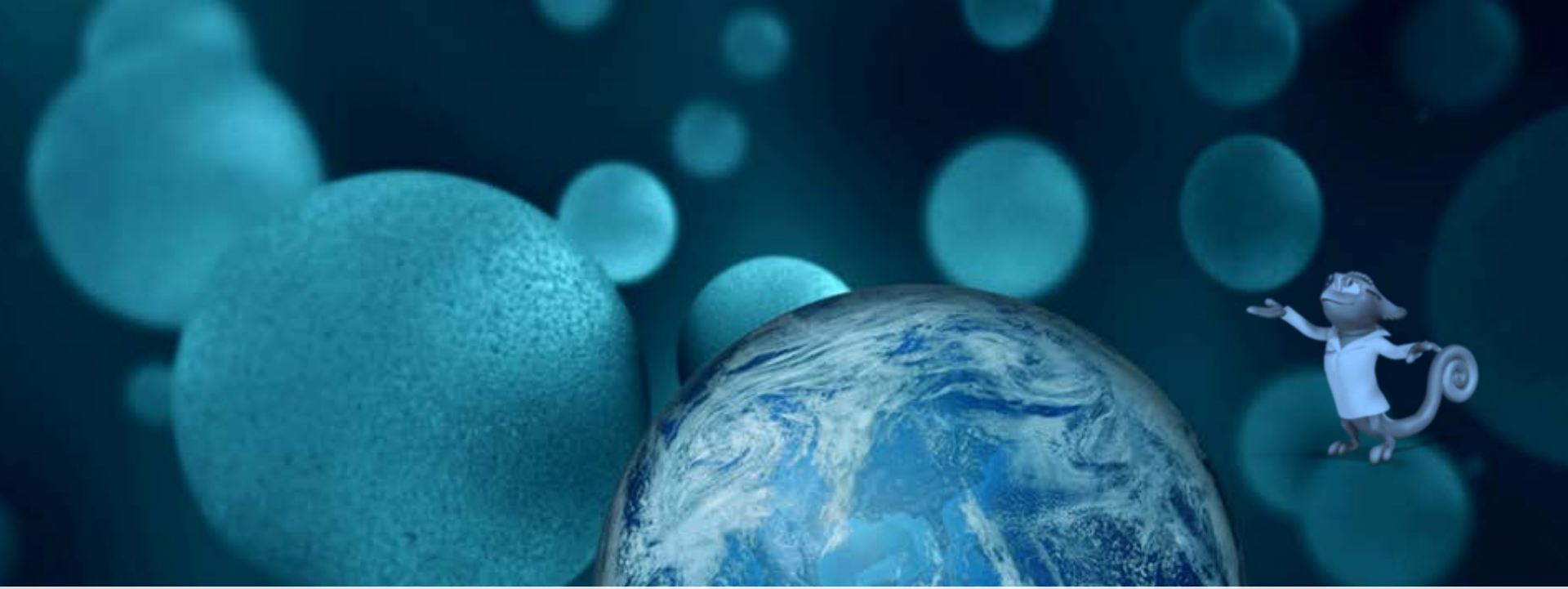

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Comply with Data Integrity Regulations with Chromeleon CDS Software

Anna Severoni
Sales Support Specialist for Chromatography
Thermo Fisher Scientific, Rodano (MI)

- Introduction
- Data integrity
- Audit trails
- Record management
- Summary
- Questions and anwers

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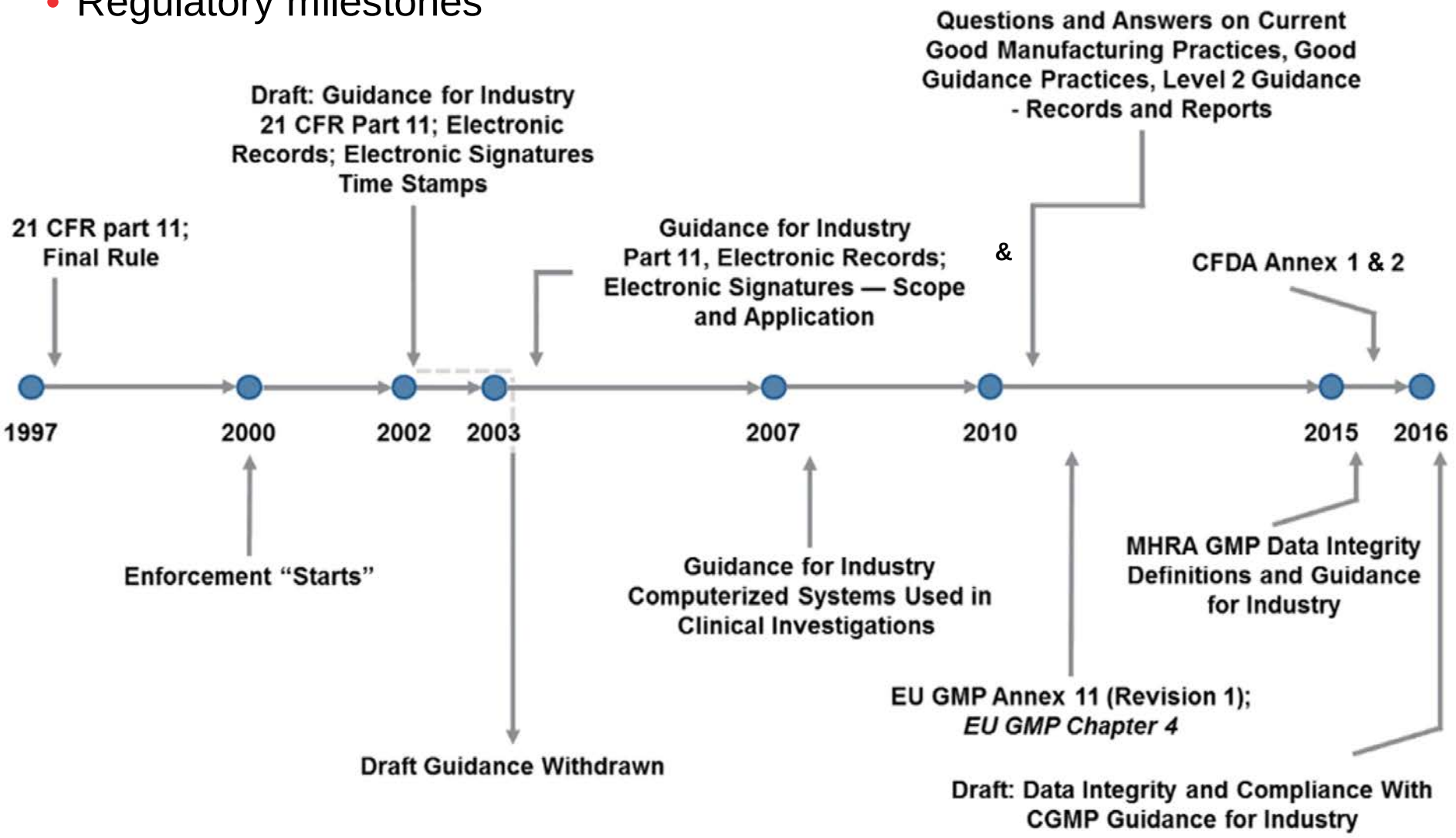
Introduction

- Regulatory milestones



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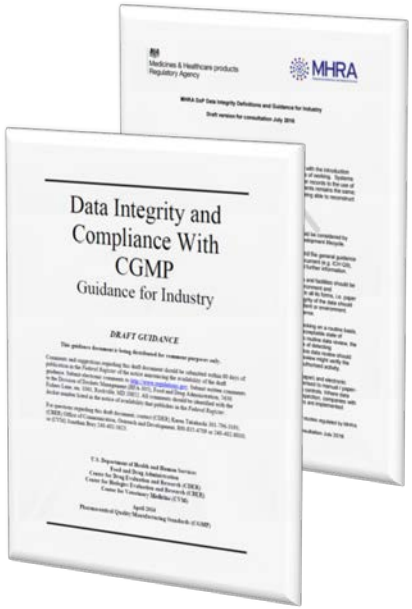
Introduction

- 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

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

ISPE Gamp

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ICH
harmonisation for better health

MHRA
Regulating Medicines and Medical Devices

CFDA China Food and Drug Administration

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Introduction

- 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?

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Data Integrity

- What is “data integrity”?
  - Completeness, consistency, and accuracy of data

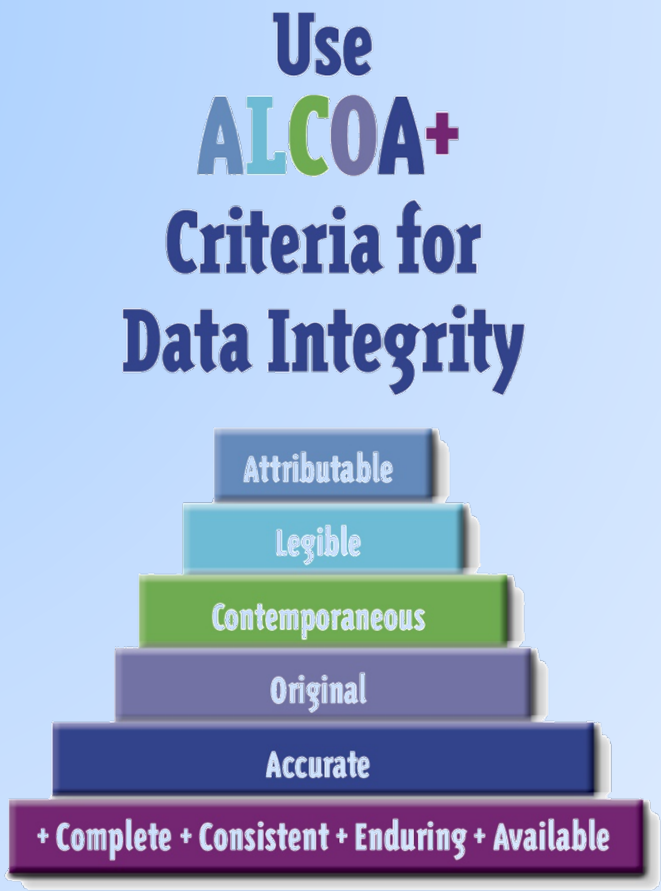
Attributable
Who performed an action and when?

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?



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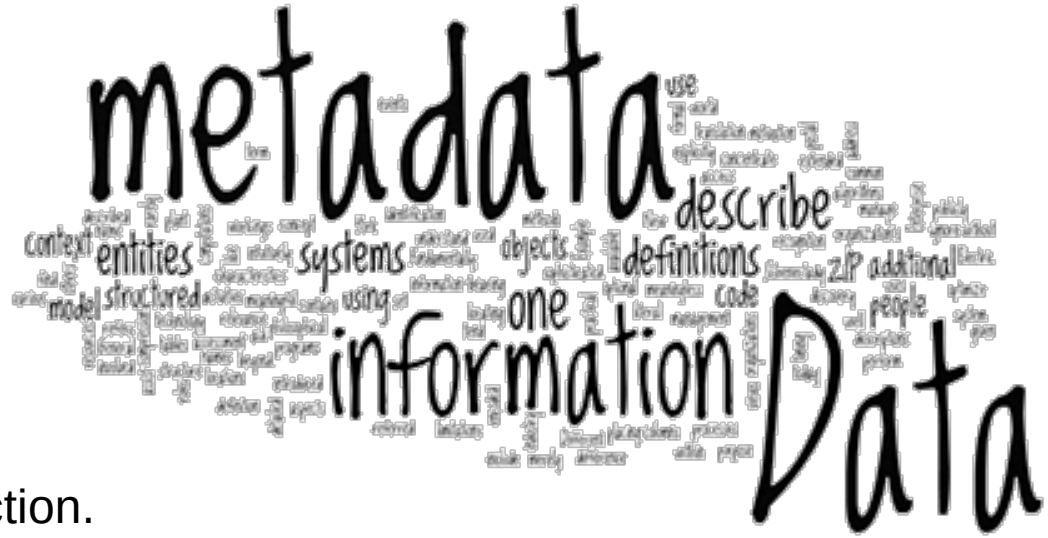
Data Integrity

- 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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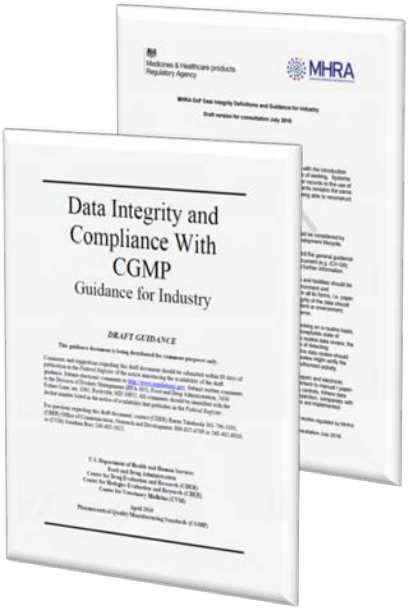
Audit Trails

- 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

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Audit Trails

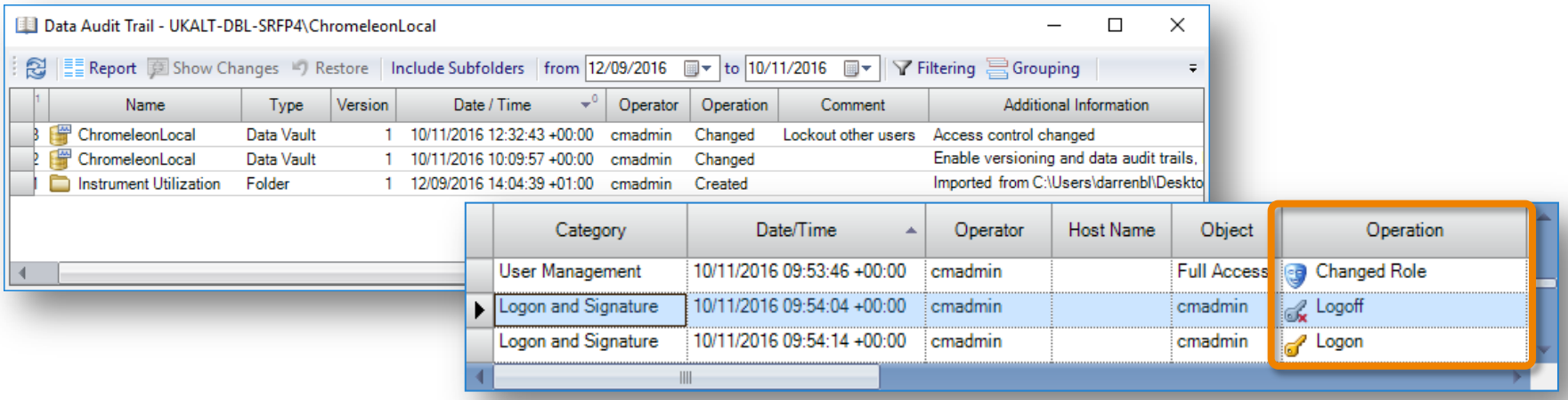
- Is it acceptable to only save final results from reprocessed laboratory chromatography?
  - No. analytical methods should be capable and stable
  - For most lab analyses, reprocessing data should not be regularly needed
  - If chromatography is reprocessed, written procedures must be established and 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

Audit Trails in Chromeleon CDS

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.



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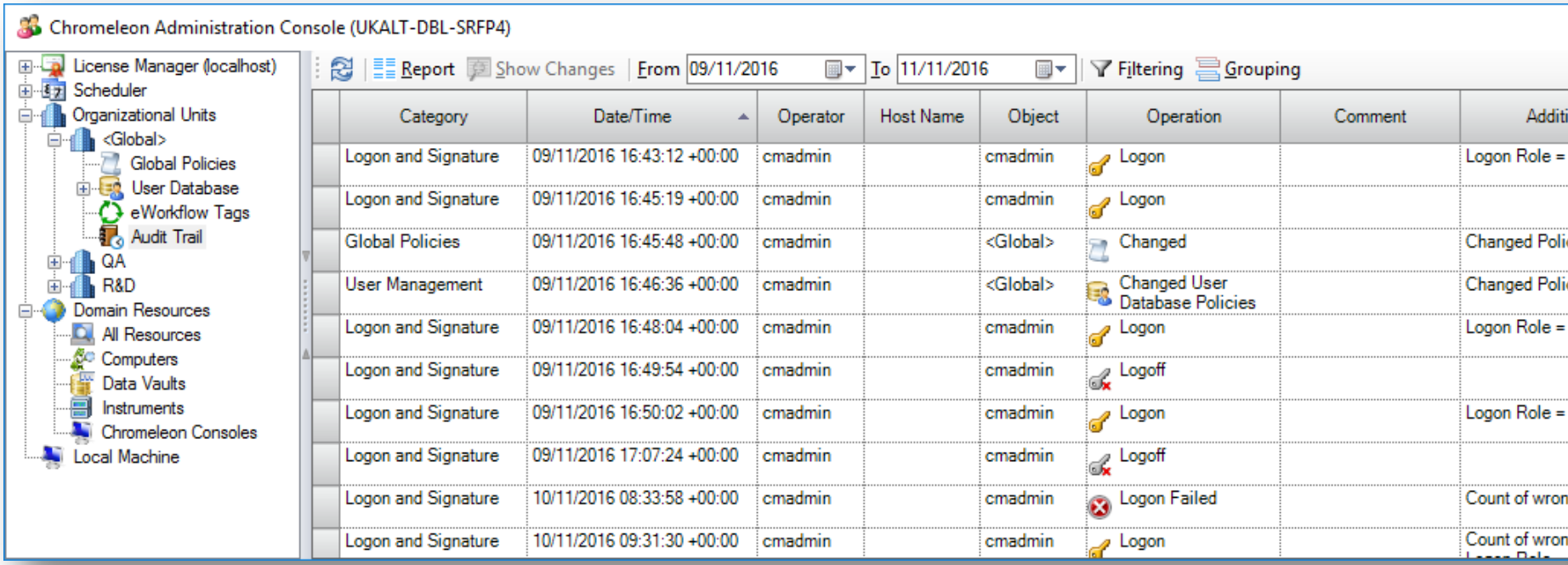
Audit Trails in Chromeleon CDS

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



Category	Date/Time	Operator	Host Name	Object	Operation	Comment	Additi
Logon and Signature	09/11/2016 16:43:12 +00:00	cmadmin		cmadmin	Logon		Logon Role =
Logon and Signature	09/11/2016 16:45:19 +00:00	cmadmin		cmadmin	Logon		
Global Policies	09/11/2016 16:45:48 +00:00	cmadmin		<Global>	Changed		Changed Poli
User Management	09/11/2016 16:46:36 +00:00	cmadmin		<Global>	Changed User Database Policies		Changed Poli
Logon and Signature	09/11/2016 16:48:04 +00:00	cmadmin		cmadmin	Logon		Logon Role =
Logon and Signature	09/11/2016 16:49:54 +00:00	cmadmin		cmadmin	Logoff		
Logon and Signature	09/11/2016 16:50:02 +00:00	cmadmin		cmadmin	Logon		Logon Role =
Logon and Signature	09/11/2016 17:07:24 +00:00	cmadmin		cmadmin	Logoff		
Logon and Signature	10/11/2016 08:33:58 +00:00	cmadmin		cmadmin	Logon Failed		Count of wron
Logon and Signature	10/11/2016 09:31:30 +00:00	cmadmin		cmadmin	Logon		Count of wron

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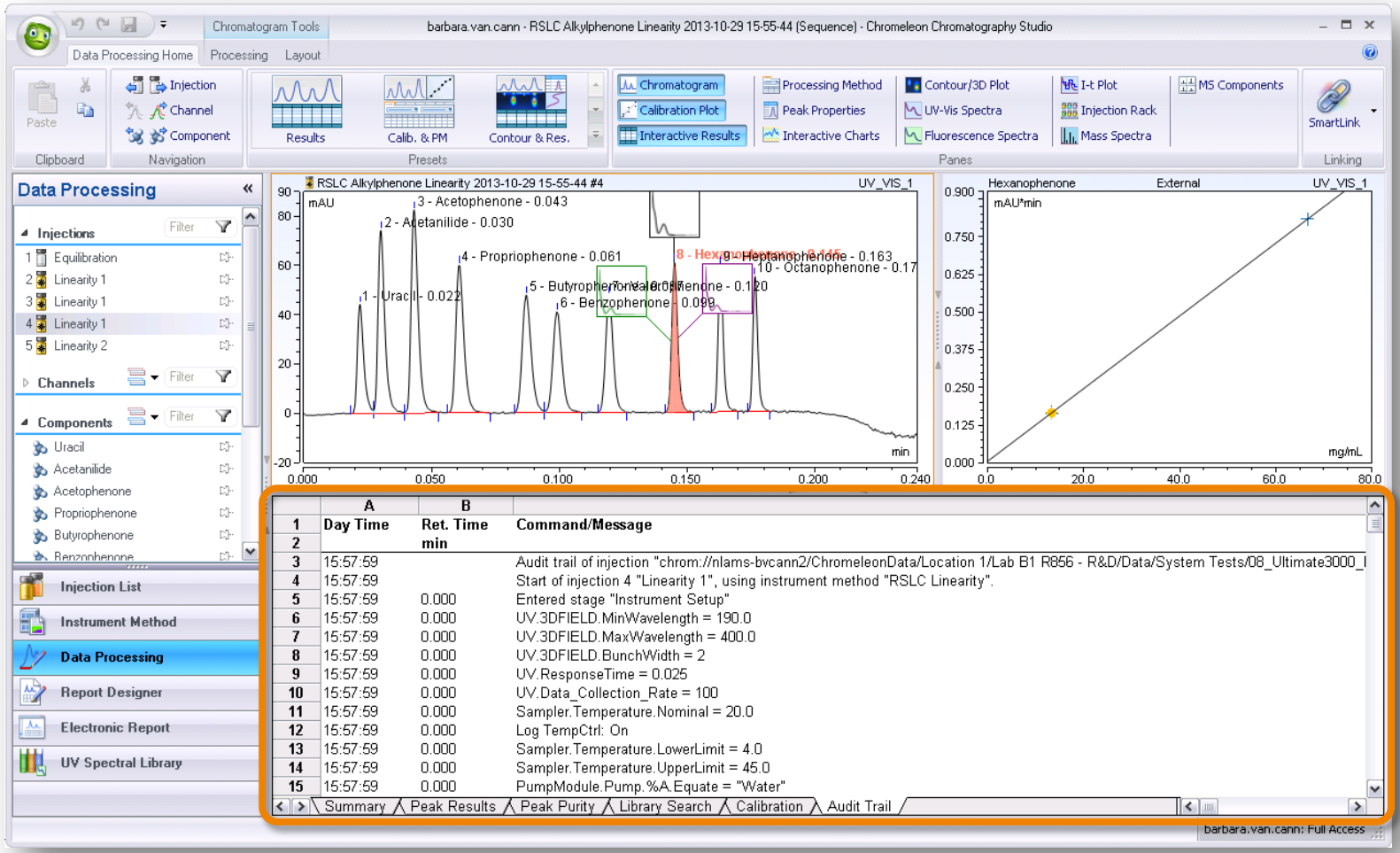
Audit Trails in Chromeleon CDS

- Instrument daily event audit trail for each injection



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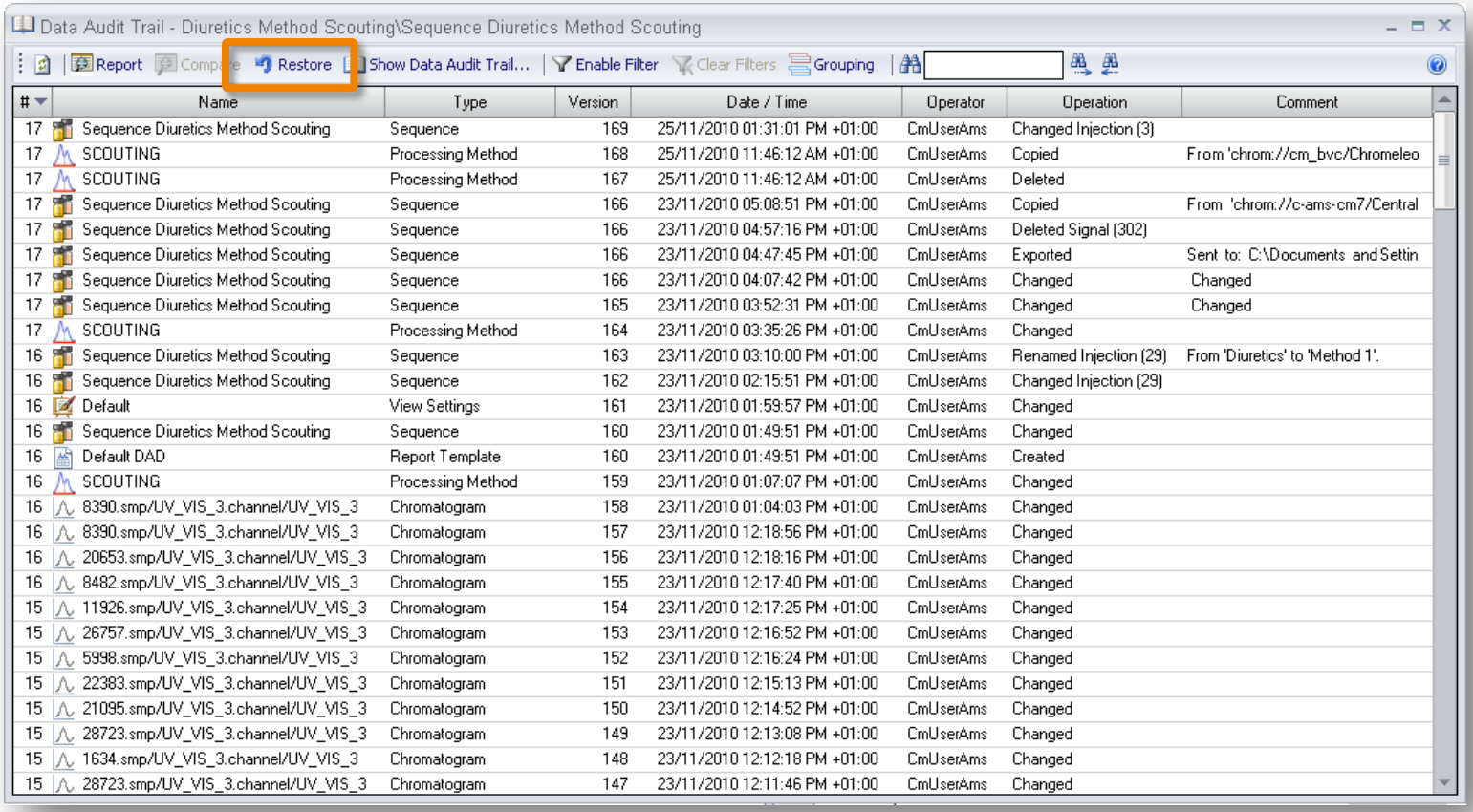
Audit Trails in Chromeleon CDS

- Modification history audit trail
  - Displays complete change history of each object (versions)
  - Can roll back (restore) a previous version



#	Name	Type	Version	Date / Time	Operator	Operation	Comment
17	Sequence Diuretics Method Scouting	Sequence	169	25/11/2010 01:31:01 PM +01:00	CmUserAms	Changed Injection (3)	
17	SCOUTING	Processing Method	168	25/11/2010 11:46:12 AM +01:00	CmUserAms	Copied	From 'chrom://cm_bvc/Chromeleo
17	SCOUTING	Processing Method	167	25/11/2010 11:46:12 AM +01:00	CmUserAms	Deleted	
17	Sequence Diuretics Method Scouting	Sequence	166	23/11/2010 05:08:51 PM +01:00	CmUserAms	Copied	From 'chrom://c-ams-cm7/Central
17	Sequence Diuretics Method Scouting	Sequence	166	23/11/2010 04:57:16 PM +01:00	CmUserAms	Deleted Signal (302)	
17	Sequence Diuretics Method Scouting	Sequence	166	23/11/2010 04:47:45 PM +01:00	CmUserAms	Exported	Sent to: C:\Documents and Settin
17	Sequence Diuretics Method Scouting	Sequence	166	23/11/2010 04:07:42 PM +01:00	CmUserAms	Changed	Changed
17	Sequence Diuretics Method Scouting	Sequence	165	23/11/2010 03:52:31 PM +01:00	CmUserAms	Changed	Changed
17	SCOUTING	Processing Method	164	23/11/2010 03:35:26 PM +01:00	CmUserAms	Changed	
16	Sequence Diuretics Method Scouting	Sequence	163	23/11/2010 03:10:00 PM +01:00	CmUserAms	Renamed Injection (29)	From 'Diuretics' to 'Method 1'.
16	Sequence Diuretics Method Scouting	Sequence	162	23/11/2010 02:15:51 PM +01:00	CmUserAms	Changed Injection (29)	
16	Default	View Settings	161	23/11/2010 01:59:57 PM +01:00	CmUserAms	Changed	
16	Sequence Diuretics Method Scouting	Sequence	160	23/11/2010 01:49:51 PM +01:00	CmUserAms	Changed	
16	Default DAD	Report Template	160	23/11/2010 01:49:51 PM +01:00	CmUserAms	Created	
16	SCOUTING	Processing Method	159	23/11/2010 01:07:07 PM +01:00	CmUserAms	Changed	
16	8390.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	158	23/11/2010 01:04:03 PM +01:00	CmUserAms	Changed	
16	8390.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	157	23/11/2010 12:18:56 PM +01:00	CmUserAms	Changed	
16	20653.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	156	23/11/2010 12:18:16 PM +01:00	CmUserAms	Changed	
16	8482.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	155	23/11/2010 12:17:40 PM +01:00	CmUserAms	Changed	
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15	26757.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	153	23/11/2010 12:16:52 PM +01:00	CmUserAms	Changed	
15	5998.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	152	23/11/2010 12:16:24 PM +01:00	CmUserAms	Changed	
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15	1634.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	148	23/11/2010 12:12:18 PM +01:00	CmUserAms	Changed	
15	28723.smp/UV_VIS_3.channel/UV_VIS_3	Chromatogram	147	23/11/2010 12:11:46 PM +01:00	CmUserAms	Changed	

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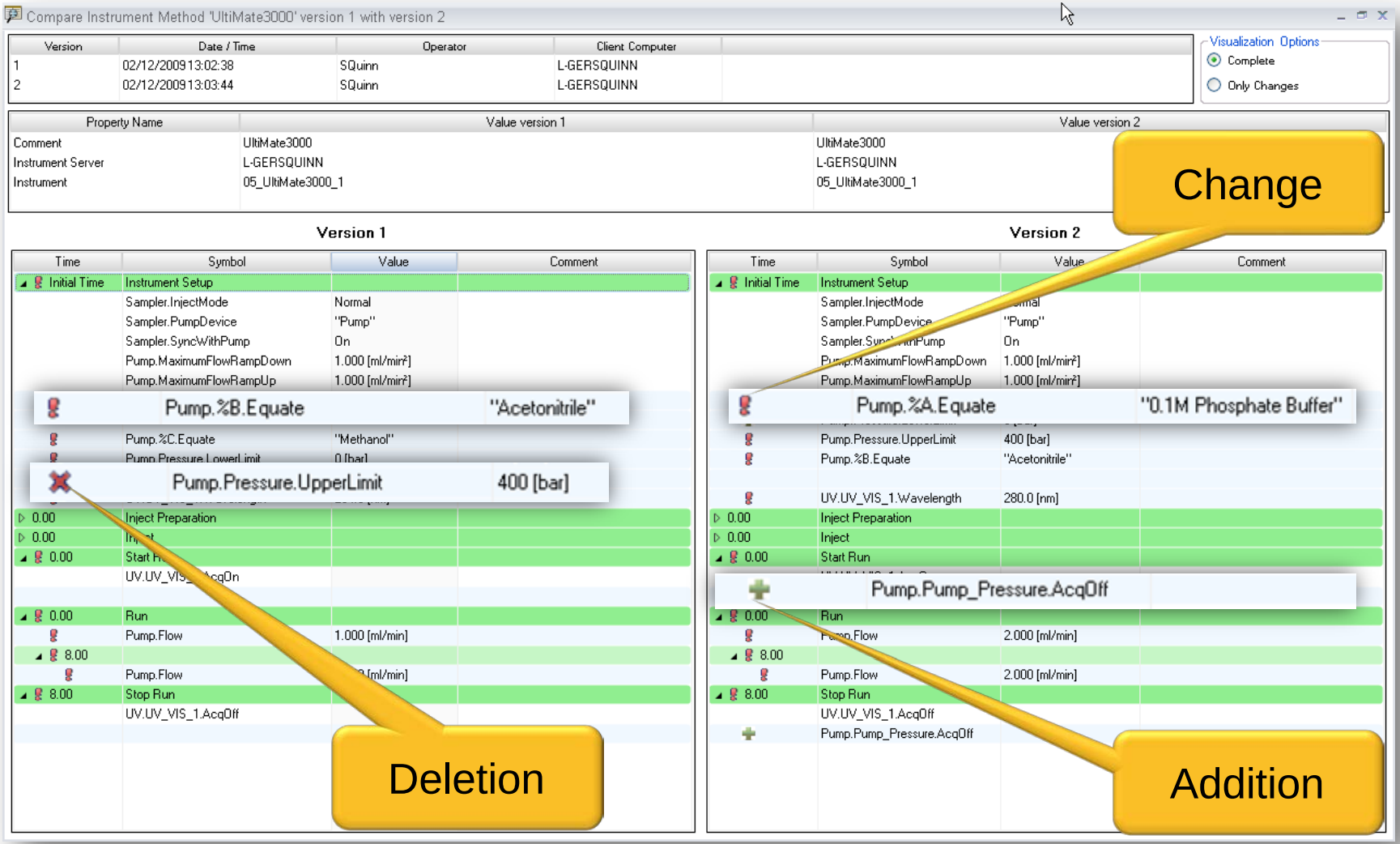
Audit Trails in Chromeleon CDS

- Version comparison tool



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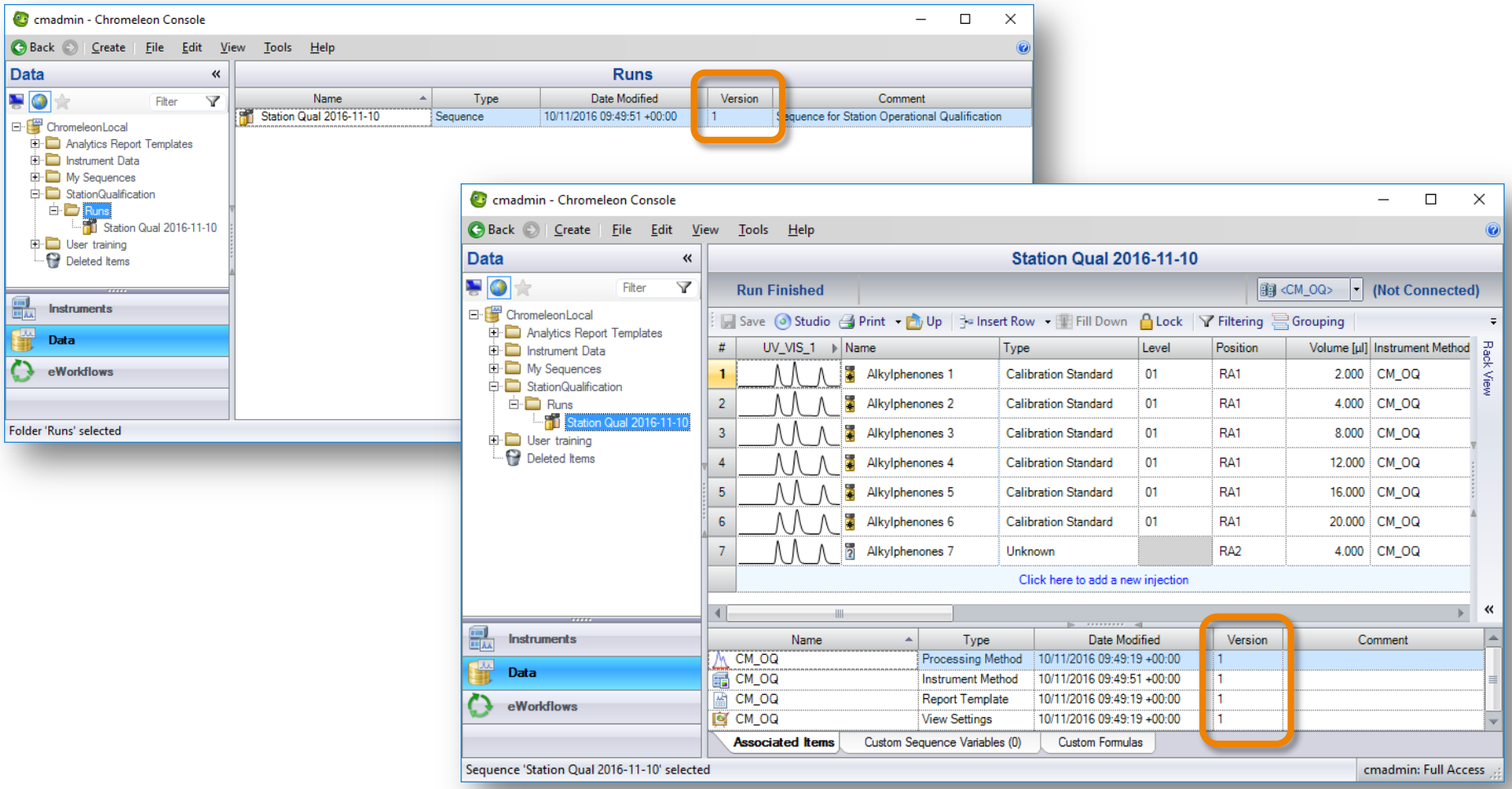
Audit Trails in Chromeleon CDS

- File section in injection list and folder view shows current version



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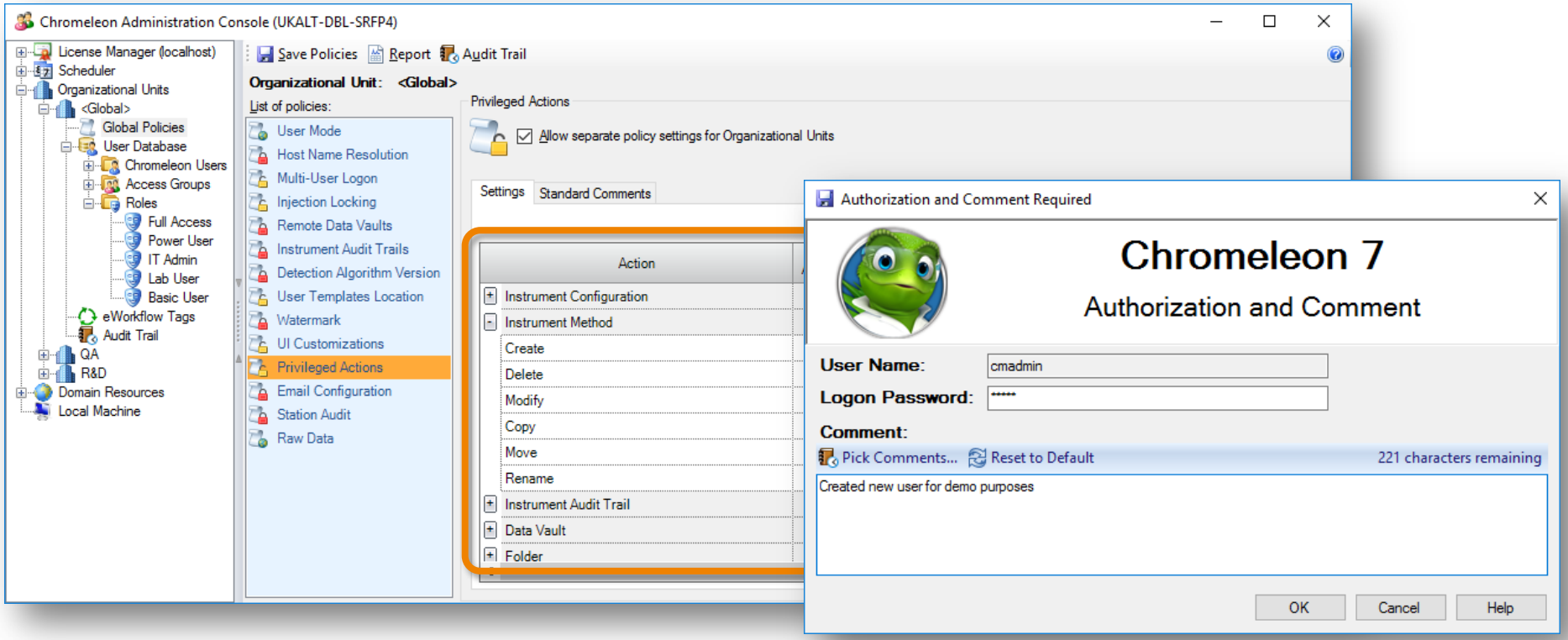
Audit Trails in Chromeleon CDS

- 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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Record Management

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

Record Management

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?

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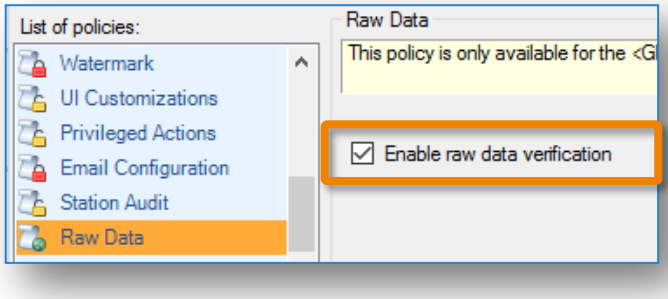
Record Management – Data Storage

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



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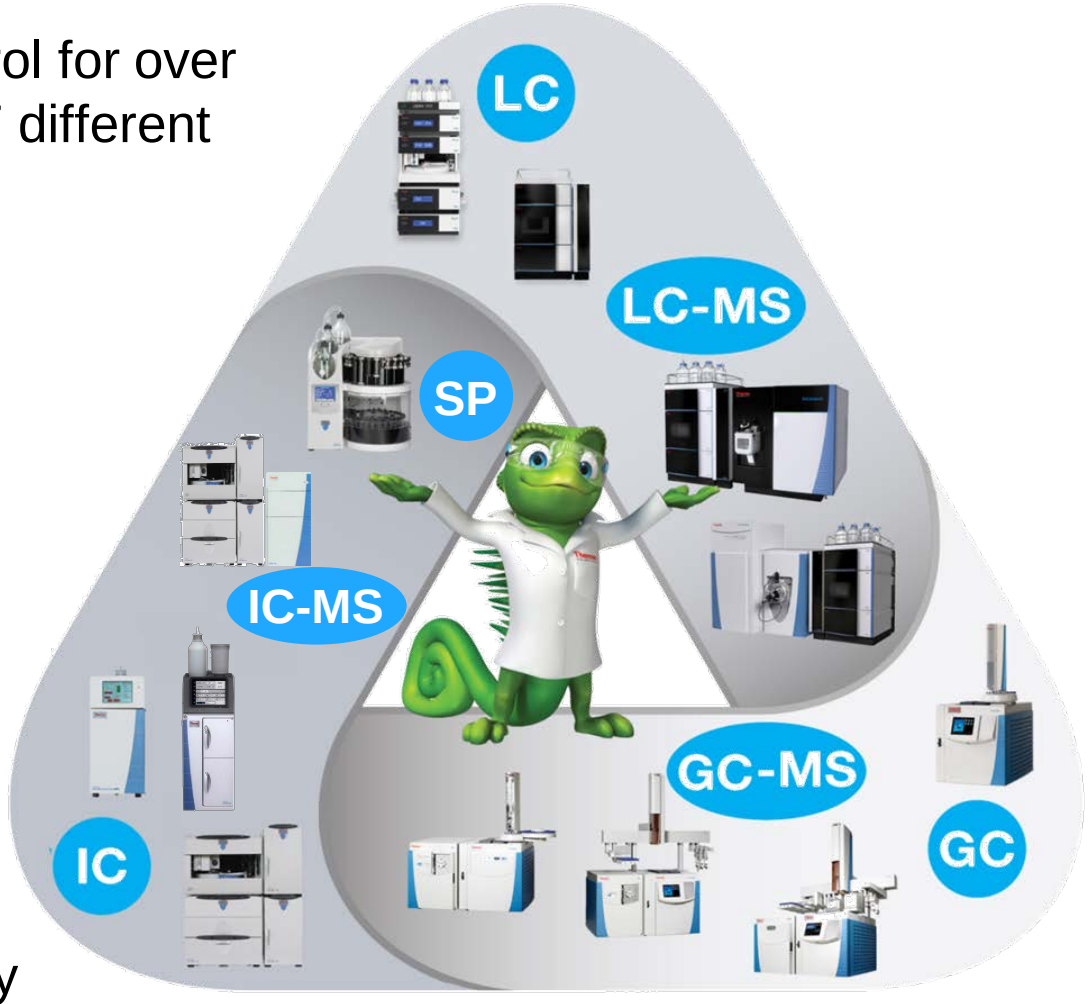
Record Management – Data Storage

- 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

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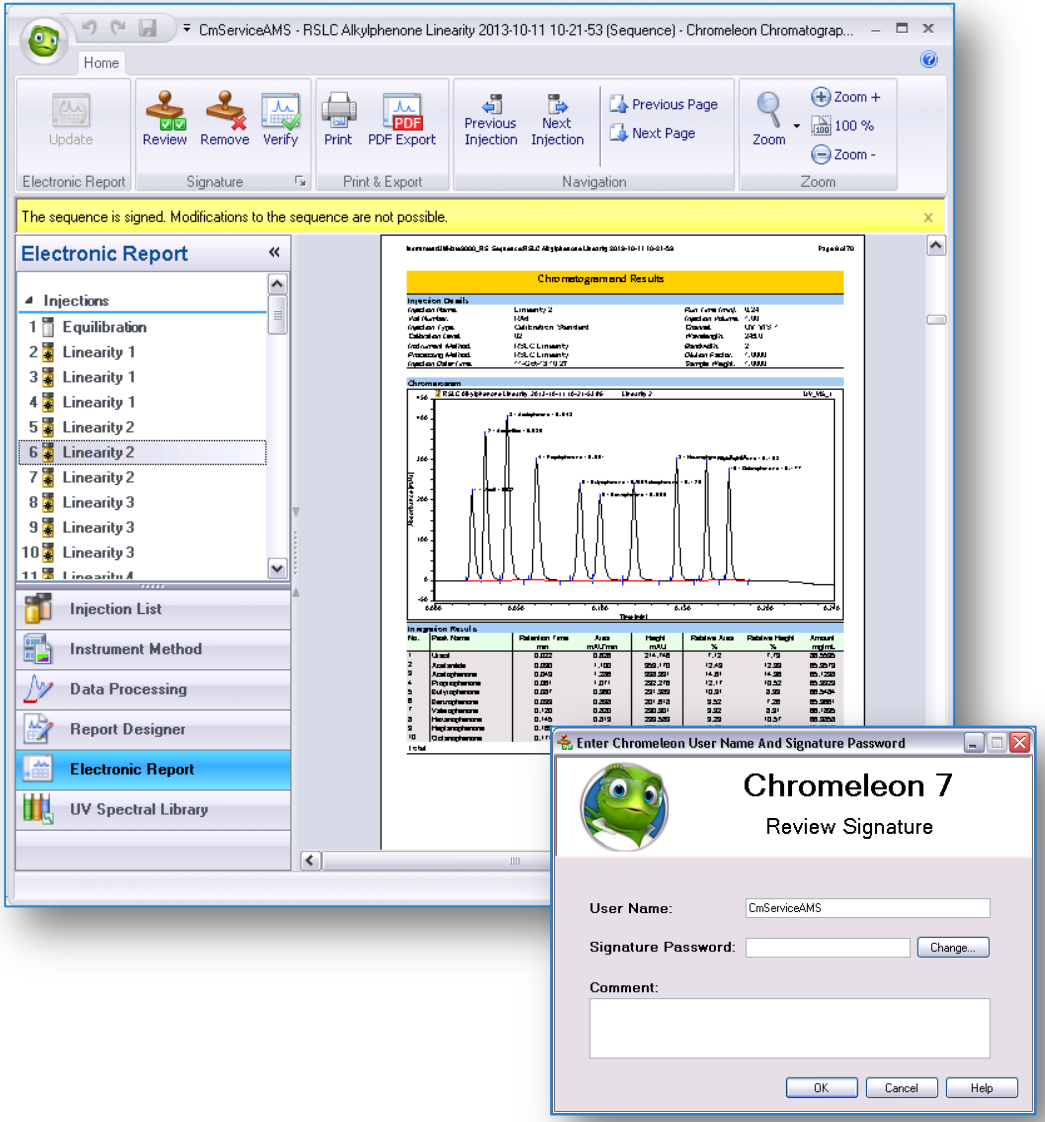
Record Management – Data Control



- 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

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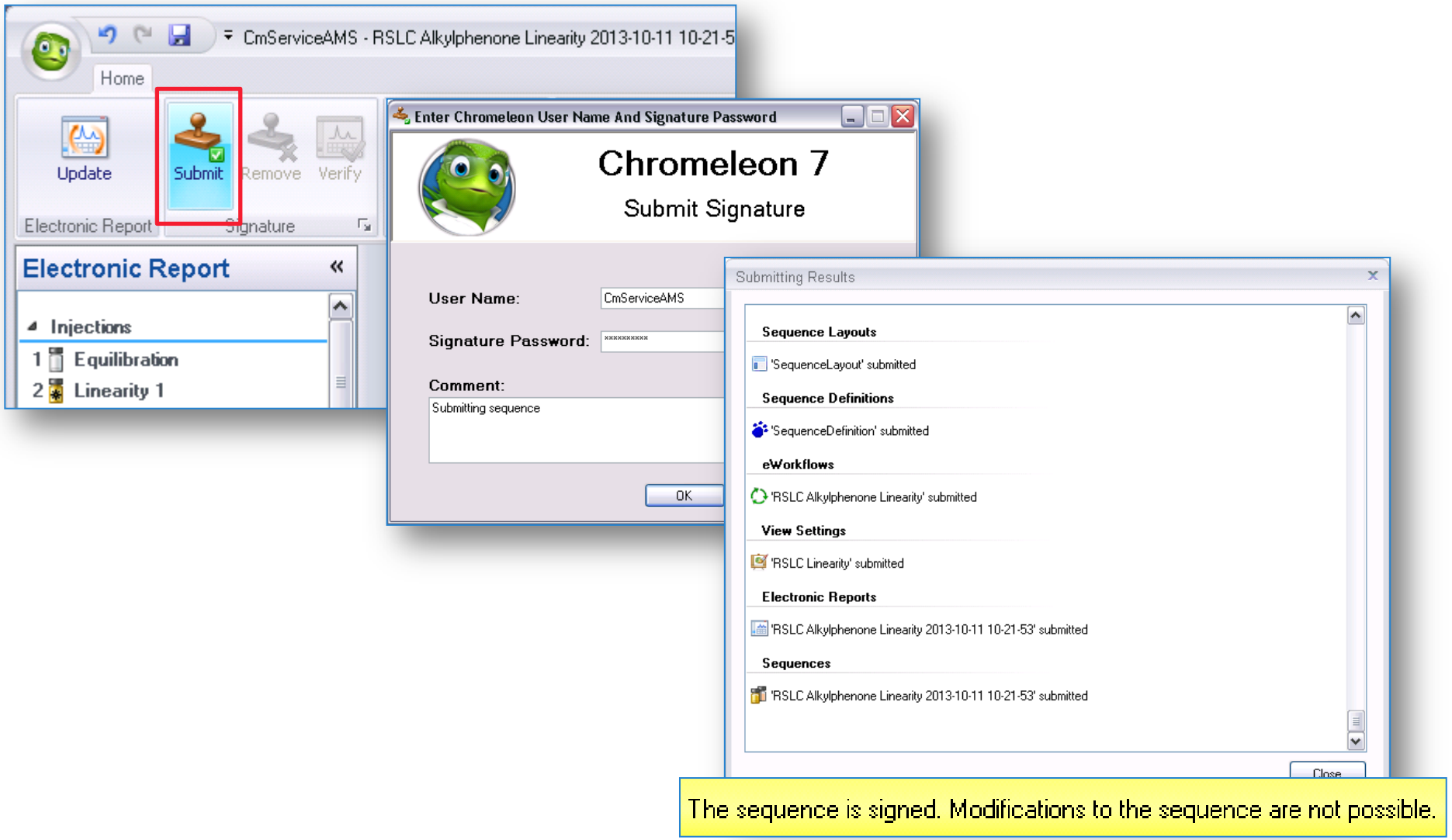
Record Management – Data Control



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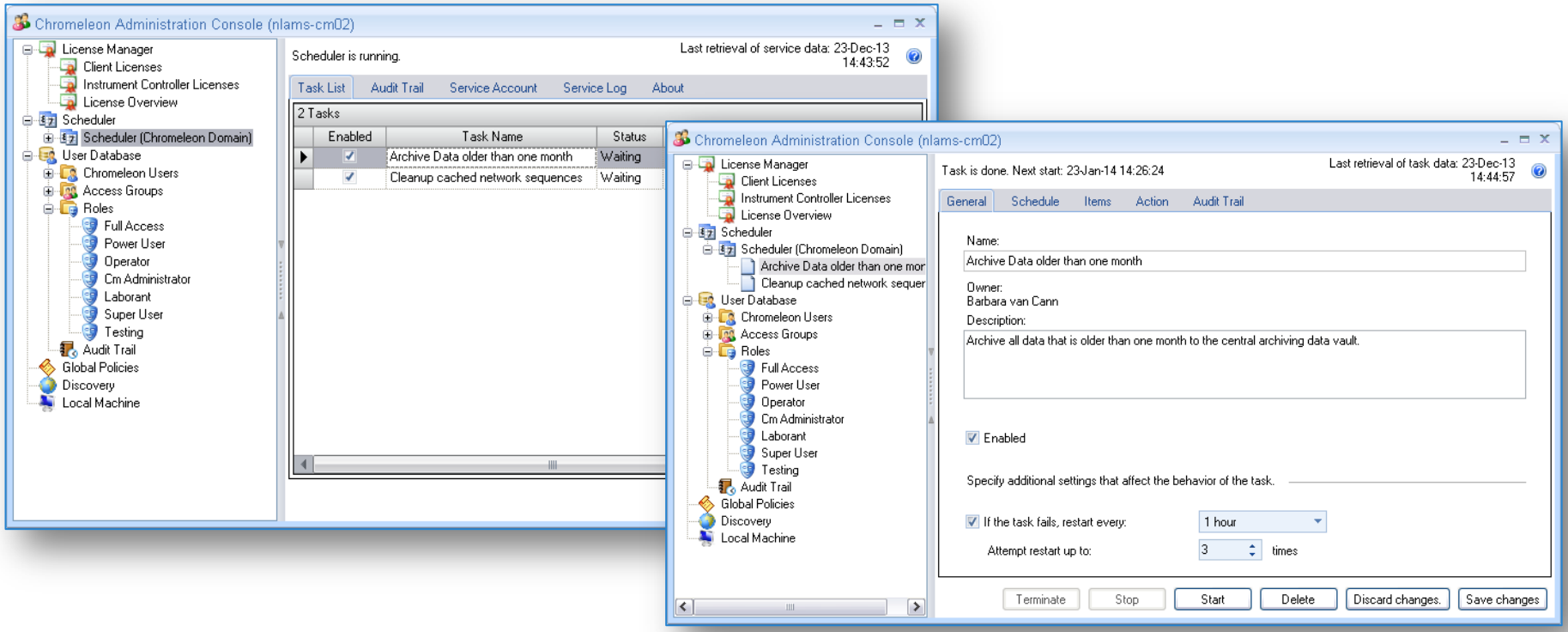
Record Management – Archive/Backup

- 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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Summary

- 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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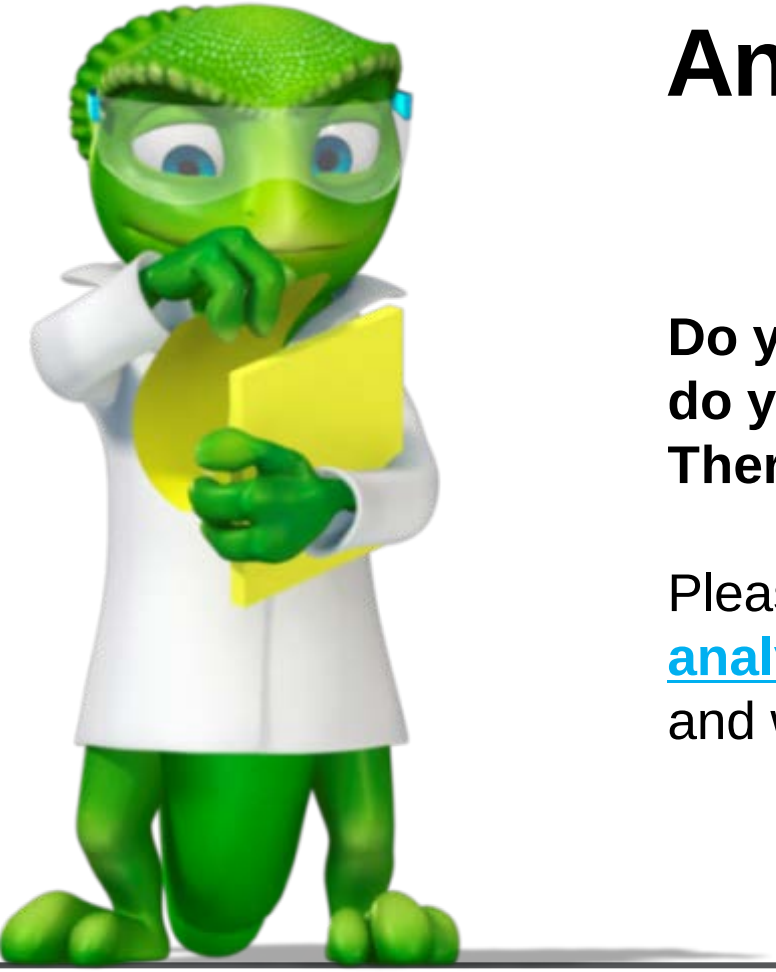
Thank you for your attention!



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.

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