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Drug Discovery and Development

SCIEX
The Power of Precision

How to ensure compliance for your biotherapeutics from development throughout quality control (QC)

Featuring SCIEX OS Software

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Mass spectrometry (MS) is increasingly used as an analytical method for the characterization and quantification of biotherapeutics across the entire production pipeline (Figure 1), from early development stages to the final production. This approach provides information-rich, specific results. It allows both specific countermeasures and a reduction in time and resources. Being used at different stages of the biotherapeutics life cycle, MS acquisition and analysis systems have to cope with very different requirements (Figure 1). While in the discovery and early development phases, freedom and flexibility are needed. During later stages, as in quality assurance and control (QA/QC), ease of use and the fulfillment of regulatory requirements (above all) are mandatory. In addition, analytical methods that are developed during early phases, without validation and regulations, need to be transferred to the later stages for routine analysis in a regulated environment. SCIEX OS Software is a GxP compliant-ready solution that integrates data acquisition and processing allowing for flexibility while meeting compliance requirements.

Key features of SCIEX OS Software

- A single, easy-to-use software for streamlining workflows through method development, data acquisition and the analysis of qualitative and quantitative data—eliminating the need for learning different software packages

- GxP compliant-ready system with great flexibility in defining customized user roles, adjusting to the specific needs for each individual laboratory

- Easy to set up and customize audit trail functionalities assuring data integrity and traceability, with the possibility to create compliant-based projects and/or workstation

- Fully customizable workflows for characterization and quantification of the biotherapeutics in a compliant environment, including intact, subunit and peptide-based MAM workflows, as well as intact, subunit and peptide-based quantification workflows
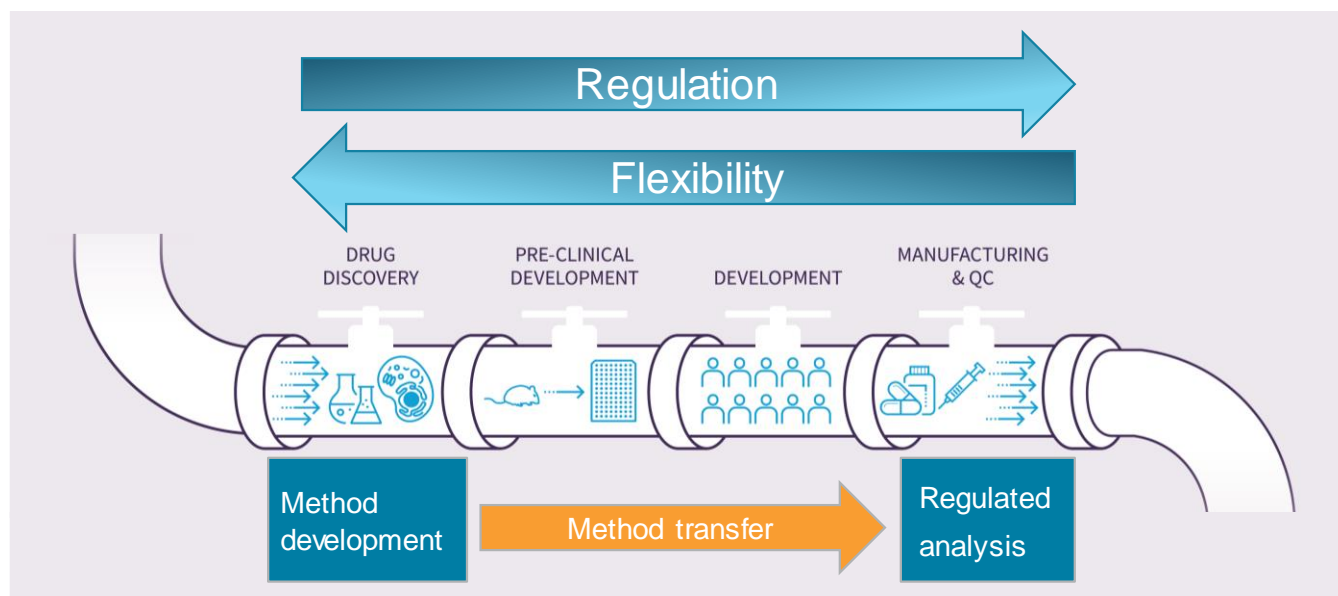

Figure 1. At different stages during the life cycle of a biotherapeutic, the analytical systems must fulfill different requirements. Moving downstream from drug discovery and early development to manufacturing and QC, the methods developed initially without regulations must be made routine and carried out in a strictly regulated manner.

Methods

***Chromatography and mass spectrometry*:** Data from two studies were used for showcasing the GxP features within SCIEX OS Software 2.0.[1,2]

The first set of data shows a liability study to monitor antibody subunit oxidation assessed by an intact multiple attribute methodology (MAM) workflow. Subunit data for the NIST mAb were acquired using an ExionLC™ System coupled to a SCIEX X500B System as described earlier.[1]

The second set is focusing on peptide quantification in rat plasma. Here, a series of surrogate peptides, spiked in a biological matrix, were quantified using an MRM approach. It was performed using an ExionLC™ System coupled to a SCIEX 7500 System as described earlier.[2]

Data processing: All data were processed using the Analytics module in SCIEX OS Software 2.0.

Overview

SCIEX OS Software is a GxP compliant-ready solution that integrates data acquisition with the SCIEX X500 Series QTOF Systems and the SCIEX Triple Quad™ 7500 LC-MS/MS System – QTRAP® Ready and processes data measured on all SCIEX platforms. By learning just one software, even less experienced MS users can be trained rapidly to acquire and convert raw MS data into product quality attribute results. The software offers

Figure 2. User and role management in SCIEX OS Software. Upper pane: system users and/or user groups with either predefined or customized roles. Bottom pane: each user has specific permissions. New roles can be configured: 1. Add new role; 2. Choose among the available roles to use as a template; 3. Configure the new role by assigning specific access privileges.

ample flexibility in defining security settings, by allowing the creation of customized user roles with different levels of access to the software's control. Traceability and data integrity is guaranteed by comprehensive and easily readable audit trails.

The audit trail function allows users to carry out a variety of qualitative and quantitative workflows while ensuring compliance, including multiple attribute methodology (MAM) at the intact, subunit and peptide level, and classical analyte quantification, such as targeted peptide quantification and intact protein quantification (including reconstruction). These workflows support the characterization and quantification of biotherapeutics in a single, compliant-ready software.

The possibility to utilize this software for data acquisition and processing in both regulated and non-regulated environments will speed up method development and facilitate the subsequent method transfer to the downstream processes.

Flexibly configurable security settings

SCIEX OS Software and Windows have integrated security features designed to control system and data access. SCIEX OS Software offers two log on modes for a compliant-ready set-up:

- Integrated security mode: the Windows user has direct access to the SCIEX OS Software upon login at Windows, if the Windows user is also being defined as a user in SCIEX OS

- Mixed mode: users log on to Windows and to the SCIEX OS Software separately

In mixed mode, a group of users can log on to Windows, but each individual requires credentials for accessing SCIEX OS Software. With this mode, additional security features can be activated, such as a screen lock after a defined period of inactivity followed by automatically logging the user off—without affecting data acquisition and processing.

Users can be managed within the SCIEX OS Software by the administrator, who is able to add or remove users and assign functional privileges to them (Figure 2). Different user roles can coexist with more or less access to critical instrument and software functions, as desired: administrator, method developer, analyst and reviewer (see Figure 2). While the administrator has the right to modify settings and has access to all actions, QC operators, for example, can be restricted to only process the acquired data and explore the results.
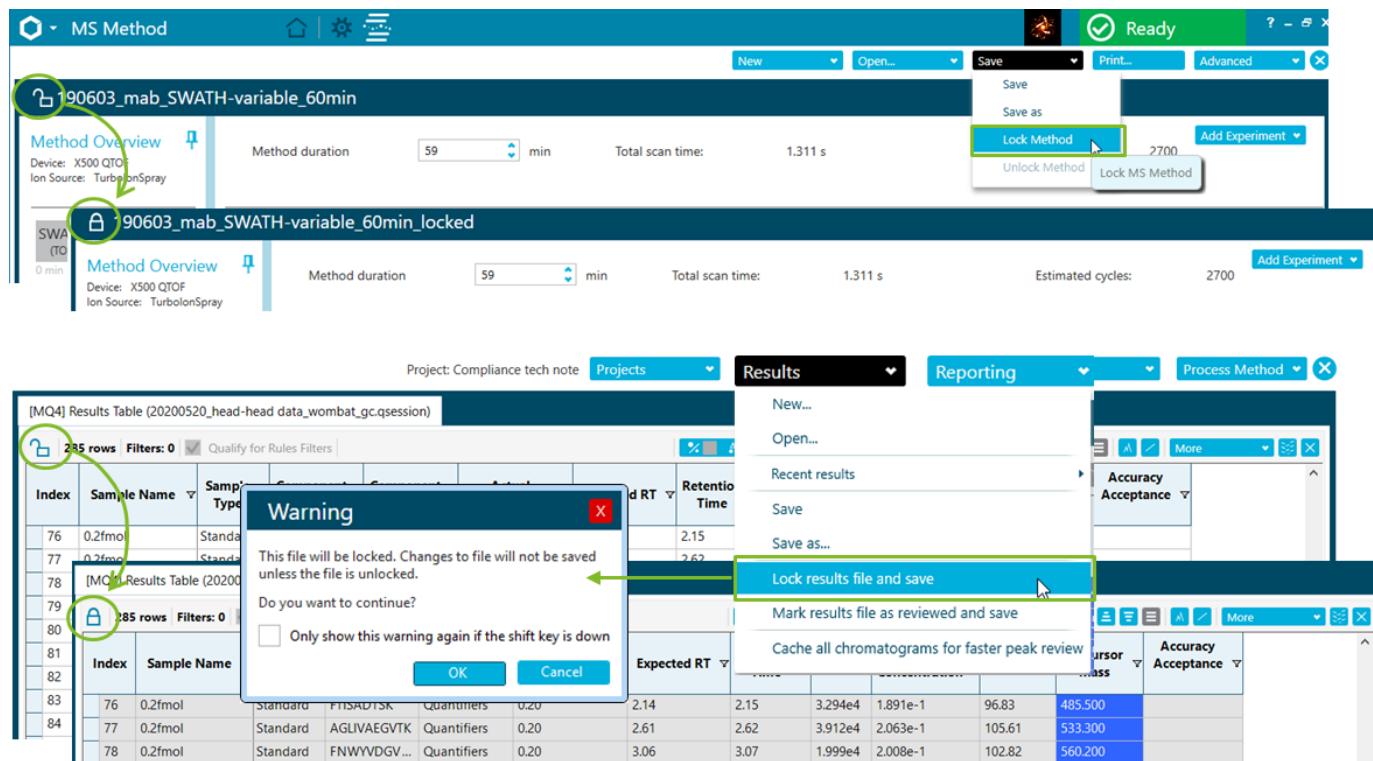
Figure 3. Locking of methods and result files. Top: defined users, such as method developers, have the right to build and modify LC or MS methods. Subsequently the methods can be locked to be used by other roles for running sample batches. Locked methods cannot be modified anymore once locked. Bottom: after processing raw data, the final result files can be locked to prevent any undesired modifications. Users with restricted permissions, as reviewers, are only allowed to review the results.

User role settings can grant permission to build LC or MS methods, to modify the existing ones and to run batches with unlocked acquisition methods to administrators and method developers only. After an LC and/or MS method has been optimized, method developers can lock the methods to protect it from further changes (Figure 3, top). Permission to run batches can be denied for other roles, or limited to locked LC and MS methods to prevent errors. In a similar way, result tables can be locked after processing the data and made available exclusively for review by specified users (Figure 3, bottom).

Audit trails ensuring full traceability

To ensure data integrity it is a requirement by regulatory agencies to record the full history of changes that are made by users within the software.[3] SCIEX OS Software provides a system of audit trails to fully meet these requirements of electronic record-keeping. Audit trails are files that store records of the audited events. The events that are audited are defined by the lab administrator within the audit maps on a workstation and/or project basis. The workstation-focused audit trail reports on actions around the MS control, like changes to the instrument configuration, tuning of the MS instrument or sample acquisition

and also tracks potential changes of the security and audit trial settings. In comparison, any actions applied to the processing methods, such as modification of the method parameters, are linked to specific projects and are reported in the project audit trail. Workstation and project-based audit trails can be set up independently. In addition, the audit trail settings allow selecting which of the events that are audited require the operator to give reasons for the change and which ones must be confirmed by an electronic signature (Figure 4).

In order to simplify the setup, ready-to-use audit map templates are available to easily create customized audit trails tailored to the specific laboratory needs. As an example, a change in the processing parameters in the Analytics module in SCIEX OS Software caused the '*Confirm Change Events*' window to pop up. As shown in Figure 4, the mass tolerance in the intact MAM workflow was changed from 5 to 2 Da (see reporting in the top panel). In this specific case, a reason for the change must be provided. The user can select from 10 pre-defined reasons, or free text can be typed in the respective field. Finally, the change has to be confirmed by entering the user's password.

All changes, whether project or workstation based, can be found and visualized in the audit trail pane in the SCIEX OS Software
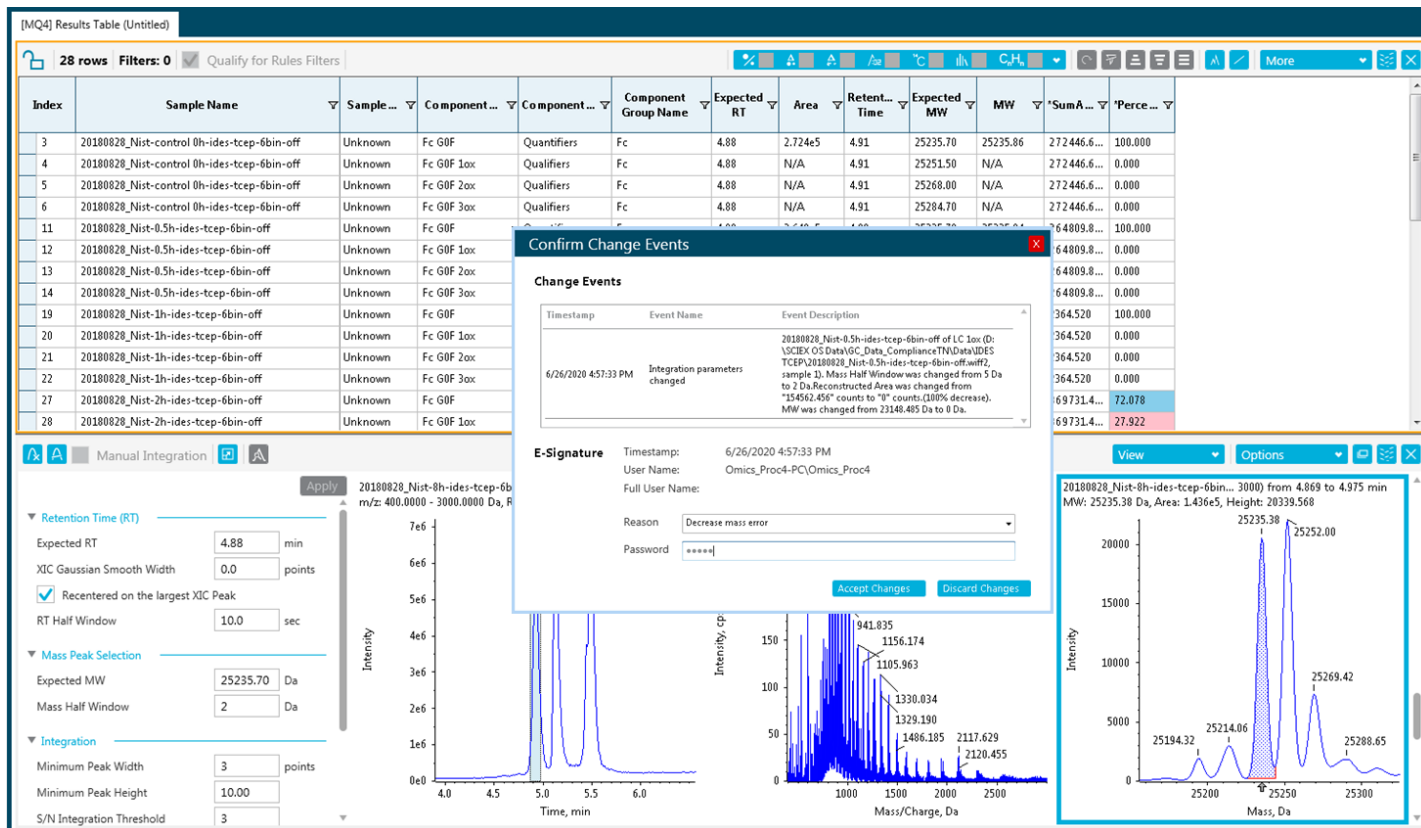

Figure 4. Request for an electronic signature in the Analytics module in SCIEX OS Software. Audit trails can be optionally configured to require a justification and password confirmation for any change made to the system. In this example a processing parameter for peak selection (*Mass Half Window)* within the intact protein MAM workflow was adjusted by the user.
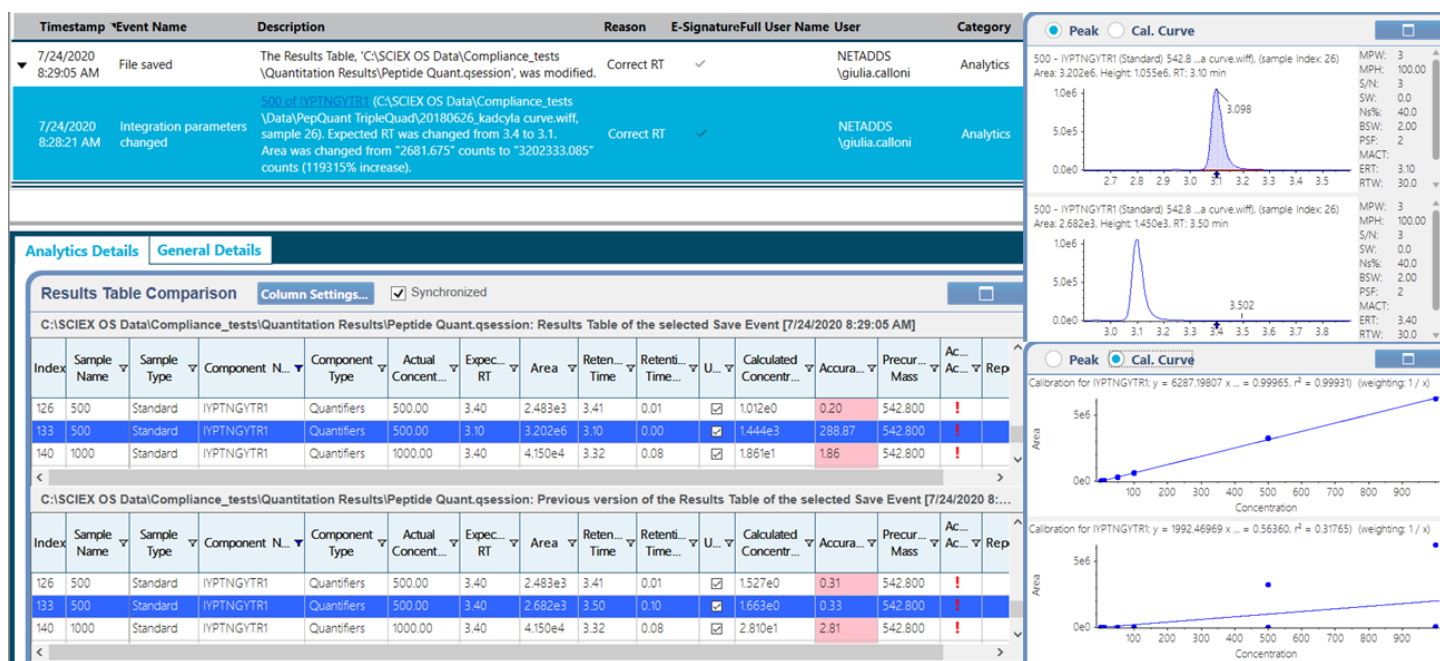
Figure 5. Audit trail window. All the workstation and project changes are tracked in SCIEX OS Software. The audited events are summarized in a table format (upper panel) reporting a description of the event and the user responsible for it. For any action that modifies the results of a processing method, the changes in the result table (left panel), peak integration and calibration curve (right panel) are displayed with a direct comparison of the results before and after the change. In this example, the expected RT parameter was adjusted within the peptide quantification workflow of SCIEX OS Software.

(Figure 5). Here, audited events are listed by reporting date and time including a description of the event and the user that signed off on the change (Figure 5, top). If the change impacted the processing method, the software visualizes the data automatically (result table, peak integration and calibration curve) and allows a direct comparison of the results before and after the change (Figure 5, bottom). The example in Figure 5 refers to a quantification workflow carried out using surrogate peptides spiked in rat plasma[2] with full audit trail activated: the user modified the peak integration parameters for one of the analytes by changing its expected retention time from 3.40 to 3.1 min, which was listed in the project audit trail including the visualization of the difference introduced by the change (Figure 5).

The comprehensive audit trail function allows for retracing all steps which were taken from the raw data acquisition to the final results guaranteeing data integrity and alignment with regulatory requirements.

Audit trails can be visualized within SCIEX OS Software in an easily navigable interface that can be searched, filtered and sorted. In addition, audit trails can be exported and saved in the .csv file format. Time audit records accumulate in the project audit trail and can create large files that become difficult to manage. When an audit trail reaches a given number of records (20,000), it is automatically archived. A final archive record is added to the

audit trail, and the audit trail is saved with a name indicating the type of audit trail, the date and time.

Conclusions

- SCIEX OS Software is a unique solution integrating data acquisition (SCIEX X500 Series QTOF Systems and the SCIEX 7500 System) and data processing of all SCIEX file formats in a compliant-ready way

- Flexible user-role definitions allow for controlled access to the software and mass spectrometer settings on a function-by-function basis

- An easily customizable project-based audit trail system offers the possibility to run compliant and non-compliant projects on the same workstation for full flexibility

- The audit trail function is compatible with any qualitative and quantitative workflow in SCIEX OS Software, allowing for processing in a single compliant environment

- All project or workstation-based events are stored in a central audit trail that allows the visualization of any change for full traceability and easy navigation through the records

- Audit trails can be exported and saved as CSV files for additional flexibility, and are automatically archived when the number of records exceeds a given number to maintain ease of navigation

References

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