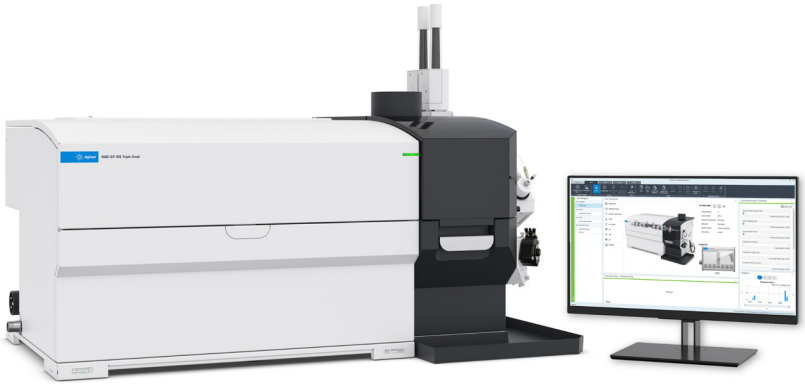
White Paper

Agilent
Trusted Answers

Meeting Regulatory Compliance Guidelines with Agilent OpenLab ICP-MS and OpenLab Enterprise Content Manager (ECM)



Overview

The United States Pharmacopeial Convention (USP) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) have developed standards to test for inorganic (elemental) impurities in pharmaceutical products and ingredients: USP General Chapters <232> (Elemental Impurities – Limits) and <233> (Elemental Impurities – Procedures) and ICH-Q3D. These standards were implemented globally between 2017 and 2018, and have since been updated and harmonized, with the latest revision of USP <233> becoming effective in 2026. The guidelines specify maximum daily exposure limits for the 24 elements listed in Table 1.

The full range of elemental impurity analysis can be performed using ICP-MS, including analysis of small sample amounts, and testing parenteral and inhalational medicines, where lower exposure limits apply and lower detection limits are thus required.

Table 1. USP <232>/ICH Q3D analytes and permitted daily exposure (PDE) limits for drugs intended for oral administration. PDEs for parenteral and inhalational medicines are significantly lower.

ICH/USP Class	Element	Oral PDE (µg/day)
Class 1	Cd	5
	Pb	5
	As (inorganic)	15
	Hg (inorganic)	30
Class 2A	Co	50
	V	100
	Ni	200
Class 2B	Tl	8
	Au	100
	Pd	100
	Ir	100
	Os	100
	Rh	100
	Ru	100
	Se	150
	Ag	150
	Pt	100
Class 3	Li	550
	Sb	1200
	Ba	1400
	Mo	3000
	Cu	3000
	Sn	6000
	Cr	11000

Apart from basic research and drug discovery, all stages of pharmaceutical product development (from pre-clinical assessment to manufacturing Quality Control) are subject to GxP guidelines. These include regulations for electronic data management as defined in Part 11 in Title 21 of the US Food and Drug Administration's Code of Federal Regulations (21 CFR Part 11), EU Annex 11 in Europe, and equivalent regulations in other regions.

Configurable compliance

Agilent OpenLab ICP-MS software can be integrated with a range of Agilent compliance solutions, covering laboratory requirements from a single instrument to a global enterprise. When integrated with OpenLab ECM and operated in combination with an overall laboratory compliance plan, OpenLab ICP-MS and its optional User Access Control (UAC) module with OpenLab Shared Services (OLSS) provide labs with the technical controls to facilitate meeting all electronic data management regulatory requirements.

With OpenLab ECM, all data and reports are stored after each run in a protected data repository. As well as providing secure data storage through a suitable server with RAID architecture, data stored in ECM is easy to find with simple keyword searching. Furthermore, ECM can delete files automatically at the end of the retention period.

ECM client access is through a web browser interface, allowing data to be downloaded for approval or reprocessing. All raw data, results, methods and reports are kept together in a protected zip package, enabling simple access to the original results for auditing throughout the retention period.

The system is configured so users must login with a unique username and password and data is always stored in the secure repository of OpenLab ECM. OpenLab ICP-MS's UAC/OLSS software module with OLSS includes an Audit Trail Map (Figure 1), which ensures that each user is assigned to a role that permits only the actions required, as appropriate for their job and training. Each action can also be setup to require user validation by password and/or reason, and all actions are included in the audit trail.

An Agilent ICP-MS or ICP-QQQ system, in combination with an Agilent data management system, is the most complete compliance solution for pharmaceutical labs implementing ICH Q3D or USP<232>/<233>.

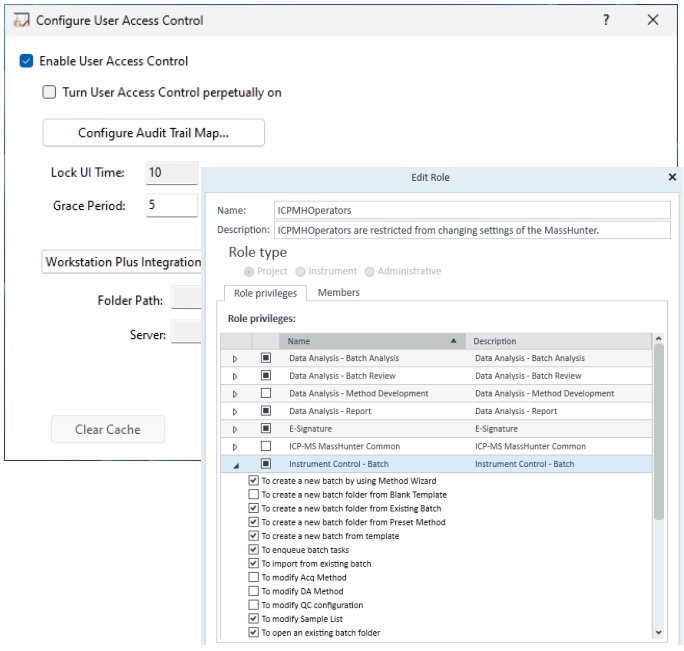


Figure 1. User Access Control pane of Agilent OpenLab ICP-MS, and a section the Audit Trail Map.

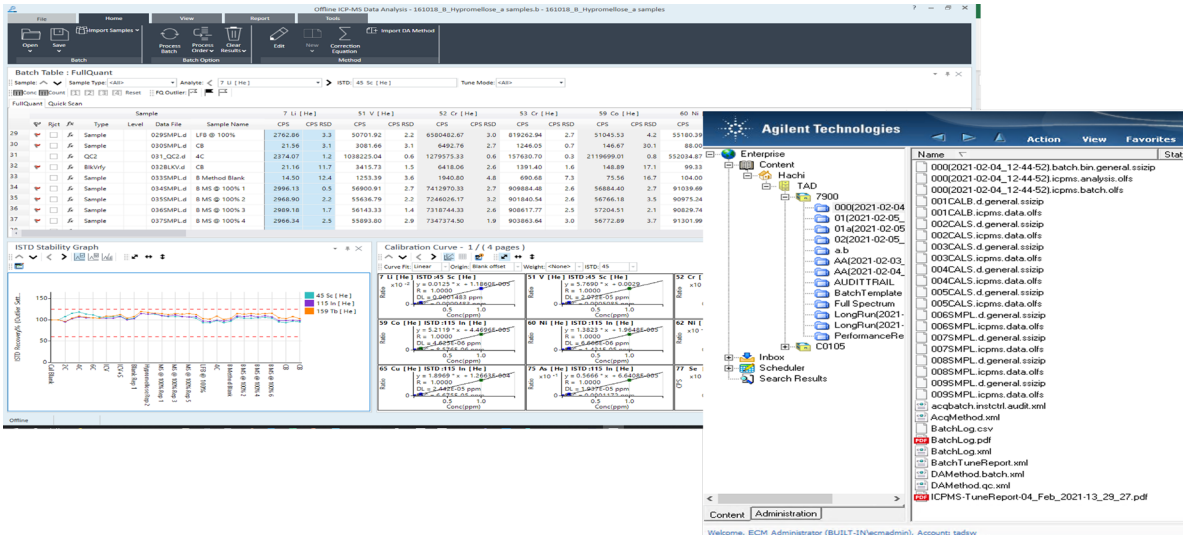


Figure 2. ICP-MS data and reports are automatically uploaded to OpenLab ECM.

Workflow overview

OpenLab ICP-MS integrates seamlessly with OpenLab ECM, with file upload occurring automatically, without user intervention. To the ICP-MS user there is no change in the normal OpenLab ICP-MS operation and acquisition workflow when connected to ECM.

A user with the appropriate level of user access rights logs onto the OpenLab ICP-MS Workstation and then operates the software in exactly the same way as standalone (not integrated with OpenLab) systems, within their level of user access rights.

As controlled records (such as tune reports, methods, batches, datafiles, and pdf reports) are generated in OpenLab ICP-MS, they are automatically stored in the secure repository of OpenLab ECM. The raw data, together with all necessary files that are needed for reprocessing of the OpenLab ICP-MS data batch, is stored in a checksum-protected zip package. This ensures that all necessary files and settings are included when the package is retrieved from the repository for audit, approval, or reprocessing. Should a record or group of records (such as a data batch) be altered and resaved, the new version is stored alongside the original version, and the version number is incremented. This ensures that no data is overwritten, all changes are traceable, and records can be audited throughout the retention period.

Finding and retrieving data

Records in the uploaded OpenLab ECM zip package are filtered so that individual records or results can easily be found with the search tools. OpenLab query items such as study name, batch name, analyst, acquisition date and time, instrument name, method name, and many more can be used to find and retrieve individual sample results or all records for a batch of samples. OpenLab's powerful search tools can also find data based on filtered metadata from the binary files.

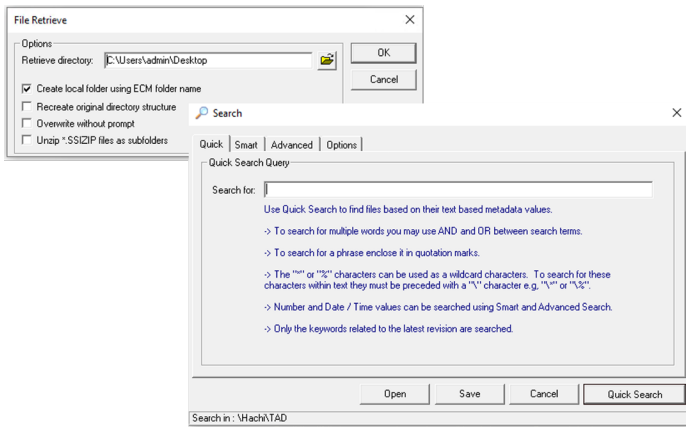


Figure 3. OpenLab ECM file retrieve and Quick Search Query dialogs.

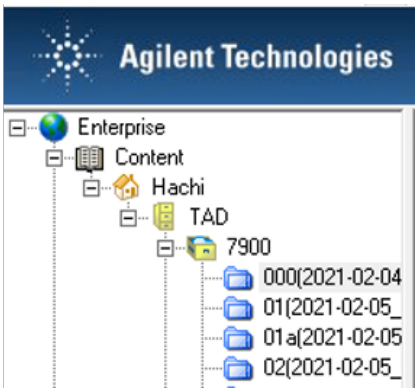


Figure 4. OpenLab ECM stores data or reports in a location > cabinet > drawer > folder (LCDF) file structure.

Meeting the Key Regulatory Requirements of 21 CFR Part 11 with Agilent OpenLab ICP-MS Software and OpenLab Enterprise Content Manager (ECM)

Part 11 or Others	Requirements*	Yes/No	If yes, how, specifically, is the requirement satisfied, or if no, what is the recommendation to customers?
1. Validation			
Part 11.10(a)	Is the system validated to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records?	Yes	Agilent has extensively validated the performance of its systems, including OpenLab ICP-MS, UAC/OLSS, and OpenLab ECM, with tests written specifically to evaluate accuracy, reliability, and consistent performance. OpenLab ECM maintains revisions of files as they are modified or altered. The solution also records any and all changes made to the system through computer-generated audit trails. Agilent recommends making use of Installation Qualification and Operation Qualification (IQ/OQ) services to qualify the on-site system.
2. Accurate Copies and Secure Retention and Retrieval of Records			
Part 11.10(b)	Is the system capable of generating accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the FDA?	Yes	Raw data, metadata and result data generated by OpenLab ICP-MS software are stored and managed in OpenLab ECM. The result set that holds all this information can be loaded at any time to the hard disk of a client PC as a copy of the original data for review. OpenLab ICP-MS software is required to read the electronic format. OpenLab ICP-MS reports (e.g., tuning reports and concentration data reports), representing the human-readable form of electronic records, can be stored as secured PDF files which can be printed or made available for review with a viewer without the source application installed on the client machine. These reports can include all data and audit trails.
Part 11.10(c):	Does the system protect records to enable their accurate and ready retrieval throughout the records retention period?	Yes	All electronic records are stored in OpenLab's secure, server-based ECM system, providing an additional level of data security beyond that provided by a single-PC based solution. Data and records are searchable and can be retrieved at any time.
3. Authorized Access to Systems, Functions, and Data			
Part 11.10(d);	Is system access limited to authorized persons?	Yes	Access to the OpenLab ICP-MS and OpenLab ECM system is controlled via a login with account username and password protection. Individual actions can be protected through the configurable system roles and permissions.
4. Electronic Audit Trail			
Part 11.10(e);	Is there a secure, computer-generated, time-stamped audit trail to independently record the date and time of operator entries and actions that create, modify, or delete electronic records?	Yes	OpenLab ECM and OpenLab ICP-MS with UAC/OLSS generate an audit entry for creation and modification of data and other files, and other relevant actions within the application software. Audit trail entries are non-editable and non-deletable. OpenLab ECM also stores all versions of the data and never overwrites previous data.
Part 11.10(e);	Is previously recorded information left unchanged when records are changed?	Yes	Strict security and revision control of the data generated by the OpenLab ICP-MS system is achieved with automatic storage of the result set or single runs in OpenLab ECM after acquisition, automatic reprocessing or any other interactive change. All entries in the OpenLab ICP-MS and OpenLab ECM audit trails are non-editable and non-deletable. Even the removal of records from OpenLab ECM by an authorized user does not affect existing entries in the audit trail.
Part 11.10(e);	Is audit trail documentation retained for a period at least as long as that required for the subject electronic record?	Yes	All audit trail information is stored in the system repository and kept throughout the electronic records retention period. The audit trails are unbreakably linked to the record. System-related activities such as logon events are also unbreakably linked to the system.
Part 11.10(e);	Is audit trail available for review and copying by the FDA?	Yes	Audit trails can be viewed through OpenLab ICP-MS software or the OpenLab ECM user interfaces. Audit trails and selected entries can be reported in a printable format.

** Descriptions taken from 21 CFR Part 11: www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=11*

Part 11 or Others	Requirements*	Yes/No	If yes, how, specifically, is the requirement satisfied, or if no, what is the recommendation to customers?
5. Operational and Device Checks			
Part 11.10(f)	Are there operational system checks to enforce permitted sequencing of steps and events, if required?	Yes	In all OpenLab ECM functions, when a sequence of events is required, the sequence is enforced by system checks. Likewise, in all OpenLab ICP-MS functions, when sequencing of events is required, system checks enforce it. For example, a method cannot be applied to data until the method has been validated for completeness. Users are prompted with an error message when steps are performed out of sequence.
Part 11.10(g);	Are there authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand?	Yes	Users cannot gain access to the Workstation, OpenLab ICP-MS software or OpenLab ECM without a valid username, password and account. Once logged in, all file access is determined by the privileges assigned n UAC/ OLSS and ECM.
Part 11.10(h)	Does the system allow to use device checks to determine, as appropriate, the validity of the source of data input or operational instruction?	Yes	Data source device identity in the form of the instrument serial number is transferred from the ICP-MS instrument to the OpenLab ICP-MS software automatically. The serial number can be displayed in the software, and it is recorded in the data files. In addition, the source computer name is recorded for files that are uploaded to OpenLab ECM from OpenLab ICP-MS software. Prior to data transfer, a device "handshake" confirms the correct link between ICP-MS and application host computer.

Architecture

Agilent OpenLab ECM is a server-based system that can be scaled from securing data from a single instrument to managing data from hundreds of instruments and users around the globe. Once OpenLab ECM is implemented by an organization, it provides secure, centralized storage for laboratory data and other records generated from multiple ICP-MS and other instruments, ensuring compliant operation across all global locations.

Metadata is automatically extracted from the files upon upload and is available to use in powerful built-in search functions to easily find specific data or records in the future. The server hardware to run the system can be supplied by Agilent if a server is not already available from your IT department. The ECM system requires a database backend and supports either Oracle or Microsoft SQL Server. See ECM configuration documentation for full compatibility information. The files are stored in a secure storage location within the database, and are accessible only through the ECM application or via a web client. A user with appropriate user privileges may also access the data after downloading to an OpenLab ICP-MS workstation.

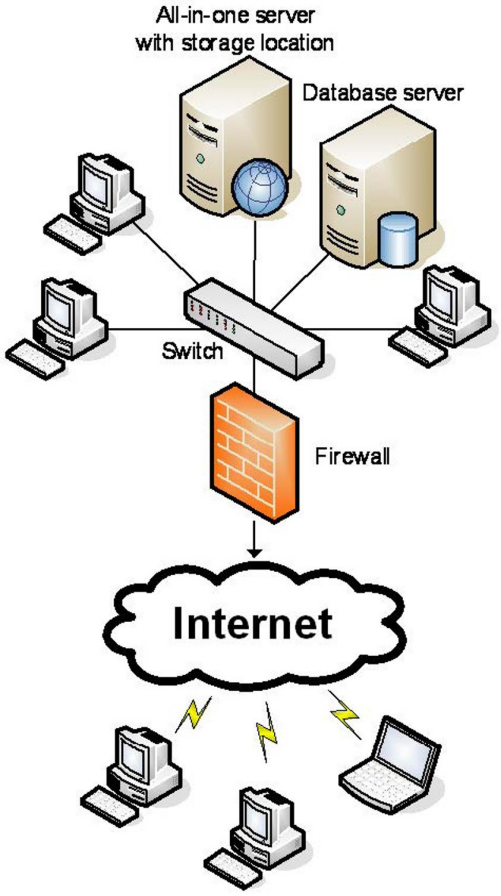


Figure 5. Schematic illustration of OpenLab ECM All-in-One server configuration. Various server configurations are supported, from all-in-one, to flexible, multi-server installations.

System requirements

The recommended server hardware specifications for OpenLab ECM are shown in Table 2 for an all-in-one (single server) system. For other supported server and system configurations, contact your Agilent representative.

Table 2. All-in-one OpenLab ECM server or workgroup server minimum hardware requirements.

Component	Description	Notes
Processor	4.0 GHz or higher	Dual Core or dual processor recommended
Memory	16 GB	32 GB or higher recommended. If the database* is also running on the same machine, review the recommendations from Microsoft as well.
Hard Drive	2 TB	Disk space sufficient for 3 years of file storage is recommended.
Optical Drive	CDROM Drive	Recommended for software installation
Network Interface	1 Gbps	

Agilent does not support running an Oracle Database on ECM Servers. Oracle databases must be hosted on a separate machine.

www.agilent.com/chem

DE-015260

Printed in the USA, June 01, 2026
5994-9269EN

Agilent
Trusted Answers