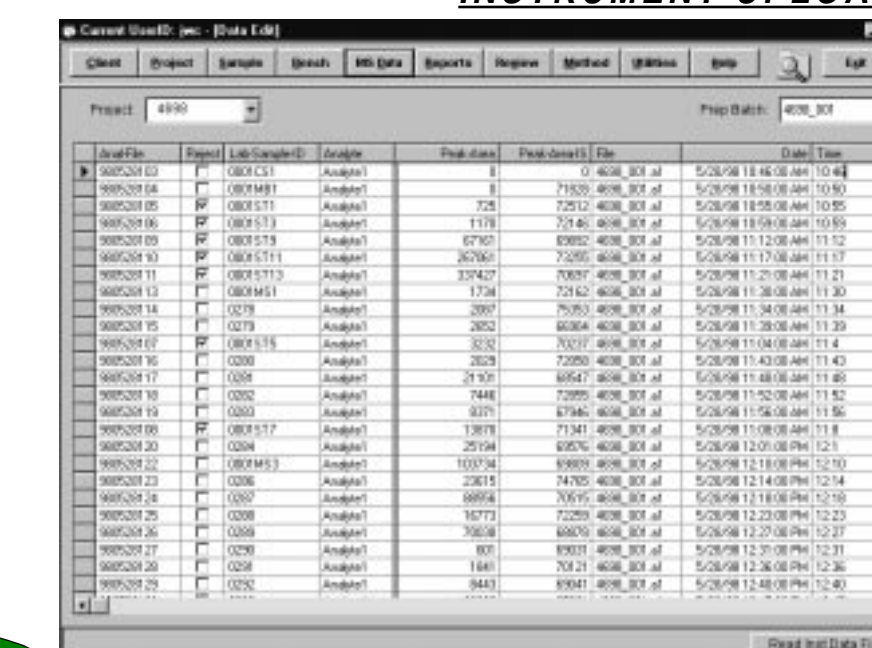
AuditID	Signature	Date	Reason
1	John W. Cornacchia-z0A-12/16/98 3:44:12 PM	12/16/98 3:44:12 PM	Sample Edit
2	John W. Cornacchia-z0A-12/16/98 9:06:56 AM	2/10/99 9:06:56 AM	Add PrepBat
3	John W. Cornacchia-z0A-12/16/98 9:07:23 AM	2/10/99 9:07:23 AM	Add PrepBat
4	John W. Cornacchia-z0A-12/16/98 9:11:13 AM	2/10/99 9:11:13 AM	PrepBat Edit
5	John W. Cornacchia-z0A-12/16/98 3:49:37 PM	3/22/99 3:49:37 PM	Add PrepBat

### ALIS98 AUDIT TRAIL

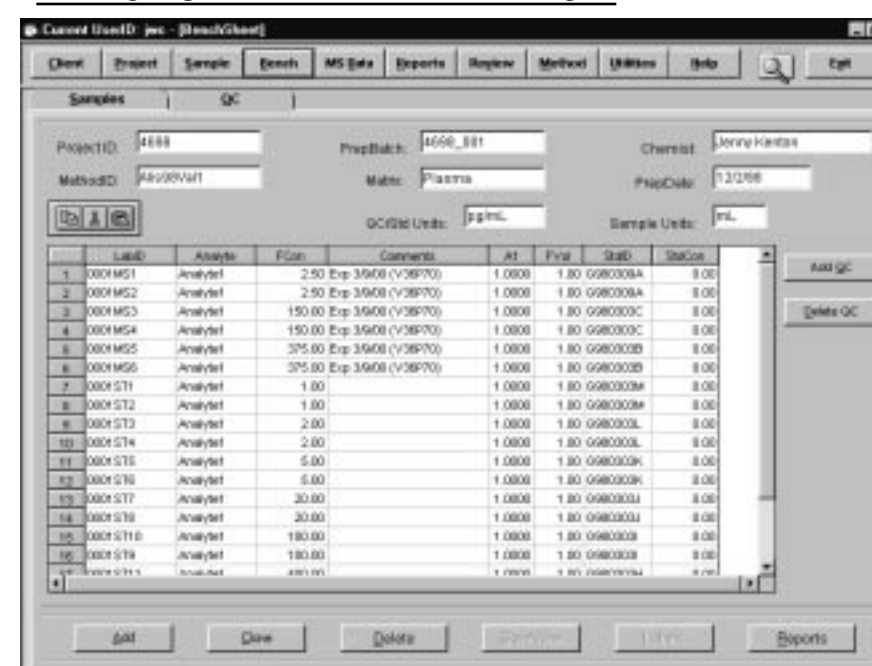
#### SAMPLE LOG-IN



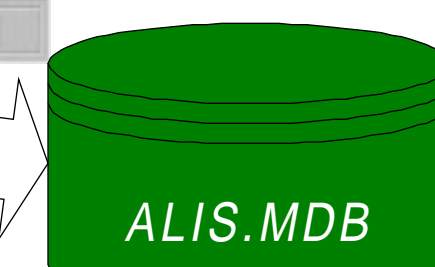
#### INSTRUMENT UPLOAD



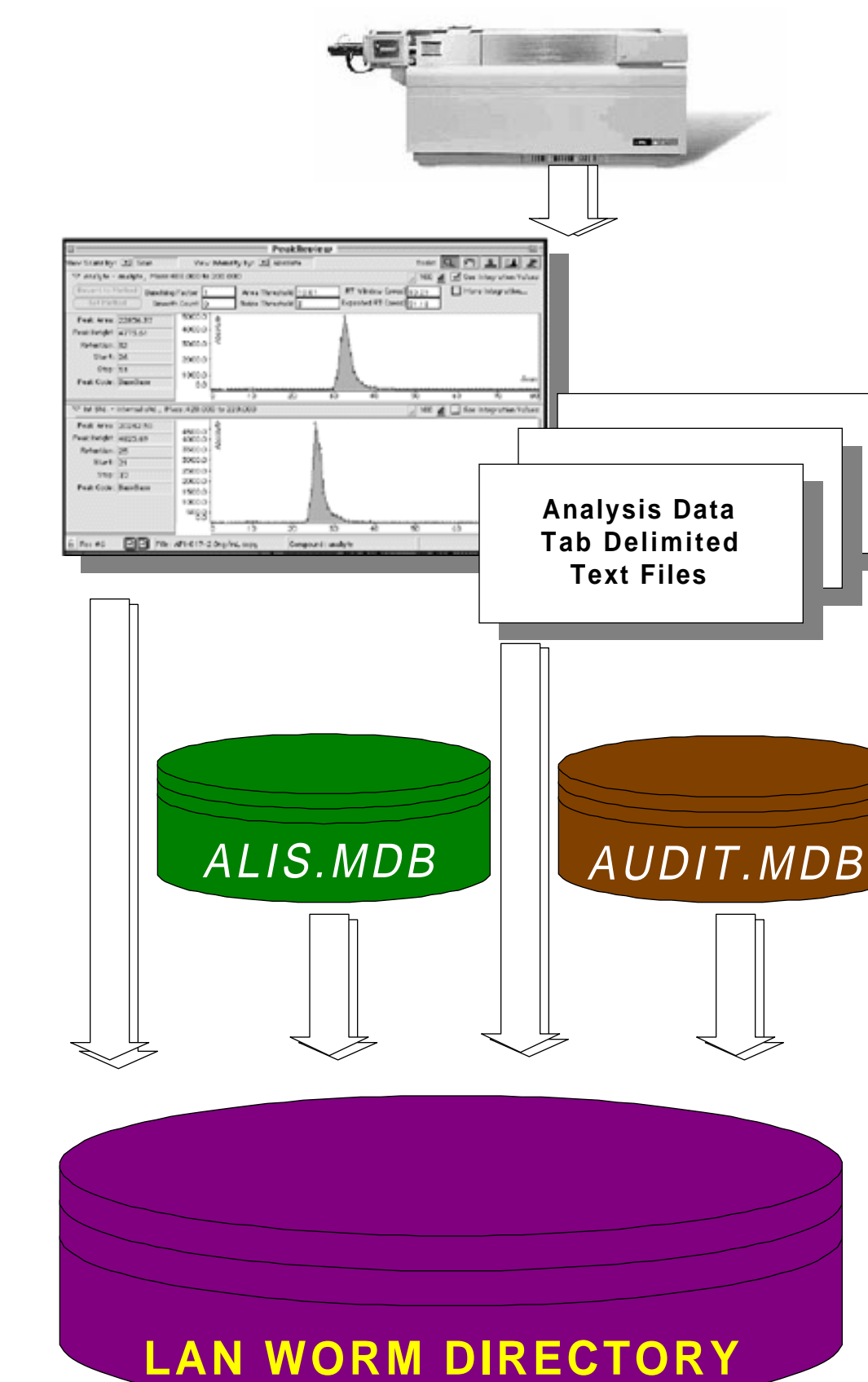
#### BENCHSHEET PREPARATION



#### DATA REVIEW



### ARCHIVING



## 3 Conclusion

In summary, we have described our approach to implementing and complying with the FDA's electronic signature and electronic record keeping requirements in a LC/MS laboratory specializing in analytical method development as well as high sample through-put. Future work will focus on the integration of emerging DVD technology and MS-Office 2000.

An electronic version of this poster and other references cited are available at: [http://www.ia-one.com/biochemistry/biochemical\\_publications.htm](http://www.ia-one.com/biochemistry/biochemical_publications.htm)

ALIS98 and ALIS2000 are trademarks of Innovative Automation.  
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