

# Audit Trails

## Data integrity: audit trails with ease of review

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### Summary

Audit Trails are an important regulatory requirement and are a proven effective means of detecting data integrity issues. It is incumbent on regulated companies to evaluate the audit trail controls and establish a documented process for review of audit trails.

The degree of effort required to configure, access and interpret electronic audit trails can vary, dependent upon the system. Electronic audit trail solutions also differ in the functionality that they provide such as searching, sorting, filtering and reporting.

This white paper describes Chromeleon CDS's audit trail controls and outlines the regulatory requirements and guidance that they pertain to and provides information how Chromeleon CDS will ease the review of audit trails.

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## Introduction

An audit trail is a regulatory requisite in situations where data is stored and there is the possibility to modify or delete said data. 21 CFR Part 11 (§11.10(e))<sup>1</sup> introduced the need to have “secure, computer-generated, time-stamped audit trails” for GMP electronic records, but audit trails are an equally important control required by all the various international regulations and guidance encompassing GMP, GLP, and GCP.

Defined within Part 11 §11.10(e), audit trails are a record of the “date and time of operator entries and actions that create, modify, or delete electronic records”. The Food and Drug Administration (FDA) has since expanded upon this definition. As written in the FDA’s Data Integrity and Compliance with CGMP Guidance for Industry,<sup>2</sup> audit trails also “...track actions at the record or system level (such as attempts to access the system or rename or delete a file)”.

Audit trails act as the body of evidence to distinguish altered or invalid electronic records. Data integrity focused inspections by regulators has brought to the forefront that not all data are being considered in lot or batch release decisions. In the worst cases, the information that was not considered was either falsified or failed specifications. The latest guidance has made it clear that audit trails, along with the electronic data they support, must be reviewed as part of the data verification process.

In an ever-increasing environment of software-driven compliance, systems provide varying controls to configure, enable or disable, and view audit trails and to interact with the “dynamic” electronic records. This white paper is written as a guide to configure and manage the audit trails in Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) software, including what information they provide to reviewers and where and how to locate them.

## Enabling, Configuration, and Security

Audit trails must be in operation before any activities regarding the collection, evaluation, deletion, and overwriting of data commence. For various reasons, audit trails are not commonly enabled by default out of the box. This means varying degrees of configuration are possible, dependent upon the system.

In the interest of data integrity, Chromeleon CDS minimizes the number of actions to enable complete auditing. There are three main areas of auditing in Chromeleon CDS: User Management, Data, and System Events and Administration.

The User Management audit trail is automatically enabled when User Mode is selected. The data audit trail including versioning is enabled during the creation of a Chromeleon Data Vault (container that stores all data) (Figure 1).

In response to the FDA’s expanded definition of an audit trail as written in their guidance, “...and those that track actions at the record or system level (such as attempts to access the system or rename or delete a file)”<sup>2</sup>, Chromeleon CDS has two Global Policies that address this latest requirement—“Enable raw data verification” applies a hashing algorithm to verify the integrity of the raw files; “Enable Station Audit Trail logging” records information that was previously only logged such as system events, e.g. failure and outages of central resources or instruments, which may have caused a run to abort (Figure 2).

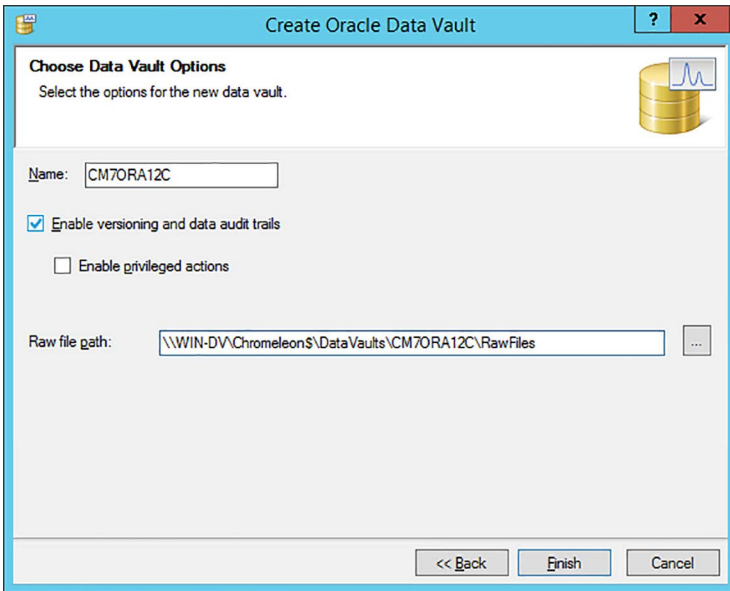


Figure 1. Enabling versioning and data audit trails at time of Data Vault creation using the Chromeleon CDS Data Vault Manager

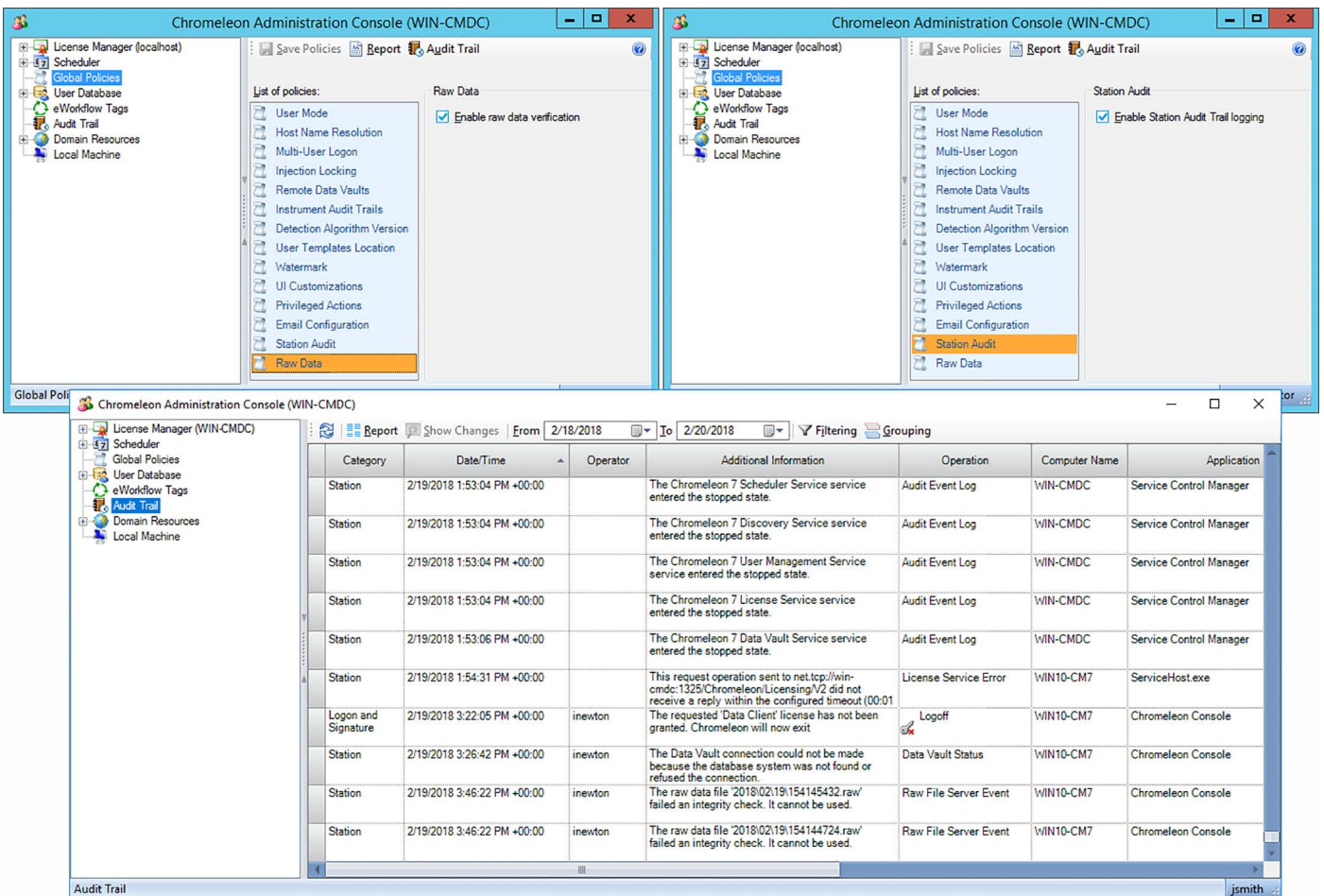


Figure 2. Chromeleon CDS Global Policies for enabling auditing of system events. Audit Trail recording system events such as raw file integrity check failures and Microsoft® Windows® services errors that aborted a run.

In accordance with the likes of the Organization for Economic Co-operation and Development (OECD) Advisory Document No. 17, which states, “The ability to make modifications to the audit trail settings should be restricted to authorized personnel”,<sup>3</sup> Chromeleon CDS Audit Trail policies and object properties are privilege-controlled. Thermo Fisher Scientific recommends that these privileges are only assigned to system administrators who do not have a vested interest in the data (Figure 3).

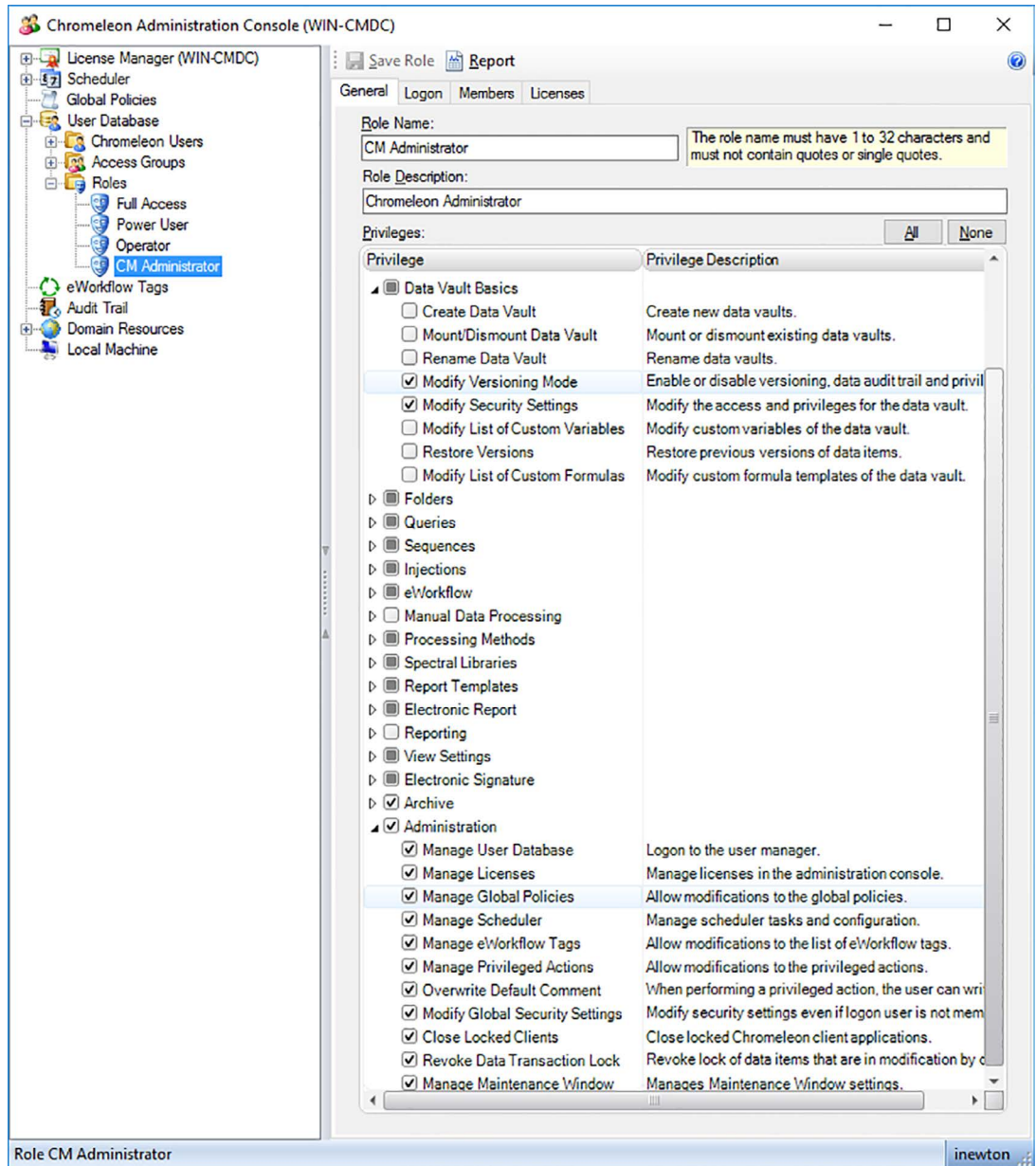


Figure 3. Audit Trail privilege controls



However, should someone change the settings, Chromeleon CDS captures these actions in the Data Audit Trail. The Data Audit Trail retains a record of these events even after disablement and it is always visible to all users (Figure 4). This allows full traceability, which in combination with the security controls and auditing of the database system, acts as the most effective deterrent against any act of malicious intent.

#	Name	Type	Version	Date / Time	Operator	Operation	Additional Information	Comment
26	CM7SQLDV	Data Vault	1	25/01/2018 13:51:58 +00:00	jmaxwell	Changed	Disable versioning and data audit trails, Disable privileged actions	disabled Data Vault au
25	DI	Folder	1	23/01/2018 11:00:53 +00:00	inewton	Moved	From 'chrom://win-dv/CM7SQLDV' to 'Deleted Items'.	
24	DI	Folder	1	22/01/2018 22:52:22 +00:00	inewton	Created		
23	Query	Injection Query	1	23/05/2017 15:16:12 +01:00	jmaxwell	Deleted Injection Query		
22	Query	Injection Query	1	23/05/2017 15:04:35 +01:00	jmaxwell	Created Injection Query		
21	Query	Injection Query	1	22/05/2017 16:27:29 +01:00	jsmith	Deleted Injection Query		
20	Query	Injection Query	1	18/05/2017 16:52:42 +01:00	jsmith	Created Injection Query		
19	Vitamin_E	Instrument Method	1	14/05/2017 14:15:17 +01:00	charlie	Copied	From 'chrom://win-dv/CM7SQLDV/ICH/Linearity/ICH Linearity.seq/V	copied instrument meth
18	New Project	Folder	1	14/05/2017 14:03:46 +01:00	inewton	Moved	From 'chrom://win-dv/CM7SQLDV' to 'Deleted Items'.	folder created in error
17	New Project	Folder	1	14/05/2017 14:02:25 +01:00	jmaxwell	Moved		
16	Ibu Assay 14 May 2017	Sequence	1	14/05/2017 14:00:54 +01:00	jmaxwell	Moved	From 'chrom://win-dv/CM7SQLDV' to 'chrom://win-dv/CM7SQLDV/D	moved sequence to rel
15	Ibu Assay 14 May 2017	Sequence	1	14/05/2017 13:44:33 +01:00	jsmith	Save As	From 'chrom://win-dv/CM7SQLDV/Data/Sequences/Ibuprofen/Ibu A	created new sequence
14	\$RecycleBin\$	Folder	1	14/05/2017 12:55:37 +01:00	jsmith	Created		
13	Default MS Report	Report Template	1	14/05/2017 12:40:54 +01:00	charlie	Moved	From 'chrom://win-dv/CM7SQLDV' to 'chrom://win-dv/CM7SQLDV/	moved Default MS Rep
12	Default MS Report	Report Template	1	14/05/2017 12:38:58 +01:00	charlie	Created		
11	Dissolution Templates	eWorkflow	1	14/05/2017 12:33:35 +01:00	charlie	Created	Imported from D:\Extension Pack\Dissolution Templates\Dissolution	imported Dissolution e
10	Environmental Workflow Templates	eWorkflow	1	14/05/2017 12:32:56 +01:00	charlie	Created	Imported from D:\Extension Pack\GCMS Environmental Analysis Te	imported Environmen
9	GPC	Folder	1	12/05/2017 08:32:30 +01:00	charlie	Created		Imported from 'C:\User
8	Spectra	Folder	1	12/05/2017 08:23:12 +01:00	charlie	Created		Imported from "\win-hp
7	MSData	Folder	1	12/05/2017 08:13:25 +01:00	charlie	Created		
6	ICH	Folder	1	11/05/2017 17:14:54 +01:00	charlie	Created		
5	Site_B	Folder	1	11/05/2017 17:14:29 +01:00	charlie	Created	Imported from \\win-hpv\Software\Thermo\Day 2 Data\DV_	
4	Site_A	Folder	1	11/05/2017 17:03:10 +01:00	charlie	Created	Imported from \\win-hpv\Software\Thermo\Day 2 Data\DV_	
3	Data	Folder	1	11/05/2017 16:40:49 +01:00	charlie	Created	Imported from \\win-hpv\Software\Thermo\Day 2 Data\DV_	
2	CM7SQLDV	Data Vault	1	11/05/2017 16:12:54 +01:00	charlie	Changed	Mounted on server 'WIN-DV'.	
1	CM7SQLDV	Data Vault	1	11/05/2017 14:12:30 +01:00	charlie	Created		

Figure 4. Data Vault property changes recorded in audit trail, which can be viewed even after disablement

## Date and Time Stamps

Securing the chronological order of audit trail events is essential. It is imperative that the source of the date and time is accurate and secured.

Chromeleon CDS relies upon the computer's operating system as its source for date and time. If the system is stand-alone, managing the date and time is more difficult. Thermo Fisher recommends that there is a Standard Operating Procedure (SOP) that describes a procedure by which an appropriately designated person with local administrative rights conducts a regular check and records any changes. The procedure should also include what actions must be taken if the time is outside of a prescribed risk-based tolerance.

In networked environments, the expectation is that time is centrally managed by IT via the use of the likes of Network Time Protocol (NTP), which ensures that all computer clocks are synchronized against a reference time source such as a National Institute of Standards (NIST) time server.

Chromeleon CDS stores time stamps in the internationally recognized Coordinated Universal Time (UTC). In so doing, no time zone configuration is required when operating in geographically dispersed operations. Also due to the confusion that time zones and daylight-saving time can cause, Chromeleon software provides various means to view and report time zones including the ability to translate the recorded date and time into the time zone of a user's computer. An example of such is the Chromeleon CDS unique tooltip shown in Figure 5.

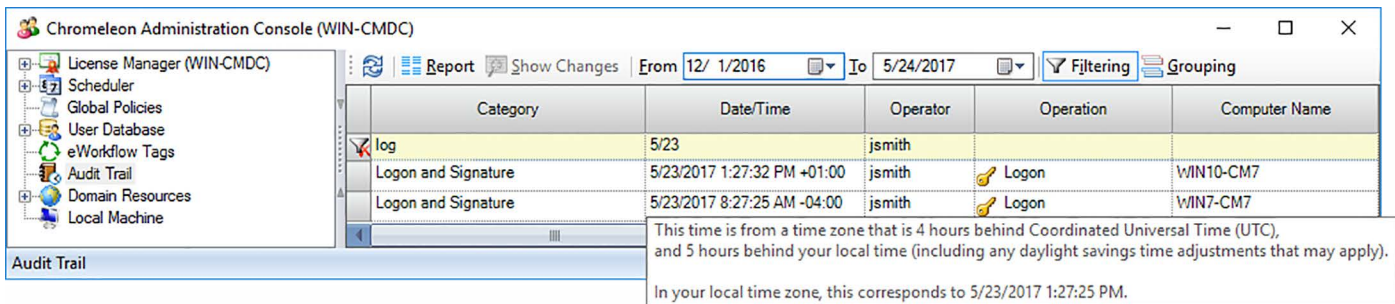


Figure 5. Example of Chromeleon's unique time zone tooltip showing timezone conversion

### 'WHY' is an Audit Trail Important?

An audit trail provides answers in the form of a documented history to questions revolving around a particular event. The critical elements of an audit trail are who, what, when, where, and why.

The elements who, what, when, and where are automatically captured and securely recorded in the audit trail by the system. However, it is not possible for the system to comprehensively understand the cause or reason for a user's action. It relies upon a user providing a justification for their actions that holds up to scrutiny.

To assist in this activity Chromeleon CDS provides the capability for a system administrator or manager to define a list of common reasons for routine actions or corrections. This list is termed Standard Comments. The system administrator or manager can then assign a comment from the list of standard comments as the default entry when a user performs a specified action (Figure 6). A set of privilege controls then determines whether a user can change the comment at all. If this is permitted, the user has the discretion to keep a default comment if one exists, select from the list of standard and recent comments, or make a change via free text entry.

As can be seen in Figure 6, Chromeleon CDS has the capability to request that a user performing a specific action confirms his or her identity through password authentication, therefore reinforcing the identity of who performed the event.

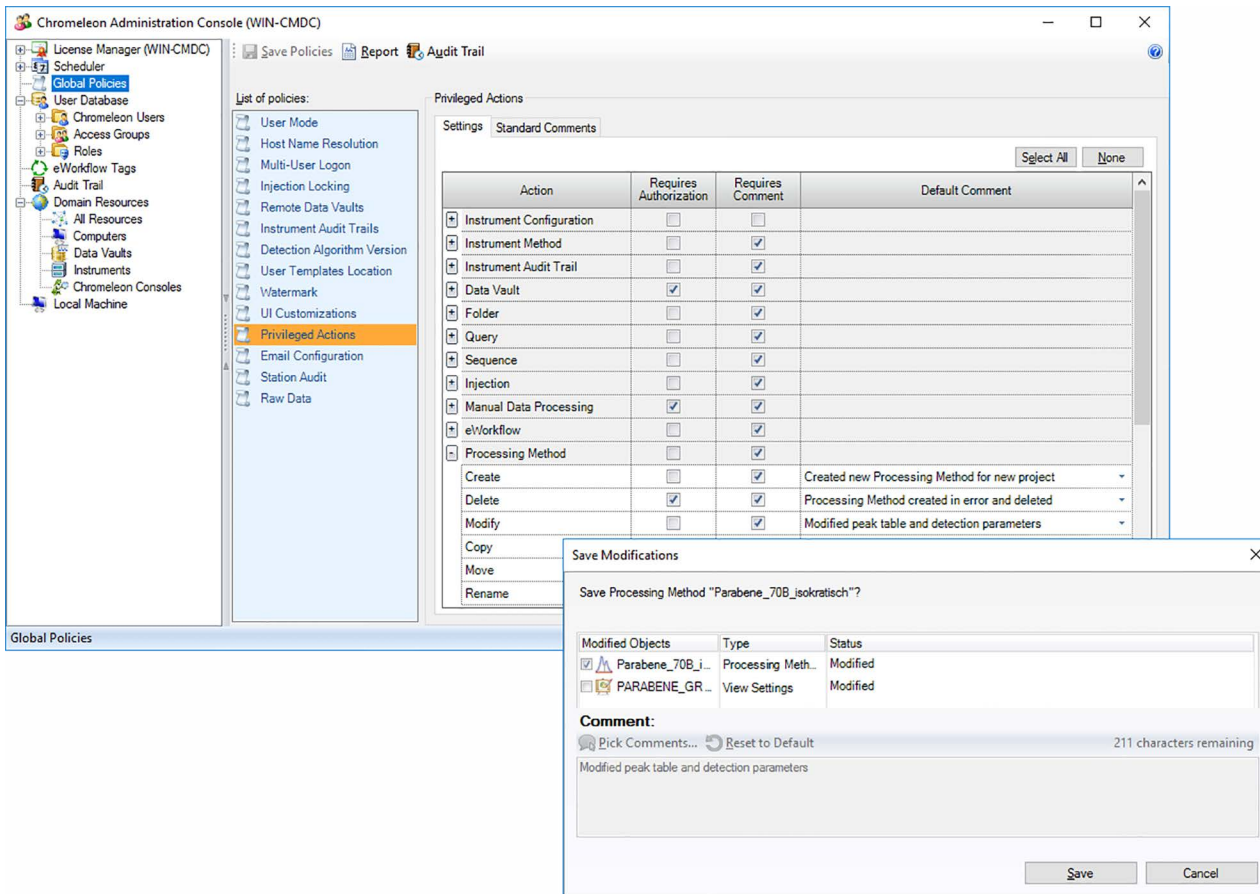


Figure 6. Chromeleon CDS Privileged Actions for which authorization and comments can be enforced for each action

## Instruments and Data Acquisition

In the interest of data security and data integrity, instruments are interfaced and integrated with systems such as the CDS and have additional controls to prevent manual intervention, for instance locking out the instrument's own control panels and preventing any instrument configuration changes during a run.

Chromeleon CDS pioneered third-party instrument control in addition to its manufacturer's instrumentation. With multi-vendor control, Chromeleon CDS maintains an audit trail of all instrument configuration settings and changes, showing old and new values. It also includes a record of any access controls, which permits or restricts certain users, or groups of users, from operating the instruments.



In terms of data creation, permanently retained with each injection record is the Injection Audit Trail that captures all activity from the instrument during the capture of raw data (Figure 7). This includes any manually executed commands or interventions by operators, if permitted. If an operator has the necessary privileges to make amendments to an already running sequence, the Chromeleon CDS Audit Trail records the details of the operator that made any change even if they were not the initiating user.

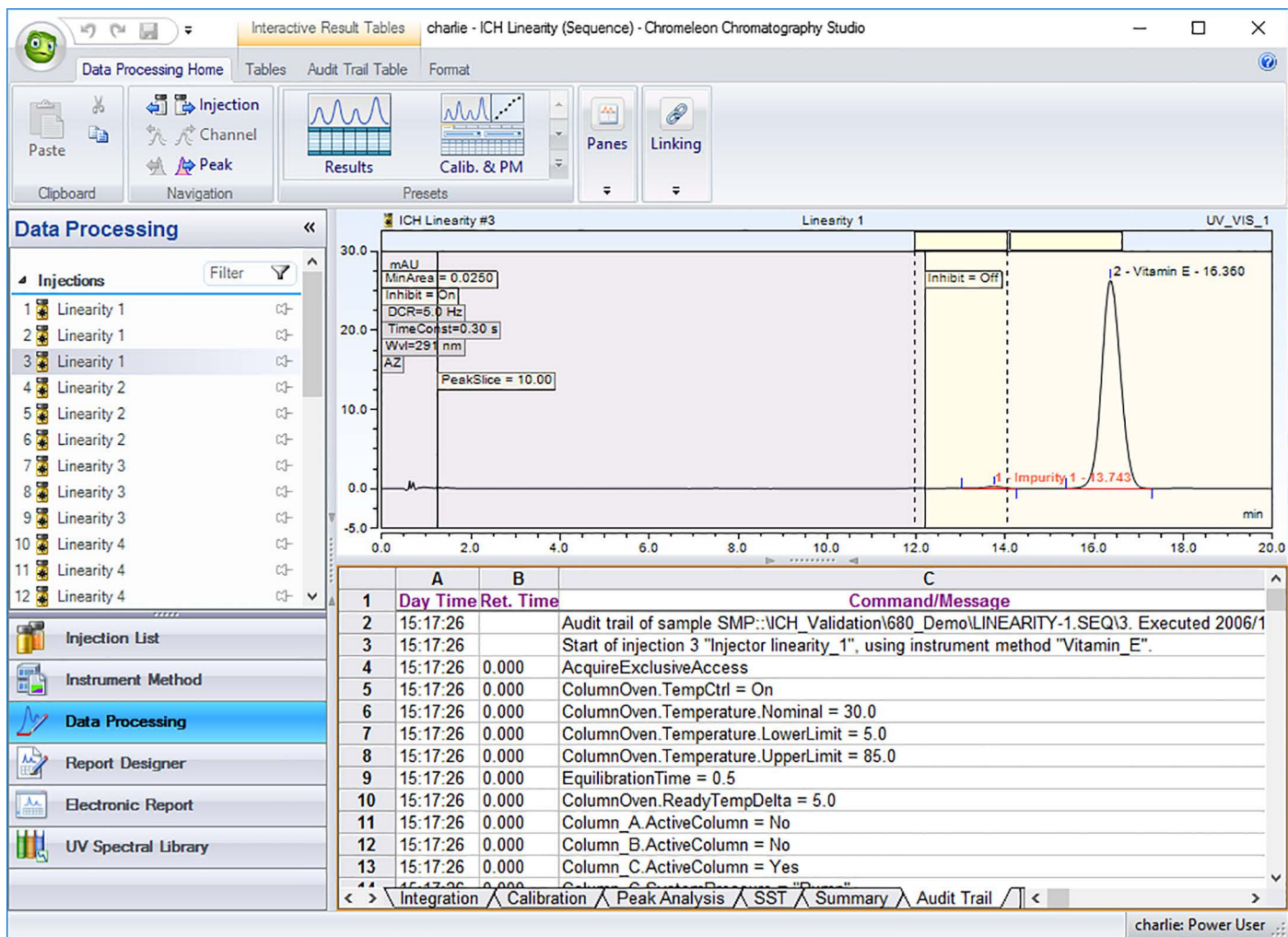


Figure 7. Injection audit trail associated with each injection of a sequence

Chromeleon CDS also maintains an Instrument Audit Trail, which is a daily event log for each instrument. The Instrument Audit Trail is a record of all events related to instrument operation, such as system events, pre-run device settings, executed commands, post-run equilibration and shutdown activities, and error messages (Figure 8).

ID	Date	Time	Retention Time	Device	Message
328	5/14/2017	10:44:09 AM +01:00		UV	UV_Lamp: On
329	5/14/2017	10:44:09 AM +01:00		UV	Connected: Connected
330	5/14/2017	10:44:09 AM +01:00			UV:
331	5/14/2017	10:44:09 AM +01:00			Precondition Log:
332	5/14/2017	10:44:09 AM +01:00			Instrument audit trail of 10_Vanquish on server WIN10-CM7. Date: 14/05/2017.
333	5/13/2017	12:49:34 AM +01:00			Finished the sequence queue run.
334	5/13/2017	12:49:33 AM +01:00			Preparing the start of the next pending sequence (if there is any).
335	5/13/2017	12:49:33 AM +01:00			End of sequence "PQ_STOP".
336	5/13/2017	12:49:31 AM +01:00		UV	Vanquish Diode Array Detector @ USB-12345678 - VH-D10-A - Serial # 12345678 - Firmware Version 0.00.01
337	5/13/2017	12:49:31 AM +01:00		UV	UV Lamp on.
338	5/13/2017	12:49:31 AM +01:00			End of injection "Restore".
339	5/13/2017	12:49:31 AM +01:00	1.000	UV	UV.SetFactoryDefaults
340	5/13/2017	12:48:31 AM +01:00	0.000		Entered stage "Run"

Found 17724 entries.

Figure 8. Chromeleon CDS automatically maintains a complete log of each instrument’s daily activities.

### Audit Trail Review












EU GMP Annex 11<sup>4</sup> released in 2011 made it a specific requirement that audit trails must be “regularly reviewed”. Although Part 11 did not explicitly list this as one of its requirements, it is cited as a predicate rule (§211.194) requirement in FDA warning letter observations.

Chromeleon CDS has always had extensive audit trails and segregates them according to their relevance, giving them a clear context so that it is easier for users to review and interpret them (Figure 9, Table 1).

Figure 9. Graphical representation of Audit Trails in Chromeleon CDS.



Table 1. Summary of Chromeleon CDS Audit Trails

	<p><b>Data Audit Trail:</b> A log of changes to a Data Vault. A separate data audit trail is maintained for each Data Vault and for each data object (Data Vaults, Folder, Sequences, Injections, Processing Methods, Instrument Methods, Report Templates, Spectra Libraries, and modified Chromatograms) in a Data Vault.</p>		<p><b>Global Policies Audit Trail:</b> A log of changes to the global policies.</p>
	<p><b>Injection Audit Trail:</b> A log of activity from the instrument during the capture of raw data for a specific injection.</p>		<p><b>Organizational Unit Summary Audit Trail:</b> A log of changes to all audit trails of an organizational unit.</p>
	<p><b>Instrument Audit Trail:</b> A daily event log that is maintained independently for each instrument. It records all events related to instrument operation, such as system events, pre-run device settings, executed commands, and error messages.</p>		<p><b>Domain Resources Audit Trail:</b> A log of manual changes to the domain resources.</p>
	<p><b>Instrument Configuration Audit Trail:</b> A log of changes to the instrument configuration.</p>		<p><b>Data Vault Manager Audit Trail:</b> A log of changes to the Data Vault management operations.</p>
	<p><b>User Management Audit Trail:</b> A log of changes to the user management.</p>		<p><b>eWorkflow Tags Audit Trail:</b> A log of changes to the eWorkflow tags.</p>
			<p><b>Station Audit Trail:</b> A log of system events (for example, failure and outages of central resources such as the Chromeleon CDS Domain Controller or Data Vault).</p>

## Ease of Review Regardless of Frequency

It is expected that regulated companies review data with a direct impact on patient safety or product quality each and every time the data set is being used in decision-making or being used in support of a batch, lot, or study release. Understanding what data and “meaningful metadata” are subject to review can often be challenging depending on the computerized system.

Chromeleon CDS’s architecture facilitates reviewing this data and metadata, including audit trails, via the Sequence. A Sequence contains an injection list that maintains the order in which injections are analyzed, including the injection results (chromatographic raw data and its acquisition metadata) and also associated methods such as Instrument Method, Processing Method, Report Template, and Spectral Library. It incorporates metadata (for example, sample weights and dilution factors), including all versions of all objects, with complete auditing (Data and Injection Audit Trails) to describe the full history of the Sequence. Having this level of containment gives reassurance and an easy means to look at the final results, work through the data, and understand the process of by whom, when, what, where, and why any changes were made during a chromatographic run.

Each Sequence can also be electronically signed. Chromeleon CDS supports signature workflows with up to three steps (Submit, Review, and Approve). In combination with adequate training and SOPs, documenting the data review for electronic records, as written in in World Health Organization (WHO) Annex 5: Guidance on Good Data and Record Management Practices,<sup>5</sup> “is typically signified by electronically signing the electronic data set that has been reviewed and approved”. As also described in Annex 5, this review procedure should include a process by which “meaningful metadata, such as audit trails” are also part of the review and electronic signature approval process.

A risk assessment, often conducted during validation of software, may also have identified a need to conduct periodic reviews of audit trails. For example, to verify a user’s privileges and access rights against their training record and ensure that nothing was changed incorrectly in the interim. It may also be the case that audit trails provide information that can assist with continual process improvements. Ad-hoc reviews of audit trails may also be necessary, for instance, if something was unexpectedly deleted and further investigation is required.

Within the Chromeleon CDS Audit Trail viewer, all events are fully searchable by filtering using “find as you type” text entry or can be grouped via simple drag and drop operations. A time period filter can also be defined, different versions of objects can be compared where applicable, a free text entry can be searched for, the audit trail information can be sorted by one or multiple columns, and the information can be reported maintaining any filters, groupings, sorting, etc. that may have been applied. As an example, you can easily identify all deletions for an entire Data Vault and check whether only authorized individuals performed such activity (Figure 10).



Data Audit Trail - WIN-DV\CM70RA12C

Report Show Changes Restore Include Subfolders from 2/ 1/2016 to 3/ 7/2018 Filtering Grouping Find Next

Operator

#	Name	Path	Type	Version	Date / Time	Operator	Operation
							delete
Operator: inewton - 1 Items							
495	FLOW0_LAMP_OFF	Data/Sequences/lbuprofen/lbu Assay 30 Oct 12	Instrument Method	2	2/26/2018 10:27:44 AM +00:00	inewton	Deleted
Operator: jmaxwell - 2 Items							
504	Stability	Data/Sequences	Folder	1	3/7/2018 3:29:26 PM +00:00	jmaxwell	Deleted
501	PARABENE_GRADIENT	Site_A/Data/Sequences/lbuprofen/lbu Assay 2 Jul 13	Report Template	2	3/7/2018 3:20:14 PM +00:00	jmaxwell	Deleted
Operator: jsmith - 1 Items							
498	lbu Assay 20 Apr 13	Site_A/Data/Sequences/lbuprofen/lbu Assay 20 Apr 13	Sequence	1	2/26/2018 10:41:35 AM +00:00	jsmith	Deleted Signal
Operator: charlie - 7 Items							
103	Query	Data/Archive Queries	Injection Query	1	3/31/2016 1:38:23 PM -05:00	charlie	Deleted Injection Query
212	GPC Templates		e/Workflow	1	3/31/2016 4:04:13 PM -05:00	charlie	Deleted
269	Query	Data/Queries	Injection Query	1	4/4/2016 2:38:28 PM -05:00	charlie	Deleted Injection Query
312	Query	Data/Queries	Injection Query	1	4/4/2016 3:12:22 PM -05:00	charlie	Deleted Injection Query
376	Query	Data/Queries	Injection Query	1	4/7/2016 4:48:39 PM -05:00	charlie	Deleted Injection Query
290	Utilization_the long way	Data/Queries/Utilization Query	Report Template	1	4/4/2016 3:00:15 PM -05:00	charlie	Deleted
392	SST	Data/Queries/SST Failures	Report Template	1	4/7/2016 5:09:36 PM -05:00	charlie	Deleted
Operator: Scheduler - 35 Items							
41	RFIC_ER Tap 5 Anion	Data/Archive Sequences	Sequence	1	3/31/2016 1:02:43 PM -05:00	Scheduler	Deleted
47	RFIC_ER Tap 7 Anion	Data/Archive Sequences	Sequence	1	3/31/2016 1:04:47 PM -05:00	Scheduler	Deleted
108	RFIC_ER Tap 5 Anion Oct 1	Data/Archive Sequences/Bulk Move	Sequence	1	3/31/2016 1:42:24 PM -05:00	Scheduler	Deleted
110	RFIC_ER Tap 5 Anion Oct 10	Data/Archive Sequences/Bulk Move	Sequence	1	3/31/2016 1:42:28 PM -05:00	Scheduler	Deleted

Figure 10. Data Vault Audit Trail including all subfolders filtered to show delete operation and grouped by operators

## Evidence of Audit Trail Review

Latest guidance from regulators also introduces the concept that the act of reviewing the audit trail must be captured and documented. As stated in the Medicines and Healthcare Products Regulatory Agency (MHRA) GMP Data Integrity Definitions and Guidance,<sup>6</sup> “There should be evidence available to confirm that review of the relevant audit trails have taken place.” This poses an intriguing technological challenge and one that may only ever truly be achieved via self-auditing audit trails and further increased automation. Until such time this needs to be procedurally controlled as described in the Pharmaceutical Inspection Convention/Pharmaceutical Inspection Co-operation Scheme (PIC/S) draft guidance; Good Practices for Data Management and Integrity in Regulated GMP/GDP Environment, PI 041-1.<sup>6</sup>

## Versioning Data Items

To verify the effects and implications of changes that are recorded in audit trails and determine whether or not they were justified and in accordance with established procedures, it is often necessary to make comparisons between pre-existing records and existing ones or it may even necessitate reverting back to a pre-existing state.

Chromeleon CDS maintains versioning for specific data items. This includes Data Vaults, Sequences, Injections, Processing Methods, Instrument Methods, Report Templates, Spectra Libraries, and modified Chromatograms. An incremental number is automatically assigned to a versioned data item and cannot be amended in any way. Differences between two versions of a data item can be viewed via the interactive version comparison dialog, and where modifications have been made, they are clearly indicated via easily identifiable icons alongside the values of all old and new records (Figure 11).



The screenshot displays the 'Data Audit Trail - WIN-DV\CM7SQLDV' window. The main table lists changes to various data objects. A secondary window titled 'Changes of Instrument Method 'Vitamin\_E' version 1 vs. version 5' provides a detailed comparison of parameters between the two versions.

#	Name	Type	Version	Date / Time	Operator	Operation	Comment
19	Vitamin_E	Instrument Method	1	5/14/2017 2:15:17 PM +01:00	charlie	Copied	copied instrument method
18	New Project	Folder	1	5/14/2017 2:03:46 PM +01:00	inewton	Moved	folder created in error
17	New Project	Folder	1	5/14/2017 2:02:25 PM +01:00	jmaxwell	Created	
16	Ibu Assay 14 May 2017	Sequence	1	5/14/2017 2:00:54 PM +01:00	jmaxwell	Moved	moved sequence to relevant location
15	Ibu Assay 14 May 2017	Sequence	1	5/14/2017 1:44:33 PM +01:00	jsmith	Save As	created new sequence via save as

Version	Date/Time	Operator	Operation	Comment
1	5/11/2017 5:30:23 PM +01:00	charlie	Created	Imported from 'C:\Use...
5	5/14/2017 2:19:38 PM +01:00	charlie	Changed	edited instrument met...

Version 1			Version 5		
Time	Symbol	Value	Time	Symbol	Value
Initial Time	Instrument Setup		Initial Time	Instrument Setup	
	Sampler.AcquireExclusiv...	On		Log	System Com...
	ColumnOven.TempCtrl	30.0 [°C]		Sampler.AcquireExclusiv...	On
	ColumnOven.Temperatur...	5.0 [°C]		ColumnOven.TempCtrl	30.0 [°C]
	ColumnOven.Temperatur...	85.0 [°C]		ColumnOven.Temperatur...	40.0 [°C]
	ColumnOven.Temperatur...	85.0 [°C]		ColumnOven.Temperatur...	5.0 [°C]
	ColumnOven.Temperatur...	85.0 [°C]		ColumnOven.Temperatur...	85.0 [°C]
	ColumnOven.Equilibratio...	0.5 [min]		ColumnOven.Equilibratio...	0.5 [min]
	ColumnOven.ReadyTem...	5.0 [°C]		ColumnOven.Equilibratio...	0.5 [min]
	ColumnOven.ReadyTem...	2.0 [°C]		ColumnOven.ReadyTem...	2.0 [°C]
	ColumnOven.Column_A...	No		ColumnOven.Column_A...	No
	PumpModule.Pump.Pres...	15 [psi]		ColumnOven.Column_A...	No
	PumpModule.Pump.Pres...	5802 [psi]		PumpModule.Pump.Pres...	15 [psi]
	PumpModule.Pump.Pres...	5802 [psi]		PumpModule.Pump.Pres...	5802 [psi]
	PumpModule.Pump.Maxi...	1.500 [ml/min...]		PumpModule.Pump.Pres...	5802 [psi]
	PumpModule.Pump.Maxi...	3.000 [ml/min...]		PumpModule.Pump.Maxi...	1.500 [ml/min...]
	PumpModule.Pump.% A...	""A"		PumpModule.Pump.Maxi...	3.000 [ml/min...]
	PumpModule.Pump.% B...	""B"		PumpModule.Pump.% A...	""A"
	Sampler.DrawSpeed	10.000 [µl/s]		PumpModule.Pump.% B...	""B"
	Sampler.DrawDelay	5000 [ms]		Sampler.DrawSpeed	10.000 [µl/s]
	Sampler.DispSpeed	20.000 [µl/s]		Sampler.DrawDelay	5000 [ms]
	Sampler.DispenseDelay	0 [ms]		Sampler.DispSpeed	20.000 [µl/s]
	Sampler.WasteSpeed	32.000 [µl/s]		Sampler.DispenseDelay	0 [ms]
	Sampler.SampleHeight	3.000 [mm]		Sampler.WasteSpeed	32.000 [µl/s]
	Sampler.Inject/Wash	No/Wash		Sampler.SampleHeight	3.000 [mm]
	Sampler.PunctureOffset	0.0 [mm]		Sampler.PunctureOffset	0.0 [mm]

Figure 11. Chromeleon CDS modification history tracks all changes to all data objects and lists the before and after state of each variable associated with each change.

The structure of versioning provides the capability to easily view changes in depth but also revert to an earlier record if desired. If the restore action is executed it is fully tracked in the audit trail and treated as an additional new record. In addition, the Chromeleon CDS versioning means that you can now also restore deleted child items with full traceability, such as the example Report Template, as shown below in Figure 12.

The screenshot displays the 'Data Audit Trail - Accuracy\ICH Accuracy 260617125111' window. The main table lists changes to report templates. A red box highlights a specific sequence of operations: a 'Deleted' operation followed by a 'Restored to version 5' operation.

#	Name	Type	Version	Date / Time	Operator	Operation	Additional Information	Comment
9	Method_Validation	Report Template	8	6/26/2017 4:09:34 PM +01:00	jmaxwell	Changed	Restored to version 5.	reverted to previous version of report template
8	Method_Validation	Report Template	7	6/26/2017 4:08:19 PM +01:00	jmaxwell	Deleted		deleted report template
7	Method_Validation	Report Template	6	6/26/2017 4:06:52 PM +01:00	jmaxwell	Changed	Restored to version 1.	restored to initial version of report template
6	Method_Validation_Accuracy	Report Template	5	6/26/2017 4:03:15 PM +01:00	jmaxwell	Renamed	From 'Method_Validation' to 'Method_Validation_Accuracy'.	renamed report template to include accuracy
5	Method_Validation	Report Template	4	6/26/2017 3:59:08 PM +01:00	jmaxwell	Changed		amended formula of tested accuracy
4	Method_Validation	Report Template	3	6/26/2017 12:58:51 PM +01:00	jmaxwell	Changed		changed statistical variable on Accuracy
3	ICH Accuracy	Processing Method	2	6/26/2017 12:56:36 PM +01:00	jmaxwell	Changed		changed detection algorithm to Cobres
2	Accuracy_IM	Instrument Method	1	6/26/2017 12:51:18 PM +01:00	jmaxwell	Changed		
1	ICH Accuracy 260617125111	Sequence	1	6/26/2017 12:51:18 PM +01:00	jmaxwell	Created	From e:\workflow\chrom\win-dv\CM7ORA12C\ICH Accuracy.proc'	

Figure 12. Restoring a deleted Report Template

## **Data Retention, Availability, and Retrieval**

“Data and document retention arrangements should ensure the protection of records from deliberate or inadvertent alteration or loss.” (MHRA: Data Integrity Definitions and Guidance<sup>7</sup>) Audit trails must also be retained and protected for as long as the original record.

Audit Trails (Data and Injection) associated with a Chromeleon CDS Sequence are preserved along with the data records that form a Sequence. If a Sequence is exported, for instance using the Chromeleon CDS data file format (.cmbx), all audit trails and versioning are safeguarded with the data.

With the exception of Instrument Audit Trails, all of the follow-on audit trails listed in Table 1 are automatically stored centrally on the Chromeleon CDS Domain Controller. In networked environments Chromeleon CDS manages the storage of these records even during periods of network outage. The records are stored centrally to ‘C:\ProgramData\Dionex\Chromeleon\UserManagement\Audit Trail’, which is, by default, a secured location of the Windows operating system. To protect against a catastrophic event, the records can subsequently be included into IT backup schedules.

The critical entries from the Instrument Audit Trail are recorded in the Injection Audit Trail and stored with the Sequence for the entire record lifecycle in the database. Depending on data retention policies, the remaining information can have an independent retention period defined. Chromeleon CDS therefore provides the option to define whether these records are stored centrally at a specified location.

## **Conclusion**

Chromeleon CDS provides easy to configure, extensive audit trails with context that makes setup, interpretation, and review simpler. In response to the latest regulatory thinking, such as the FDA’s expanded definition of an audit trail, Chromeleon CDS also captures information that was previously only recorded in non-permanent log files to its audit trails.

Having comprehensive audit trails in combination with the Chromeleon CDS User Management controls that secure the sequence, instrument control, data acquisition, and processing files minimizes the review effort and risk, and allows organizations to define a more effective data review process that promotes sound scientific practices.

## References

1. U.S. Food and Drug Administration (FDA). Title 21 Chapter 1 Subchapter A Part 11 (21 CFR Part 11) Electronic Records; Electronic Signatures. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11> (accessed March 13, 2018).
2. U.S. Food and Drug Administration (FDA). Data Integrity and Compliance With CGMP Guidance for Industry. <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM495891.pdf> (accessed March 13, 2018).
3. Organisation for Economic Co-operation and Development (OECD). OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Advisory Document No. 17. [http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2016\)13&doclanguage=en](http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)13&doclanguage=en) (accessed March 13, 2018). EudraLex Volume 4 GMP Medicinal Products for Human and Veterinary Use; EU GMP Annex 11
4. European Commission. EudraLex Volume 4 Good Manufacturing Practice (GMP) Medicinal Products for Human and Veterinary Use; EU GMP Annex 11. [https://ec.europa.eu/health/documents/eudralex/vol-4\\_en](https://ec.europa.eu/health/documents/eudralex/vol-4_en) (accessed March 13, 2018).
5. World Health Organization (WHO). Technical Report Series No. 996, 2016: Annex 5 Guidance on good data and record management practices. [http://www.who.int/medicines/publications/pharmprep/WHO\\_TRS\\_996\\_annex05.pdf](http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf) (accessed March 13, 2018).
6. Pharmaceutical Inspection Convention Pharmaceutical Inspection Co-operation Scheme (PIC/S) Good Practices for Data Management and Integrity in Regulated GMP/GDP Environment, PI 041-1 (draft). <https://picscheme.org/layout/document.php?id=714> (accessed March 26, 2018)
7. Medicines and Healthcare Products Regulator Agency (MHRA). GMP Data Integrity Definitions and Guidance for Industry March 2015. [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/412735/Data\\_integrity\\_definitions\\_and\\_guidance\\_v2.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/412735/Data_integrity_definitions_and_guidance_v2.pdf) (accessed March 13, 2018).



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