Comply with Data Integrity Regulations with Chromeleon CDS Software

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Introduction

Data integrity

Audit trails

Record management

Summary

Questions and answers
Introduction

- Regulatory milestones
Introduction

- Data integrity requirements
  - New guidelines in 2015 & 2016 from MHRA, CFDA and FDA
  - Covers authenticity and security of data
  - Clarifies role of data integrity in current good manufacturing practice (CGMP) for drugs
  - Contains current thinking on creation and handling of data in accordance with CGMP requirements

- Software needs to meet regulatory requirements
  - Includes requirements for 21 CFR Part 11 compliance
• In recent years, FDA and MHRA have increased focus on data integrity during CGMP inspections

• Observed CGMP violations involving data integrity during inspections

• Ensuring data integrity is important
  • Industry’s responsibility to ensure safety, efficacy, and quality of drugs
  • Regulatory responsibility to protect the public health

• How can Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) software help?
• What is “data integrity”?
  • Completeness, consistency, and accuracy of data

Attributable
Who performed an action and when?

Legible
Can you read the data file and written entries throughout the life cycle?

Contemporaneous
Documented at the time of the activity?

Original
Original record or a certified copy?

Accurate
No errors or editing without documented amendments?
Data Integrity

• What is “data”?
  • Any recorded information
    2 types:
    • **Static** - Fixed-data document such as paper record or electronic image
    • **Dynamic** - Record format that allows interaction between user and record content
      – E.g. chromatogram allowing user to change baseline or reprocess data so peaks may change size; user modifiable formulas or entries in spreadsheet

• What is “metadata”?
  • Metadata is data about data
    • Contextual information required to understand data
    • A data value is meaningless by itself without additional information
  • Metadata can describe a single piece of data, a data set or collection.
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What is an “audit trail”? 
• Secure, computer-generated, time-stamped electronic record that allows for reconstruction of events relating to creation, modification, or deletion of an electronic record.
• Electronic audit trails include those that track creation, modification, or deletion of data and those that track actions at the record or system level.
• CGMP-compliant record-keeping practices prevent data from being lost or obscured. Electronic record-keeping systems, which include audit trails, can fulfil these CGMP requirements.

Chronology of the “who, what, when, and why” of a record
• Is it acceptable to only save final results from reprocessed laboratory chromatography?
  • No. analytical methods should be capable and stable
  • For most lab analyses, reprocessing data should not be regularly needed
  • If chromatography is reprocessed, written procedures must be established and followed and each result retained for review
  • Must have complete data in lab records, which includes raw data, graphs, charts, and spectra from lab instruments

• Predicated rules show this refers to reprocessing of samples, not data.
  • Must keep all data (and metadata) relating to each analysis
  • Versioning helps track changes to objects
Chromeleon CDS provides industry-leading audit trails.

- Detailed audit trails for:
  - Chromeleon console and chromatography studio
  - Administration console, instrument configuration manager, data vault manager
  - Chromeleon CDS station

- Logs all user, instrument and system actions
  - E.g. user logon/logoff, instrument setup, sequence start/stop, data processing, admin changes, services startup/shutdown, etc.
Audit Trails in Chromeleon CDS

- Chromeleon CDS consolidated audit trail viewer
  - Combines all audit trails within organizational unit
  - Events are categorized for filtering and grouping
  - Entries contain significant detail
Audit Trails in Chromeleon CDS

• Instrument daily event audit trail for each injection
Modification history audit trail

- Displays complete change history of each object (versions)
- Can roll back (restore) a previous version
Audit Trails in Chromeleon CDS

- Version comparison tool

<table>
<thead>
<tr>
<th>Version</th>
<th>Date / Time</th>
<th>Operator</th>
<th>Client Computer</th>
</tr>
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<tbody>
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<td>SQuinn</td>
<td>LGER SQUINN</td>
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<tr>
<td>2</td>
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<table>
<thead>
<tr>
<th>Property Name</th>
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<tbody>
<tr>
<td>Version</td>
<td></td>
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</tr>
<tr>
<td>Change</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Addition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deletion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Change
- Addition
- Deletion

[Image of the version comparison tool interface with highlighted changes, additions, and deletions]
Audit Trails in Chromeleon CDS

- File section in injection list and folder view shows current version
Audit Trails in Chromeleon CDS

- Privileged actions
  - Require authorization for specified actions
  - Ensure users add appropriate comments for specified actions
  - Use standardized comments or free entry
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All data should be stored, controlled and archived correctly.

- When does electronic data become a CGMP record?
  - When generated to satisfy any CGMP requirement, all data becomes a CGMP record
  - Must document, or save, data at time of performance (contemporaneous)
    - E.g. chromatograms should be sent to long-term storage upon run completion
  - Not acceptable to record data on paper that will be discarded after data are transcribed to permanent laboratory notebook
  - Not acceptable to store data electronically in temporary memory, in manner that allows for manipulation, before creating permanent record
All data should be stored, controlled and archived correctly.

• How do regulatory bodies use the term “backup”?
  • A true copy of original data that is maintained securely throughout records retention period.
  • Backup file should contain data (with associated metadata) in original format or in format compatible with original format.

• Must not be confused with backup copies!
  • Created during normal computer use and temporarily maintained for disaster recovery (e.g. in case of a computer crash or other interruption)

• How does Chromeleon CDS help?
Immediate transfer to long-term storage

- Chromeleon CDS uses relational database
  - Microsoft® SQL® Server Express (2005 SP3, 2008 R2 SP2 & 2014 SP2)
  - Microsoft® SQL® Server (2008 R2, 2012 & 2014 SP2)
  - Oracle® Database 11g & 12c
  - Oracle® Database 12c on Red Hat® Enterprise Linux® 7

- Detect changes to raw files
  - Automatic detection of raw files being manipulated outside Chromeleon CDS
• Bi-directional instrument control for over 450 different modules from 17 different manufacturers including:
  • Thermo Scientific systems (LC, IC, GC, MS, Sample Prep)
  • Agilent (LC, GC)
  • Waters (LC)
  • Shimadzu (LC, GC)
  • Varian (LC, GC)
  • Perkin Elmer (LC, GC)
  • Gilson (LC)
  • CTC PAL (Sample Prep)

• Highest data transport security
  • Communication secured using latest standards
Electronic report
- Snapshot in time of sequence
- Any changes tracked
- Can be sent for review

Electronic signatures
- 3 Levels of signature: Submit, Review, Approve
- Applied to electronic report
- Complete sequence protected by checksums
- Controlled by privileges
Record Management – Data Control

The sequence is signed. Modifications to the sequence are not possible.
Record Management – Archive/Backup

- Chromeleon scheduler – Automatically archive/backup data using powerful injection queries
- Transfer to another data vault – Direct access with full metadata
- Export to cmbx or other format (e.g. PDF, GAML, XLS, etc.)
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• Data integrity and compliance go hand-in-hand
  • Subject to elevated scrutiny by regulatory bodies

• Chromeleon CDS meets all of your data integrity needs:
  • Ensures completeness, consistency, and accuracy of data
    • ALCOA+
  • Comprehensive audit trails
    • Who, what, when and why of data
  • Maintains record authenticity
    • Contemporaneous collection
    • Automated long-term data retention with easy accessibility
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Thank you for your attention!

Any questions 🎨

Do you have additional questions or do you want to talk to an expert from Thermo Fisher Scientific?

Please send an E-Mail to analyze.eu@thermofisher.com and we will get back to you.