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Technical Report

Data Integrity Compliance: An Innovative Solution for Molecular Spectroscopy

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Abstract:

A recent topic related to analytical data is the lack of data integrity due to data modification and replacement. Regulatory authorities for analytical instruments are not only interested in chromatography systems, such as liquid chromatographs (LC) and gas chromatographs (GC), but are also turning their interest to spectroscopy systems, such as UV and IR systems. Consequently, many analytical laboratories are urgently considering how to ensure data integrity for spectroscopy systems. This report describes an innovative solution for ensuring data integrity for such spectroscopy systems.

Keywords: Data integrity, spectroscopy system, and orphan data

1. References to Spectroscopy Systems by Regulatory Authorities

Compliance with data integrity requirements is already a pressing issue for companies that require GxP compliance. In addition to chromatography systems, such as LC and GC systems, regulatory authorities have now turned their attention to spectroscopy systems, such as UV and IR spectrophotometers. (See below.)

• MHRA (Medicines and Healthcare products Regulatory Agency) [1)]

It is common for companies to overlook systems of apparent lower complexity. However, with these systems, it may be possible to manipulate data or repeat testing to achieve a desired outcome with limited opportunity for detection (e.g. stand-alone systems with a user-configurable output such as ECG machines, FTIR, UV spectrophotometers).

• FDA (U.S. Food and Drug Administration) [2)]

For example, a spectral file created by FT-IR (Fourier transform infrared spectroscopy) can be reprocessed, but a static record or printout is fixed. This does not satisfy CGMP requirements to retain original records or true copies (§ 211.180(d)).

• WHO (World Health Organization) [3)]

Original dynamic electronic spectral files created by FT-IR, UV/Vis, and chromatography instruments can be reprocessed, but a pdf or printout is fixed or static and the ability to expand baselines, view the full spectrum, reprocess and interact dynamically with the data set would be lost in the PDF or printout.

• PIC/S [4)]

QC supervisors and managers should not be assigned as the system administrators for electronic systems in their laboratories (e.g., HPLC, GC, UV-Vis).

• PMDA (Pharmaceuticals and Medical Devices Agency) [5)]

Ensuring appropriate data integrity:

The following practices never occur in workplaces, do they?
PDF files of past IR test results are modified and printed.

⇒ Recycling test results

The above shows that regulatory authorities are not only interested in chromatography systems, such as LC and GC systems, but are also turning their attention to spectroscopy systems, such as UV and IR systems.

1 Analytical & Measuring Instruments Division

Table 1 Typical Data Integrity Compliance

		Chromatography (Data Acquisition and Management)	Spectroscopy *1	
			(Data Management)	(Data Acquisition)
Data	Acquisition	Yes	—	Yes
	Management	Yes	Yes *2	—
Audit Trail (Metadata)		Yes	—	Yes *2
Users		Yes	Yes *3	Yes *3
Security		Yes	Yes	Yes
Time (Time Stamp)		Yes		
Remarks		• Requires two servers, one for chromatography and one for spectroscopy. • Requires three types of software: (1) For chromatography data acquisition and management (2) For spectroscopy data management (3) For spectroscopy data acquisition • Not compatible with electronic data		

*1: This table is based on a case of using a data management system to manage spectroscopy data that differs from the brand of the spectroscopy system.
*2: In this example, spectroscopy data and audit trail data cannot be reviewed and managed in a unified manner.
*3: In this example, users that acquire spectroscopy data cannot be managed in the same manner as users that manage spectroscopy data.

2. FDA Warning Letters

The FDA website includes several examples of warning letters for spectroscopy systems that show how warning letters are now being issued specifically for UV and IR systems. (See below.)

• Warning Letter—Example (1) [6]

In response to this letter, provide details of your retrospective review of the HPLC and other laboratory data, such as Fourier transform infrared spectroscopy, gas chromatography, UV spectrophotometry, and (b)(4) analyzer data.

• Warning Letter—Example (2) [7]

You lacked controls to prevent the unauthorized manipulation of your laboratory's electronic raw data. Specifically, your infrared (IR) spectrometer did not have access controls to prevent deletion or alteration of raw data.

3. Data Integrity Compliance for Spectroscopy Systems

So, what sort of compliance is required for ensuring the integrity of data from spectroscopy systems?

In terms of the form of the data, spectroscopy data are considered dynamic data, as indicated in the FDA and WHO excerpts on the previous page, just like it is for chromatography data. Therefore, presumably a key point for compliance will be ensuring equivalence with chromatography systems.

4. Obstacles for Ensuring Data Integrity Compliance for Spectroscopy Systems: Audit Trail and User Management

As illustrated in Fig. 1, compliance is based on Good Manufacturing Practice (GMP), which is premised on the validation of systems and analytical methods. Furthermore, data, audit trail (metadata), and user operations must be correctly time-stamped in a secure environment. If a laboratory has both chromatography and spectroscopy systems, the elements shown in Fig. 1 apply to both chromatography and spectroscopy systems, such that compliance with data integrity requirements results in the complicated operations indicated in Table 1.

Typical systems retain audit trail data (metadata) within the spectroscopy data acquisition system as indicated in Table 1, but cannot manage spectroscopy and audit trail data in a unified manner. (That means the data cannot be managed in a linked state.) The same applies to the user management. Typical systems cannot manage data management users and data acquisition users in a unified manner.

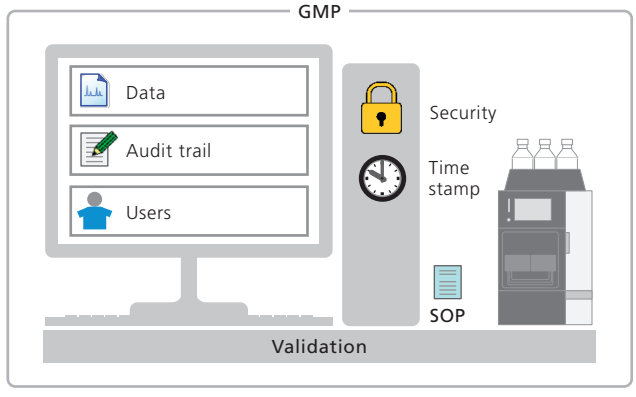

Fig. 1 Illustration of Data Integrity Compliance

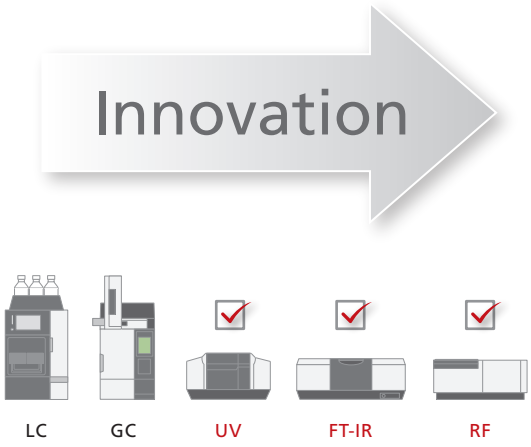

Table 2 Innovative Data Integrity Compliance

		Chromatography and Spectroscopy (Data Acquisition and Management)
Data	Acquisition	Yes
	Management	Yes
Audit Trail (Metadata)		Yes *4
Users		Yes
Security		Yes
Time (Time Stamp)		Yes
Remarks		• One server • One software program *5 • Compatible with electronic data

*4: Spectroscopy data and audit trail data can be reviewed and managed in a unified manner.
*5: In this case, "one software program" means all the elements indicated in Fig. 1 can be managed in a unified manner.

Due to the current attention on data integrity, focus has shifted toward providing evidence to reviewers that no improper operations were performed with respect to analytical results. However, this approach represents a policy of punishing any practice that appears suspicious, which is a major departure from the approach used in previous investigations.[8)] This approach applies to both chromatography and spectroscopy systems, which means the conventional approach cannot be used to ensure appropriate compliance.

5. Innovative Data Integrity Compliance

Therefore, considering that data integrity compliance for spectroscopy systems could present a major obstacle for operating analytical laboratories in a regulated environment, there is a need for an innovative approach to ensuring data integrity that solves such problems. That is exactly what LabSolutions achieves.

LabSolutions takes full advantage of Shimadzu's unique position as a developer and manufacturer of a wide variety of analytical instruments. Therefore, Shimadzu is able to offer a unique solution for data integrity compliance that is not limited to chromatography systems, but can also comprehensively include UV and IR systems and other spectroscopy systems in the LabSolutions family. (See Table 2.)

In other words, Shimadzu successfully integrated operations for ensuring data integrity by deploying the LabSolutions Report Set function [9)], which received excellent reviews for ensuring compliance with data integrity requirements for chromatography systems, for use in ensuring data integrity compliance for spectroscopy systems. A key feature of the report set is that it includes all the information necessary for validating data integrity, as shown in Fig. 2, step (3) Complete a set of reports.

6. Procedure for Using LabSolutions to Create a Report Set for Spectroscopy Systems

The procedure for creating a report set for spectroscopy systems corresponds to the procedure for chromatography systems, so the report set can be created using the same simple operations for both types of systems. As shown in Fig. 2, the procedure steps are (1) select the desired files, (2) right-click on the files and click [Create Report Set] on the right-click menu, and (3) complete the report set. Completed report sets are automatically stored in a database to prevent replacing, altering, destroying, or otherwise tampering with the data.

When a report set is created, it generates an electronic link between the electronic data and the report set, which also automatically disables (locks) editing the electronic data. That means editing or otherwise tampering with electronic data can be prevented after reports are created.

In this case, electronic signatures can be used not only for reviewing and approving report sets, but also for reviewing and approving the electronic data (analytical results) on which report sets are based. Using electronic signatures also eliminates the need to print out and sign reports manually and enables a paperless operation, which eliminates the need for redundant management of both electronic and paper records. That also solves the problems associated with paper records, such as replacement, alteration, or disposal of records.

Additionally, as shown in Fig. 2, data lines are color-coded when electronically approved, so they can be easily differentiated from remaining data that has not been reviewed or approved. That ensures orphan data can be identified easily, just as it can be for chromatography systems.

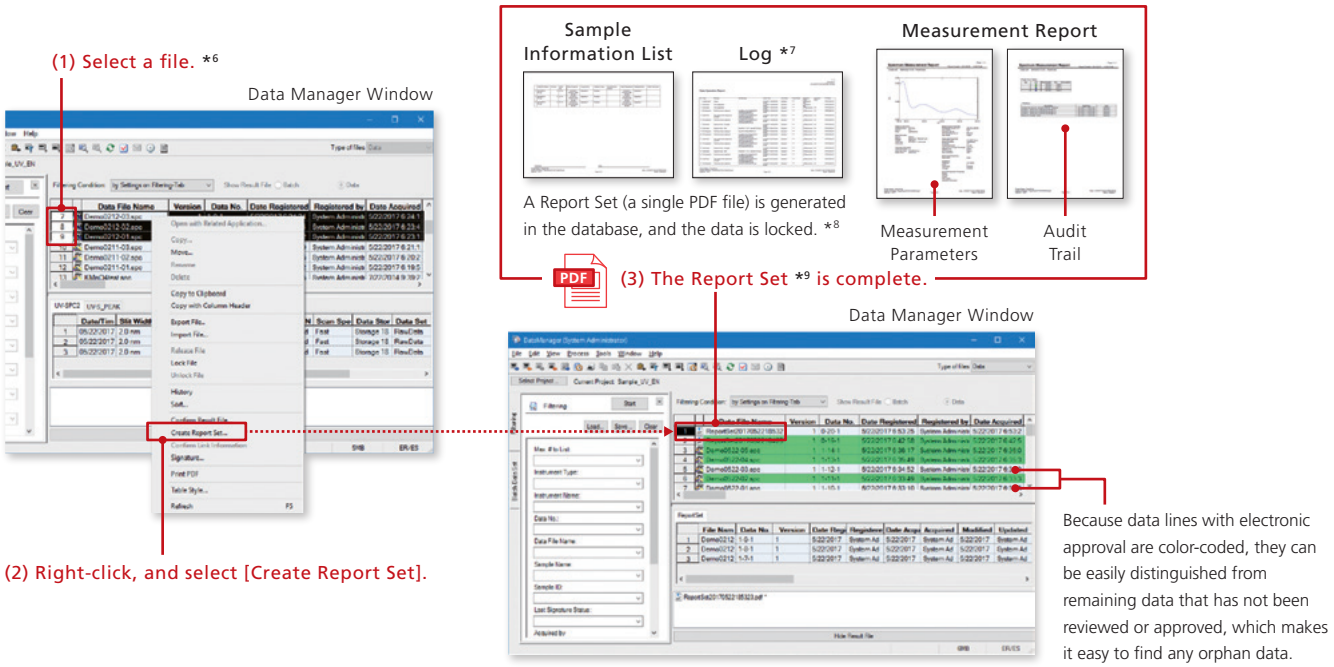

Fig. 2 Procedure for Using LabSolutions to Create a Report Set for Spectroscopy Systems *6

*6: If one UV photometric data file is selected for creating a report set, then the created report set will include files related to the selected file. If there are multiple related files for UV, FTIR, or RF confirmation testing, then the related files are selected manually.
*7: The log file includes information recorded during measurements (a log record of operations performed between logging in for measurements and logging out). If postrun analysis is performed, a postrun analysis log is recorded (a log record of operations performed between logging in for postrun analysis and logging out) separately from the measurement log.
*8: Locked files can only be unlocked by people with the right to do so.
*9: For UV, FTIR, and RF report sets, support for functions (1) to (3) will be available in the future.
(1) Assigning ID codes to measurement methods (2) Avoiding superimposed printing of measurement methods for multiple sets of data
(3) Measuring sequences. However, this is already supported for UV quantitative testing (photometric). See *6.

Reference

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