Customer collaboration article

Implementing chromatography data systems for increased data integrity and regulatory compliance

Data integrity is a primary focus for pharmaceutical and manufacturing companies whose products must be of the highest quality. Monitoring not only product excellence but also the quality of processes significantly improves both data integrity and laboratory efficiency. While paper-based records and audits still exist, processes can be improved with electronic-based records and electronic signatures that play a key role in creating and maintaining data integrity.

As an increasingly greater emphasis is continuingly being put on data integrity, companies must be highly vigilant to ensure accuracy in all levels of a process, and to meet current regulatory guidelines. Determining requirements for chromatography data systems (CDS) that comply with both the Food and Drug Administration (FDA) and Medicines and Healthcare Products Regulatory Agency (MHRA) regulations includes considerations across lab conformity, data integrity, and efficiency. The FDA's regulatory section 21 CFR part 11 outlines electronic options for audit trail compliance as an alternative to paper documentation. The regulations also incorporate the ALCOA+ principles to ensure the most robust and comprehensive procedures.

Introduction

Data integrity provides evidence that analytical results are valid and accurate. While this concept should already be an important focus of any lab, it has become an increasing priority for regulatory organizations such as the FDA and the MHRA.

The significance of data integrity in lab compliance is encompassed in the ALCOA+ principles, as defined by FDA guidance. These guiding principles outline nine expectations set up to identify weaknesses in a data lifecycle and strengthen both paper and electronic elements of data generation.

- Attributable: Who did what, when and why?
- Legible: Data must be recorded in a permanent and durable medium.
- Contemporaneous: Data must be recorded as observed and in real-time.
- Original: Data must be raw and directly from the source.
- Accurate: Data must be correct and free from errors. Corrections must be documented.
- Complete: All data, good and bad, must be recorded.
- Consistent: Good documentation must be practiced at all times.
- Enduring: Records must exist for an entire study period.
- Available: Records must be available for review at any time.

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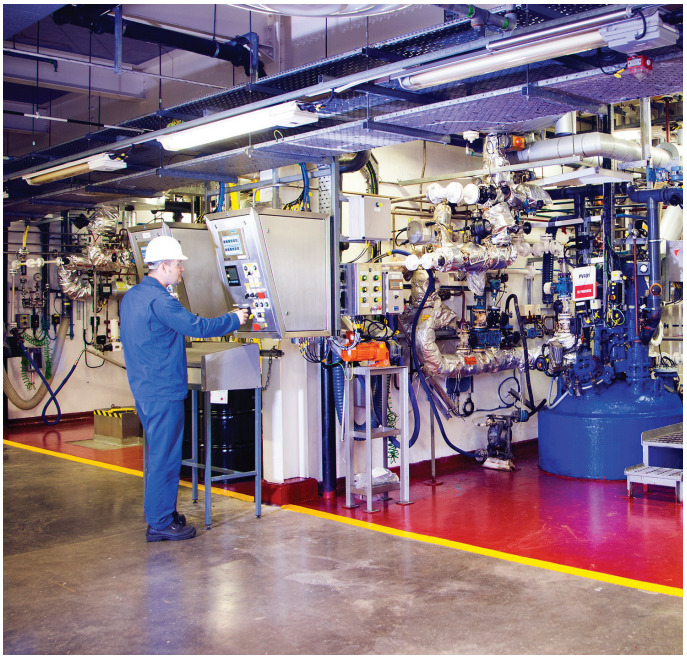
Regulatory guidelines support validated documentation and outline parameters such as audit trails, electronic signatures, and thorough reviews. Advanced chromatography data systems not only organize requirements needed to comply with regulations but can automate systems, so all lab processes can be standardized and cohesive.

Evaluating audit trails

Under current regulations, a critical aspect to data integrity is the documentation of the who, what, why, and when of every activity and process. This vital information, or metadata, provides context and meaning to recorded data and displays it as attributable to an individual user. Though the 21 CFR part 11 and MHRA GMP guidelines are not new, they have not changed in their requirement to include the requirement for computer-generated time stamped audit trails, the ability to show any and all changes to the data, and reviews to be confirmed and recorded.

The design and set-up of audit trails in a CDS can be built-in to certain systems and be ready to meet regulatory requirements automatically. The CDS can help ensure compliance with features such as an automatic audit trails function, unique and password-protected user accounts, automated time stamps and date entries, and required comment areas on data modifications. When setting-up systems, training of all users and reviewers on what to look for, how to complete an entry, and how to properly review a procedure can help support success of the automated system. Similarly, enabling report templates allows trained users to obtain a sequence overview and list of all audit trails with how many versions of an activity there are.



Version numbers, the number of times that an activity was performed or changed, plays a significant role in data integrity. If methods are performed correctly and chromatograms pass with no question, only one version is likely recorded, resulting in an easy review. However, if several different version numbers are recorded, there will be a need to examine the audit trail and learn why so many steps had been adjusted or repeated. With such transparency of processes comes the ability to easily and quickly improve upon methods. Nevertheless, this does depend on the application as some activities typically involve more than one version regardless of optimal technique and results. Successful audit trail documentation and reviews show that a process is attributable and accurate.

Transitioning integration

Data integration into the system can be manual or automated. Both can be employed within a process depending on the application, though automated integration is preferred for absolute integrity of results. When an auditor observes manual integration, the question arises as to whether the user is integrating into compliance. Are they manipulating the results?

While manual integration may be required for certain methods, it is important to control its use and identify where it is and is not used. When manual integration is necessary, robust review procedures are essential that scrutinize all chromatography results, especially those that have barely passed. Setting formal monitoring procedures combined with official limits and reviewing both electronic and printed versions of chromatography data ensures quality in compliance and creates a strict platform where manual integration cannot be hidden. In addition, CDS queries can be used to measure and report integration on a monthly basis, as well as highlight the need to monitor accuracy in user activities. System monitoring may reveal patterns of particular users and evidence of “system suitability polishing” that in turn can be used to drive improvement in the overall process.

In order to be compliant and successful with data integration, it is important to automate integration wherever possible, identify methods where manual integration is required, and prepare processing methods where detection parameters can be recorded in method documentation. Proper integration review allows for assessment of methods and where manual integration can be improved.

Data completeness

The requirement of data completeness evaluates if orphan data is present and whether a complete record is being documented. There are two questions that can be asked when auditing a process: When reviewing data, is every sequence recorded in batch records? And who decides what to report?

First of all, if a sequence has no link to a batch, it is an orphan. While this data is unreported, it still remains in the system and so is auditable. Secondly, if analysts are recording only successful results, failed results could be deleted, hidden, or ignored. For example, an auditor could inquire about a specific batch number and that search could reveal multiple unreported injections. In this case, data is being manipulated and potentially invalidated without justification. It is imperative that review processes detect this behavior.

Running a risk assessment on a review process can expose data that may be hidden or deleted. In a sophisticated CDS, data cannot be deleted and changes cannot be made to submitted sequences, helping immensely with data integrity. In addition, many systems require electronic signatures by at least two people, necessitating all sequences to be submitted electronically and activities to be validated. Within a CDS, visual indication of a review status, whether unsigned, submitted or reviewed, provides a real-time check of what stage each process is at. electronically and activities to be validated. Within a CDS, visual indication of a review status, whether unsigned, submitted or reviewed, provides a real-time check of what stage each process is at.

Resulting audit trails relay who did what, when and why across all sequences. Reviewers can then assess the validity of a sequence and discover orphan or unreported data quickly and easily. CDS queries can again check for unsigned or unreviewed sequences to ensure completeness of data

A case study: Sterling Pharma Solutions

Sterling Pharma Solutions, a contract research and manufacturing organization, replaced their original chromatography data system in 2012 with Thermo Scientific™ Chromeleon™ CDS. The company's goal was to have one system that could span across its laboratories and work with the existing instrumentation. One comprehensive CDS could bring cohesion between the laboratories and provide improved compliance, data integrity and efficiency.

Addressing data integrity and meeting modern compliance in the lab had been an important aspect in the decision to change CDS. Transcribing data into a spreadsheet, for example, is not only an inefficient process but one wrought with risk. Between errors, deletions, or manipulations, moving from manually transferring data to electronic raw data entry meets, and can exceed, regulations. The new CDS platform also included security requirements for electronic data, instilling confidence that all data is secure and enduring throughout the data lifecycle.

Sterling recognized that customers can visit and audit processes at any time, which it welcomed. Compliance to regulations shows control of processes, giving customers confidence in data output and investment. An important aspect of compliance for customers includes comprehensive audit trails, or the ability to track everything the user and system does. When users regularly review the audit trails for each sequence, they can ensure correct versions of files such as instrument methods and report templates are used for each analysis. These consistent reviews and confirmations assure its customers that procedures are being performed correctly. Sterling's personnel utilized all aspects of Chromeleon CDS in this respect, even the version comparison tool that could easily demonstrate changes between versions, where all changes could be clearly identified.

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Increasing lab efficiency

The new CDS brought an enhanced level of laboratory efficiency to Sterling through ease of use and speed of data processing and retrieval. While data processing is typically known to be time-consuming, bringing in the intuitiveness and speed of an advanced CDS significantly reduced both training requirements and time spent. Additional tools helped set-up optimum integration parameters quickly for consistent and smooth integration practices. Manual integration is also in the process of being phased out in favor of automated integration, for improved compliance and data integrity.

The ability to monitor laboratory-wide performance on such activities as instrument utilization or data input improved data sharing and instrument visibility, thereby also increasing efficiency. This cohesiveness in procedures from a single and centralized system simplified activities and made data easily accessible. It also allowed the labs to share instruments and transfer methods, bringing labs and customers together for successful results while making all methods more transparent to everyone. Method validation report templates then enabled the sharing of data with customers, which encouraged collaboration and built on partnerships.

Driving method improvement

Sterling has a wide range of methods that need different system suitability and calculation requirements. By setting-up method, product, and project specific reporting structures, Sterling was able to improve their reporting efficiency and streamline operations on a stable system. Implementing electronic signatures and eWorkflow™ procedures minimized paper usage and also ensured correct methods and reports were applied and analyses were performed in line with current standard operating procedures (SOPs). This saved time in data review and maintained data integrity with automated inputs.

Conclusion

Given the regulatory climate surrounding pharmaceutical research, development, and manufacturing companies, implementing checks and balances across all systems and procedures provides companies with the confidence that their data output is ultimately accurate, and resulting products are high quality. Following guidelines like the ALCOA+ principles and enforcing FDA and MHRA requirements becomes second-nature as chromatography data systems enable automatic compliance while enhancing lab processes. Updated CDS systems can alleviate pressures and time when tracking user activities and paper audit trails by automating the audit trail process and all activities involved. These improvements ensure data integrity and make regulatory compliance much simpler, emphasizing the importance of reviewing audit trails and automating integration, as well as setting limits to drive improvement.

Find out more at **thermofisher.com/oneCDS**

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