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Ensuring Regulatory Compliance and Data Integrity with MassHunter Software Solutions

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Introduction

Paper based approaches to laboratory data integrity are no longer enough to meet today’s increased scrutiny of computerized systems. Per the regulations1,2, it is the responsibility of the user and their organization to ensure that the technical controls provided in the software are used appropriately to achieve compliance-readiness for laboratory data acquisition and data processing. When the technical controls are enabled, the SOPs have been implemented and are being enforced. Automated audit trails independently record user actions thus connecting laboratory staff to the work they perform. When combined, this enables a lab to show attribution of work3. In this study, several key biopharma analysis workflows are demonstrated with technical controls enabled.

Figure 1 Agilent 6545XT AdvanceBio LC/Q-TOF.

Experimental

Instrumental Analysis

All LC/MS data files used in the data analysis were generated on an Agilent 1290 Infinity II UHPLC system coupled with an Agilent 6545XT AdvanceBio LC/Q-TOF system equipped with an Agilent Dual Jet Stream ESI source (Figure 1). The instrument system was controlled by MassHunter Networked Workstation for LC/TOF and LC/Q-TOF 11.0 .

Data Analysis

Data analysis was performed using Agilent MassHunter BioConfirm Networked Workstation 11.0.

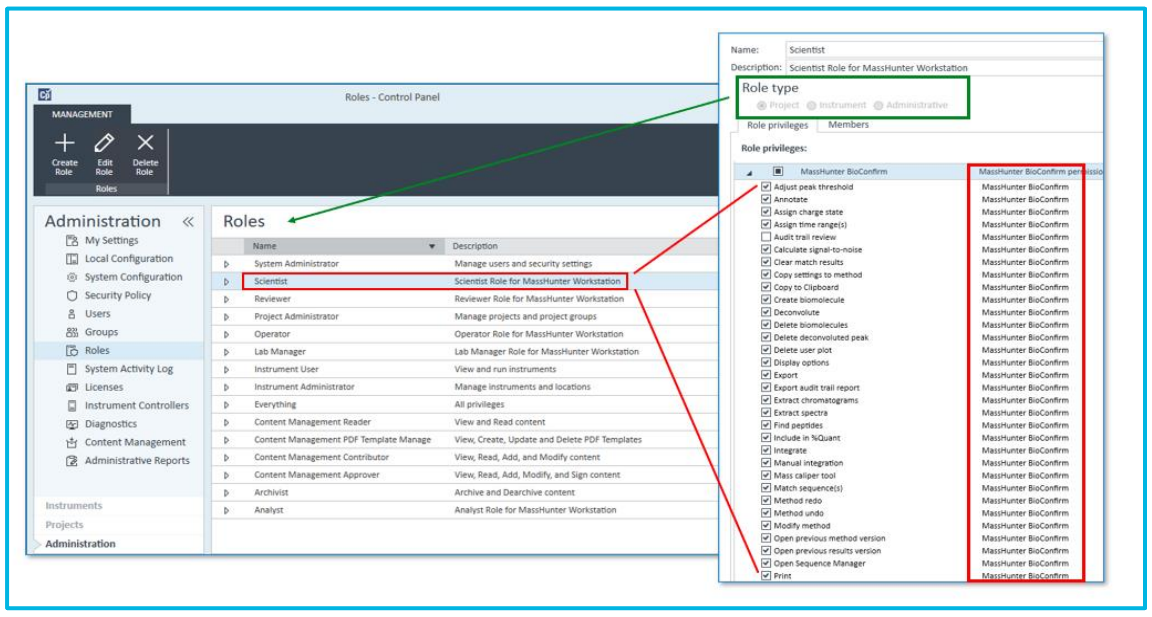
The acquisition and data analysis PC was connected by secure Ethernet to an OpenLab ECM XT 2.5 server.

Highlights on key features

- One location for user and project management for MassHunter Acquisition, Quantitative Analysis, and BioConfirm.
- Data integrity with OpenLab Server/ECM XT content management.
- Traceability with audit trails and activity logs.
- Software feature restricted with permission controls.

User Management

User management is one of the key requirements for labs whit data integrity obligation. A user can be defined as an individual who operates instruments where data is being collected or an individual who processes the acquired data and generates reports. For the administrator, they need to be able to restrict access to electronic records. Electronic records can be defined as Worklists, Methods, Data Analysis Methods, Reports, Report Templates, and Audit Trails (Figure 2 and 3).



Name	Description
System Administrator	Manage users and security settings
Scientist	Scientist Role for MassHunter Workstation
Reviewer	Reviewer Role for MassHunter Workstation
Project Administrator	Manage projects and project groups
Operator	Operator Role for MassHunter Workstation
Lab Manager	Lab Manager Role for MassHunter Workstation
Instrument User	View and run instruments
Instrument Administrator	Manage instruments and locations
Everything	All privileges
Content Management Reader	View and Read content
Content Management PDF Template Manage	View, Create, Update and Delete PDF Templates
Content Management Contributor	View, Read, Add, and Modify content
Content Management Approver	View, Read, Add, Modify, and Sign content
Archivist	Archive and Dearchive content
Analyst	Analyst Role for MassHunter Workstation

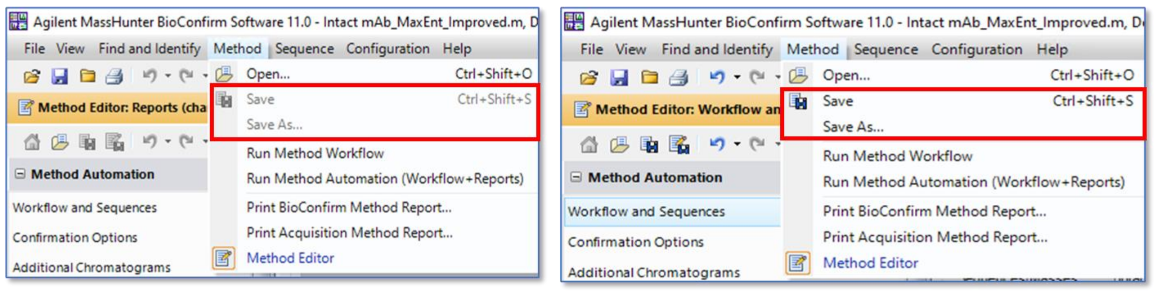
Name: Scientist

Description: Scientist Role for MassHunter Workstation

Role privileges:

■ MassHunter BioConfirm	MassHunter BioConfirm permissio
☑ Adjust peak threshold	MassHunter BioConfirm
☑ Annotate	MassHunter BioConfirm
☑ Assign charge state	MassHunter BioConfirm
☑ Assign time range(s)	MassHunter BioConfirm
□ Audit trail review	MassHunter BioConfirm
☑ Calculate signal-to-noise	MassHunter BioConfirm
☑ Clear match results	MassHunter BioConfirm
☑ Copy settings to method	MassHunter BioConfirm
☑ Copy to Clipboard	MassHunter BioConfirm
☑ Create biomolecule	MassHunter BioConfirm
☑ Deconvolute	MassHunter BioConfirm
☑ Delete biomolecules	MassHunter BioConfirm
☑ Delete deconvoluted peak	MassHunter BioConfirm
☑ Delete user plot	MassHunter BioConfirm
☑ Display options	MassHunter BioConfirm
☑ Export	MassHunter BioConfirm
☑ Export audit trail report	MassHunter BioConfirm
☑ Extract chromatograms	MassHunter BioConfirm
☑ Extract spectra	MassHunter BioConfirm
☑ Find peptides	MassHunter BioConfirm
☑ Include in %Quant	MassHunter BioConfirm
☑ Integrate	MassHunter BioConfirm
☑ Manual integration	MassHunter BioConfirm
☑ Mass caliper tool	MassHunter BioConfirm
☑ Match sequence(s)	MassHunter BioConfirm
☑ Method redo	MassHunter BioConfirm
☑ Method undo	MassHunter BioConfirm
☑ Modify method	MassHunter BioConfirm
☑ Open previous method version	MassHunter BioConfirm
☑ Open previous results version	MassHunter BioConfirm
☑ Open Sequence Manager	MassHunter BioConfirm
☑ Print	MassHunter BioConfirm

Figure 2. In the Control Panel, the system administrator has full control over all roles with defined privileges for data acquisition and data analysis.


Agilent MassHunter BioConfirm Software 11.0 - Intact mAb_MaxEnt_Improved.m, D
File View Find and Identify Method Sequence Configuration Help
Method Editor: Reports (cha
Method Automation
Workflow and Sequences
Confirmation Options
Additional Chromatograms
Open... Ctrl+Shift+O
Save Ctrl+Shift+S
Save As...
Run Method Workflow
Run Method Automation (Workflow+Reports)
Print BioConfirm Method Report...
Print Acquisition Method Report...
Method Editor
Agilent MassHunter BioConfirm Software 11.0 - Intact mAb_MaxEnt_Improved.m, D
File View Find and Identify Method Sequence Configuration Help
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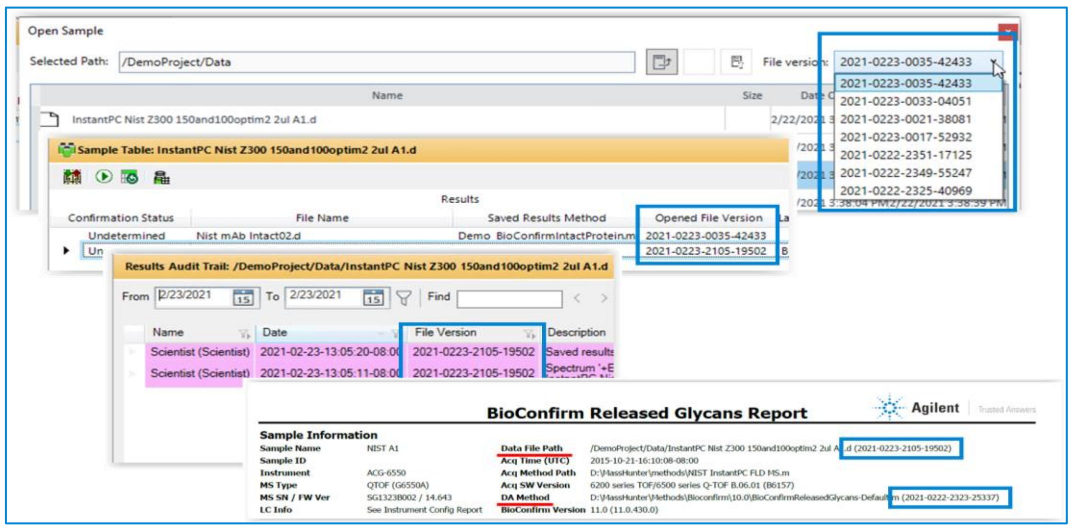
Workflow and Sequences
Confirmation Options
Additional Chromatograms
Open... Ctrl+Shift+O
Save Ctrl+Shift+S
Save As...
Run Method Workflow
Run Method Automation (Workflow+Reports)
Print BioConfirm Method Report...
Print Acquisition Method Report...
Method Editor

Figure 3. The system admin can assign specific permissions to certain roles. For example, 'Lab Operator' (left) can only open data file but cannot save method or create/run/save worklist as 'Scientist' (right) does.

Data integrity with OpenLab Server/ECM XT content management

MassHunter 11.0 with OpenLab Server/ECM XT and Control Panel integration supplies several tools for data integrity. These tools include secured and central storage, file encryption, built-in archiving, life cycle management, and file versioning (Figure 4 and 5).



Selected Path: /DemoProject/Data

File version: 2021-0223-0035-42433

2021-0223-0035-42433
2021-0223-0033-04051
2021-0223-0021-38081
2021-0223-0017-52932
2021-0222-2351-17125
2021-0222-2349-55247
2021-0222-2325-40969

InstantPC Nist Z300 150and100optim2 2ul A1.d

Sample Table: InstantPC Nist Z300 150and100optim2 2ul A1.d

Confirmation Status	File Name	Saved Results Method	Opened File Version
Undetermined	Nist mAb Intact02.d	Demo BioConfirmIntactProtein.m	2021-0223-0035-42433
Un			2021-0223-2105-19502

Results Audit Trail: /DemoProject/Data/InstantPC Nist Z300 150and100optim2 2ul A1.d

From 2/23/2021 To 2/23/2021 Find

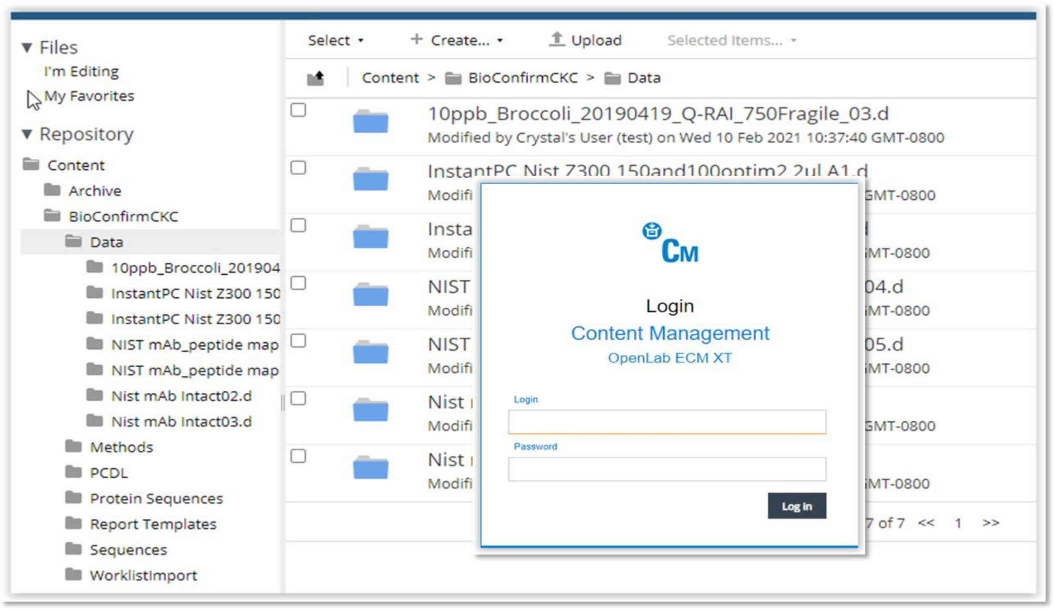
Name	Date	File Version	Description
Scientist (Scientist)	2021-02-23-13:05:20-08:00	2021-0223-2105-19502	Saved results
Scientist (Scientist)	2021-02-23-13:05:11-08:00	2021-0223-2105-19502	Spectrum '+E

BioConfirm Released Glycans Report

Sample Information

Sample Name	NIST A1	Data File Path	/DemoProject/Data/InstantPC Nist Z300 150and100optim2 2ul A1.d (2021-0223-2105-19502)
Sample ID		Acq Time (UTC)	2015-10-21-16:10:08-08:00
Instrument	ACG-6550	Acq Method Path	D:\MassHunter\methods\NIST InstantPC FLD MS.m
MS Type	QTOF (G6550A)	Acq SW Version	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)
MS SN / FW Ver	SG1323B002 / 14.643	DA Method	D:\MassHunter\Methods\Bioconfirm\10.0\BioConfirmReleasedGlycans-Default.m (2021-0222-2323-25337)
LC Info	See Instrument Config Report	BioConfirm Version	11.0 (11.0.430.0)

Figure 4. Versioning is enabled in MassHunter data analysis programs.



10ppb_Broccoli_20190419_Q-RAI_750Fragile_03.d
Modified by Crystal's User (test) on Wed 10 Feb 2021 10:37:40 GMT-0800

InstantPC Nist Z300 150and100optim2 2ul A1.d
Modifi GMT-0800

Insta
Modifi MT-0800

NIST 04.d
Modifi MT-0800

NIST 05.d
Modifi MT-0800

Nist
Modifi GMT-0800

Nist
Modifi MT-0800

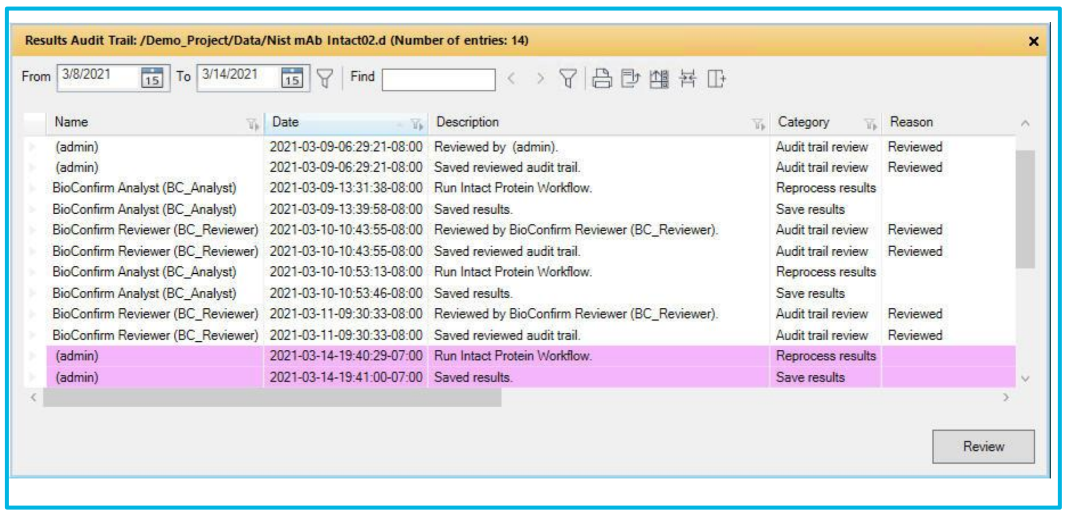
Figure 5. Data is securely backed up and stored in the ECM XT server. User login/password is required to export data out of content management.

Traceability

Another vital component of regulatory compliance is traceability. Traceability is to understand the lifetime of a record. What was done to it, who did it, why it was done, and when it was done are all critical pieces of information necessary to be able to trace the lifetime of a record.

Two types of audit trails are included in MassHunter: System activity logs, and application record audit trails. The system activity log tracks any changes that happen, at an elevated level to the system, such as login/logout actions, opening applications, etc. Application audit trails track any changes to specific records on the system, such as a change to a method or result file (Figure 6).

Results and Discussion



Results Audit Trail: /Demo_Project/Data/Nist mAb Intact02.d (Number of entries: 14)

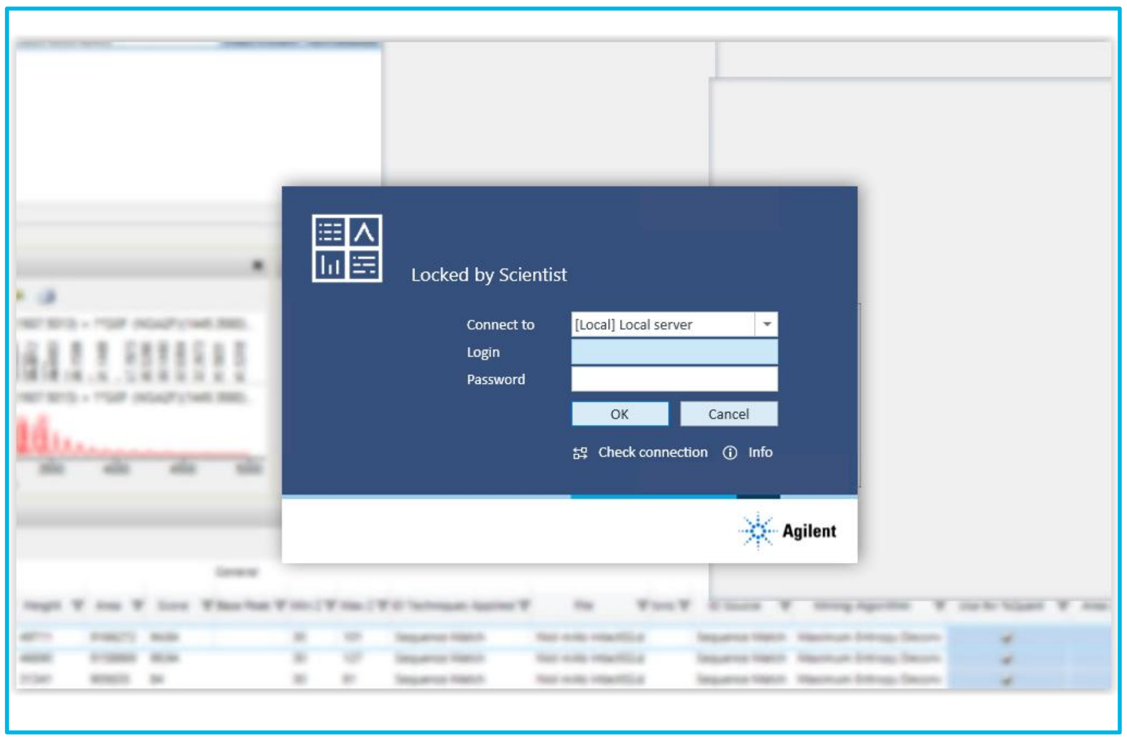
From 3/8/2021 To 3/14/2021 Find

Name	Date	Description	Category	Reason
(admin)	2021-03-09-06:29:21-08:00	Reviewed by (admin).	Audit trail review	Reviewed
(admin)	2021-03-09-06:29:21-08:00	Saved reviewed audit trail.	Audit trail review	Reviewed
BioConfirm Analyst (BC_Analyst)	2021-03-09-13:31:38-08:00	Run Intact Protein Workflow.	Reprocess results	
BioConfirm Analyst (BC_Analyst)	2021-03-09-13:39:58-08:00	Saved results.	Save results	
BioConfirm Reviewer (BC_Reviewer)	2021-03-10-10:43:55-08:00	Reviewed by BioConfirm Reviewer (BC_Reviewer).	Audit trail review	Reviewed
BioConfirm Reviewer (BC_Reviewer)	2021-03-10-10:43:55-08:00	Saved reviewed audit trail.	Audit trail review	Reviewed
BioConfirm Analyst (BC_Analyst)	2021-03-10-10:53:13-08:00	Run Intact Protein Workflow.	Reprocess results	
BioConfirm Analyst (BC_Analyst)	2021-03-10-10:53:46-08:00	Saved results.	Save results	
BioConfirm Reviewer (BC_Reviewer)	2021-03-11-09:30:33-08:00	Reviewed by BioConfirm Reviewer (BC_Reviewer).	Audit trail review	Reviewed
BioConfirm Reviewer (BC_Reviewer)	2021-03-11-09:30:33-08:00	Saved reviewed audit trail.	Audit trail review	Reviewed
(admin)	2021-03-14-19:40:29-07:00	Run Intact Protein Workflow.	Reprocess results	
(admin)	2021-03-14-19:41:00-07:00	Saved results.	Save results	

Figure 6. Results Audit Trail from BioConfirm 11.0. Audit Trail entries that have not been reviewed are highlighted in color.

Security of electronic records

To support the security requirements, OpenLab Server/ECM XT software performs automatic collection, organization, and storage of data. All data archived is versioned on the server so that older results can be reconstructed if necessary. Users can access results and reports remotely, allowing instruments and staff to continue working during data reviews and inspections. All data acquisition and data analysis programs can be locked to prevent unauthorized access. A valid user login and password is needed to unlock the programs. (Figure 7).



Locked by Scientist

Connect to: [Local] Local server

Login:

Password:

Figure 7 Locked BioConfirm with login screen and deliberately obscured software panel below it.

Electronic signatures

While 21 CFR Part 11 does not require the use of electronic signatures (eSignatures), without them a lab is committing to a hybrid paper/electronic record solution. The software system provides a means of eSigning documents. Opening the Content Browser on the OpenLab ECM XT Server allows users to access the files under content management. Browsing to a file in the project there is a check summed file set manifest which users with the appropriate permission can eSign to approve and lock the file. eSigning process requires user to enter Username, Password and selecting a Reason, e.g., approving the document**.**

Conclusions

Agilent MassHunter 11.0 which includes Acquisition, Quantitative Analysis, and BioConfirm, provides customers with excellent technical control tools for user management, data integrity and traceability. These tools have been carefully designed to enhance flexibility and improve the productivity of system administrators, end users and data reviewers, while providing the data integrity required by regulatory agencies.

References

11U.S. Food and Drug Administration. CFR - Code of Federal Regulations Title 21. Title 21—Food and Drugs, Chapter I—Food and Drug Administration Department of Health and Human Services. Part 11 Electronic Records; Electronics Signatures.
2Support for Title 21 CFR Part 11and Annex 11 Compliance: Agilent MassHunter for LC/TOF and LC/Q-TOF Systems, Agilent Technologies, publication number 5994-2902EN.
3Ensuring Regulatory Compliance and Data Integrity with MassHunter Software Solutions, Agilent Technologies, publication number 5994-3546EN.

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