

Agilent MSD Security ChemStation for GC/MS Systems

Rev. A.02.00

Specifications

December 2005

General Description

The Agilent MSD Security ChemStation controls data acquisition, performs library searches and quantitation, and generates selected reports via methods or sequences.

The software addresses all aspects of data security, integrity, and traceability mandated by FDA's 21 CFR Part 11.

The solution represents a significant productivity advance for pharmaceutical laboratories. Access to the application is protected by a mandatory logon with a user identification code and password. Paper trails are replaced by audit-proof and reliable electronic records. The software manages versions electronically and provides a user-independent audit trail along with electronic signing capabilities. Electronic records generated by the application are always linked to all related raw, meta, and result data.

The MSD Security ChemStation software is designed to run on personal computers with Microsoft® Windows® operating environments.

The MSD Security ChemStation software is supplied on CD-ROM and contains extensive online help with both task and reference information about system operation. The example methods and data files supplied with the software can be used to practice and learn the MSD Security ChemStation software.

The MSD Security ChemStation software can be configured to support a single online instrument, with a maximum of one MSD and one GC detector. The following Agilent instruments are supported:

- The new 5975 series MSDs 5973A, 5973N, and 5973 inert MSDs
- 6850 GC platform and supported accessories
- 6890A, 6890 Plus, and 6890N GCs
- Agilent automatic liquid samplers (ALS)
- Agilent HeadSpace samplers

The software controls 5973N, 5973 inert, and 5975 MSDs with 6850 GC or 6890 Series GCs using standard LAN communications, while using GPIB communications for 5973A MSDs with 6890 Series GCs.

It is possible to acquire GC/MS data as well as to acquire and review mixed mode (GC/detector and GC/MS) data.

A GC-only instrument is not available.



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What's New?

Hardware

- Support for the new 5975 series MSDs. This instrument offers increased mass range to m/z 1050.
- Support for the 6850 GC platform and supported accessories.
- The 5973 and 5975 series MSDs chemical ionization (CI) valving and flow control is now automated.
- The capability to run electronic impact (EI) with a CI source has been added.
- Automatic sensing of the installation of the integrated vacuum gauge option.

Electronic Methods (eMethods)

- To enable easy sharing and distribution of methods, the capability to export an MSD Security ChemStation or MSD ChemStation method into an electronic method (eMethod) and import an eMethod into an MSD Security ChemStation or MSD ChemStation method is provided.
- This means you can easily exchange methods between different systems and even share methods between 5973 and 5975 MSDs.

SIM/Scan Capabilities

- A SIM/Scan (selective ion monitoring) acquisition mode was added for all 5975 instruments. This mode is also extended to 5973 instruments with Performance Electronics and the 100 mbyte instrument controller (the local control panel indicates "100 mbyte" when the instrument is first powered up).
- The functionality of acquiring SIM and Scan data in the same run is enabled via synchronous (alternating) SIM/Scan.
- The number of SIM ions and SIM ion groups was extended from 50 groups of 30 ions to 100 groups of 60 ions. The minimum dwell time was reduced from 10 ms to 5 ms.
- A new SIM group spreadsheet editor was added to Data Analysis.

Instrument Control Enhancements

- The Top view was eliminated, and its menus, toolbars and functionality were merged into Instrument Control. Now you can set up and control your system including sequencing all from one easy view.
- Two new toolbar buttons let you tune the MSD and easily access the maintenance schedule and log.
- A new Help menu item lets you view the IP address(es), serial numbers and revision information for your GC and MS

instruments. You can easily print this information and store it in a logbook or with the instruments.

- The Sample Log Table (sequence) can be configured to display only the column headings that you want to use and more right mouse-click menu items were added to simplify editing a sequence .
- Print Method lets you select which sections of a method you want to print.

Data Analysis Enhancements

- The new Explorer-style window provides easy navigation of method and data files. You have the ability to show or hide the Explorer window, and right-click menus are provided for quick data and method file actions.
- Right mouse-click actions are available in the Chromatogram/Spectrum windows and can be easily accessed via a toolbar button. (The classic mouse actions are also available.)
- The Reprocessing Top was removed and its functions were integrated in the Data Analysis menu.
- Custom reports can be created in MSD Security ChemStation. Bar code (expected or actual) was added to the report items for custom reports.
- Peak Purity is available now and performance reports can be created.

- This revision of MSD Security ChemStation offers a series of performance reports. The reports show the following details; based on total ion chromatogram (TIC): Peak Width at half height, Resolution, Tailing at 10% height, peak to peak S/N (signal-to-noise) ratio, RMS S/N, number of theoretical plates
- A spreadsheet-like SIM Parameters Table is provided for easy editing using right mouse-click actions and can be easily accessed via a toolbar button.
- QEdit functionality is improved to allow generating custom and quantitation reports from QEdit, custom configuring X-axis to be shorter so that user does not have to zoom all the time, and quick review of the integration.
- You can create a Windows metafile from the right mouse-click menu on the data variable watch window.
- Retention Time is displayed to 0.xxx minutes in windows and all reports.
- You can double click on a compound in Edit Compound to view the highlighted compound.

Specifications - At a Glance

Supported Operating Systems

The MSD Security ChemStation software is supported with the following operating systems:

- Windows 2000 Professional, Service Pack 4
- Windows XP Professional, Service Pack 2

The MSD Security ChemStation software is **not** supported on Windows 2000 Server software, Windows 2003 Server software, or Windows NT® Workstation. The recommended browser is Internet Explorer 5.5 with Service Pack 2 or Internet Explorer 6.0.

Supported Instruments

Current compatible hardware products include the following:

- 5973A MSD (GPIB or LAN)
- 5973N MSD
- 5973 inert MSD
- 6890A GC (GPIB or LAN)
- 6890 Plus GC
- 6890N GC
- 6850 GC

- 7683 family Autosamplers
- G2612A ALS controller
- G1888A, G1289B, G1290B Agilent HeadSpace samplers

Minimum PC Requirements

The minimum requirements for operation of the MSD Security ChemStation software are:

- Pentium® III computer, 600 MHz or faster
- SVGA color monitor
- 128 MB of RAM
- 80 GB of hard disk storage
- CD-ROM drive
- Sound card and speakers or headphones for viewing avi files
- Windows supported mouse

Recommended PC Requirements

For optimum system performance, the following PC capacity is recommended:

- Pentium IV computer, 2.8 GHz (or faster)
- 512 MB (or greater) of RAM
- 80 GB of hard disk storage (or greater)

MSD Communication Card

The interface from the ChemStation PC to the analytical instruments is through a LAN (local area network) card or a GPIB internal card depending on the configuration:

- A LAN card is used for 5973N, 5973 inert, 5975 series MSDs, and 6850, 6890 Plus, and 6890N GCs
- An Agilent 82350B GPIB Control Card can be used for 5973A MSDs and 6890A GCs that have not been upgraded to LAN
- The required GPIB (SICL) driver version is M.01.01.

Supported Printers

- HP LaserJet 2200d or 2300dn, Post Script, revision 5.02
- HP LaserJet 4050 or 4100, PCL 5e or 6, revision 5.02
- HP LaserJet 4020, PCL 6
- HP DeskJet printers are not supported.
- Network printers are not supported.

Supported Spectral Libraries

- G1033A NIST05 MS Library (NIST search algorithm NOT supported)
- G1041A NIST MS Library Upgrade
- G1035B Wiley Library
- G1036A NIST Chemical Structures Database

Supported GC Detector(s)

- Thermal Conductivity detector (TCD)
- Flame Ionization detector (FID)
- Electron Capture detector (ECD)
- Micro-ECD detector (μ -ECD)
- Flame Photometry detector (FPD)
- Nitrogen Phosphorus detector (NPD)

Supported GC Inlet(s)

- Split/Splitless (electronic pressure/flow control only)
- Temperature-programmable cool on-column (electronic pressure/flow control only)
- Programmable temperature vaporization (electronic pressure/flow control only)
- Volatiles interface (electronic pressure/flow control only)

Supported ALS Bar Code Reader and HeadSpace Samplers

- G2613A - 7683A Injector (A.10.07)
- G2612A - 7683A Controller (A.02.01)
- G2614A - 7683A Tray (A.02.01)
- G2615A - 7683A Bar Code Reader
- G2912A 7683B Controller (A.02.01)
- G2913A 7683B Injector (A.11.00)
- G2916A 7683B Tray (A.02.01)
- G1888A - HeadSpace sampler
- G1289B - 7694 HeadSpace sampler (EPC ready)
- G1290B - 7694 HeadSpace sampler (without EPC)

File Compatibility

- Long file names are supported. Data file and method paths can be up to 100 characters long. The names of individual data files and methods can be up to 50 characters long.
- Data and sequence files created on previous versions of the MSD Productivity ChemStation can be imported into the MSD Security ChemStation.
- Recent methods can be imported directly. Methods and quant databases prepared on earlier versions of the MSD Productivity ChemStation software (prior to G1034C, revision C.03.04) must be modified.
- Custom report databases are supported.

Installation, Qualification Services and Training

Agilent Technologies offers a full range of training and qualification services including installation, familiarization, and operational qualification service to ensure that the Agilent MSD Security ChemStation is installed and functioning correctly, and is in the right environment. A certificate of system validation is shipped with the products.

Product Description

The key requirements mandated by FDA's 21 CFR Part 11 are summarized in Table 1. Generally, to bring a system into compliance, an implementation consists of both procedural controls that must be established in the laboratory, and product functionality built into the paperless data system. The MSD Security ChemStation addresses those requirements that are marked as technical controls. It is important to understand that the design of the Agilent software is based on a closed system. This is achieved by implementing procedural controls and access security rules established in the lab so that only authorized individuals physically have access to the systems.

Table 1. Requirements Mandated by 21 CFR Part 11

Section	Requirement	Responsibility
11.10a	Systems must be validated	Procedural*
11.10b	Accurate and complete copies	Technical**
11.10c	Protection of records	Procedural, Technical
11.10d	Access limited to authorized individuals	Procedural, Technical
11.10e	Secure, computer-generated, time-stamped audit trail	Technical
11.10f/g/h	Checks (device, authority, system checks)	Technical
11.50	Signature manifestations	Technical
11.70	Signature/Record linking	Technical
11.100	Uniqueness of electronic signature to the individual	Procedural, Technical
11.200	Electronic signature components and controls	Procedural, Technical
11.300	Controls for identification codes and passwords	Procedural, Technical

*Procedural: The user's company is usually responsible to develop procedural controls.

**Technical: The supplier of the data system is usually responsible for implementation of technical controls.

Software Validation lies in the responsibility of the organization using the software. However, the vendor can help in making the validation procedure easier. Agilent validates each product before it leaves the factory. It also provides documented and certified evidence of successful software validation. Optional Installation Qualification and Operational Qualification services complement this.

The MSD Security ChemStation software provides:

- Storage of electronic records generated by the application in a protected proprietary format using a secure file hash algorithm. If such a record is altered through another application, this will be detected by the system when trying to read the record.
- The ability to create accurate and complete copies of electronic records in human

readable, as well as electronic format for inspection and review by the FDA.

- Protection of records to enable their accurate and ready retrieval throughout the records retention period (for example, by providing archive and restore functionality). Again, record protection is also subject to procedural controls.
- Restriction of system access to authorized individuals.

- Secure, computer-generated, time-stamped audit trails (previous information is not obscured).
- Authority checks to ensure that only authorized individuals can use the system, electronically sign a record and access the security features of the system.
- Operational system checks (to enforce permitted sequencing of steps and events, as appropriate).
- Signature manifestation - the signed record contains date and timestamp, name of the signer, and reason for signing.
- Linking of each signature to its record.
- Unique combination of password and UserID only known to the individual. This can only be achieved in combination with written procedures controlling the setup and management of user accounts and their access to the application, including password policies.

A user's company must provide the following procedural safeguards:

- The establishment of, and adherence to, written policies that hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification.
- Use of appropriate controls over systems documentation (controlled distribution of, access to, and use of documentation for system operation and maintenance).

- Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.
- Sufficient education, training and experience for persons who operate the system.

Product Design Overview

The MSD Security ChemStation is a standalone application that addresses the requirements of 21 CFR Part 11 through a combination of operating system facilities and programmatic controls. It runs on Microsoft Windows operating systems and takes advantage of their inherent user access security capabilities. The operating system security features are used to protect data and manage user access to it. User-based file access is achieved by making use of individual file and folder permissions, and local user and group management.

A mandatory logon requires users to enter their user-ID and password when starting the application. The user must be a member of a MSD Security ChemStation user group. The access level is determined by the user group membership. The logon is independent of the user who logged on to the operating system. See Figure 1.

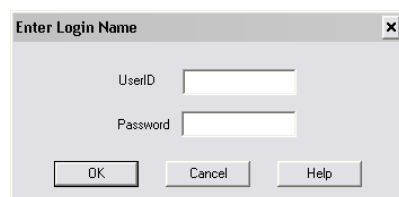


Figure 1. Logon screen.

Electronic records generated by the application are always stored along with all related raw, meta, and result data and are unbreakably linked to the record audit trail as well as to electronic signatures that were applied.

The software also includes interactive as well as automatic library searching for additional result confirmation. See "Mass Spectral Libraries" on page 21 for more information.

Data can be stored to durable media by using the built-in data archival tool. The integrated archival function is a convenient way to archive electronic data after completion of the review and approval cycles, while ensuring data integrity and retaining full traceability. A detailed description of the archival functionality is given in "Data Archival, Backup, and Recovery" on page 28.

The user interface of the MSD Security ChemStation is guarded by the MSD Security Monitor. It provides means for locking a session privately, when leaving the system unattended, or non-privately, for example, during shift changes. In addition the application includes a configurable time-based session lock.

System Requirements

Computer Hardware

The MSD Security ChemStation consists of Hewlett-Packard/Compaq personal computer hardware and MSD Security ChemStation software. The hardware is an IBM-compatible personal computer with a positive chemical ionization (PCI) interface bus.

The personal computer is interfaced to the analytical instruments through a LAN card or a GPIB internal card. All cards plug directly into the computer's PCI interface bus.

For latest hardware specifications please contact your local sales representative.

Note: *The MSD Security ChemStation software has been tested on Agilent Technologies ChemStation (PC) hardware that conforms to the above specifications. Although the software is also designed to be run on other IBM-compatible PCs, Agilent is not responsible for defects reported on third party hardware.*

Computer Hardware Considerations

The minimum PC configuration required to use the MSD Security ChemStation software includes:

- A Pentium III computer (Pentium IV, 2.8 GHz or faster recommended)
- An SVGA color monitor
- 1024 × 800 × 65,536 colors video display resolution (maximum supported resolution is 1600 × 1200 × 16,000,000 colors)
- 128 MB (512 MB or more recommended) of RAM
- At least 40 GB of hard disk storage (MSD ChemStation program files use approximately 115 MB). 80 GB or more is recommended.
- A CD-ROM drive
- A sound card and speakers or headphones
- A Windows 2000- or XP supported mouse
- A data backup device is strongly recommended
- BIOS which supports Windows 2000 with Service Pack 4 (or later) or Windows XP with Service Pack 2
- All power-saving features of the BIOS disabled
- All power-saving programs removed

Software

The operating system must be either Windows XP Professional (Service Pack 2), or Windows 2000 Professional (Service Pack 4). MSD Security ChemStation software is not supported on Windows 2000 Server, Windows 2003 Server, or Windows NT Workstation.

The hard disk partition that is used for installation of the MSD Security ChemStation must be formatted with NTFS.

Data Storage and Printing

Active data is stored on the local hard drive of the acquisition PC hosting the application. Data storage on networked drives is not supported. After review and final approval, data can be archived to another location such as external disk drive, networked drive, or other durable media.

Printers

The ChemStation software can print to any Microsoft Windows compatible printer directly connected to the computer through a parallel interface or connected through a LAN.

The ChemStation is designed to use the Windows default local printer. The typical system is sold with an HP LaserJet printer, which is intended to be the local printer on the parallel port of the ChemStation computer.

- HP LaserJet 2200d or 2300dn printers are fully tested and supported. Supported drivers are Post Script, revision 5.02.
- HP LaserJet 4050 or 4100 printers, although not tested with this release, are supported due to testing on older revisions. Supported drivers

include PCL 5e or 6, revision 5.02.

- HP LaserJet 4020 printer is fully tested and supported. Supported driver is PCL 6.
- HP DeskJet printers are not tested or supported

Agilent service engineers are not trained to configure and support network printers. The system requires a local printer. Shared network printers are not supported.

Disk Sizing Considerations

The local storage of data is limited by the size of the hard disk. The estimated required disk space depends on the acquisition parameters. For example, the storage of raw, meta, and result data from a sequence with 100 runs (with a run time of 40 minutes, sampling rate

2.94 scans/s, scan rate: 50–550 amu) will require approximately 50 MB of disk space. Provided two sequences are executed per week, 1 year of analytical data will require 5 GB of disk space. The real amount might vary greatly with the specific acquisition conditions. We strongly recommend you determine your personal disk space requirements in order to plan for appropriate archival intervals. It is important to implement an archiving procedure that both archives and locally deletes data from the hard disk, after completion of review and approval, in frequent time intervals. This will ensure sufficient disk space availability and thus optimum system performance.

Data Security

User Management and Data Access

Access Control requires procedural controls (by implementing Standard Operating Procedures, SOPs) in the lab. These SOPs define physical access controls and authorization levels of the individuals working in the lab. The employed computerized system has to provide automatic system controls. These controls must be enabled and configured to match the established access control SOPs. Most automatic system controls can be implemented using the means provided by the Windows operating system.

Examples for access controls are:

- User authentication through secure logon
- Protection of files and folders using NTFS security
- Inactivity timeouts
- System policies (for example, disable access to the command prompt)

Typically, the information technology (IT) department of a regulated facility has already implemented several layers of security in the operating system of the end-users. IT groups define security and password policies and apply formal rules for assigning user account names and passwords. In many cases, access

restrictions are already implemented on the file servers to ensure integrity and confidentiality of data. Ideally, a chromatography data system should just tie into the security mechanisms offered by the operating system.

In the MSD Security ChemStation users are entirely organized by making use of the local Windows user management. Users are grouped in local Windows user groups. It makes use of three user groups - MSDOperators, MSDAnalysts and MSDManagers - with predefined tasks. Users have to have valid Windows user accounts in order to be able to gain access to the application. A

Windows administrator is able to add any Windows user to any of these three groups without the need of having direct access to the application itself, that is, the administrator does not need to be a member of one of these groups. By adding the user to a group, the administrator grants the privileges of this user group (by job type) to the user. The administrator must supply a login name and a full user name for each user, and must require that the actual user log in and change his or her password at first use (Figure 2 on page 10).

By making use of the Windows logon, there is one central user administration on the system, the Windows user management console. However, the user who has logged onto the operating system is not necessarily the application user. This is important when the operator

changes while data acquisition is running. The user doesn't have to relog on to the operating system but just to the application. For example, when working in shifts, it might be useful to have a dedicated global logon to the computer, while having the users using their personal windows account to enter the application.

The implementation in the laboratory environment strongly depends on the individual requirements and use model.

The MSDOperator, MSDAnalyst, and MSDManager Local Groups

At installation, the install process creates three additional local user groups corresponding to the three levels of user privilege supported by the application: MSDOperator, MSDAnalyst, and MSDManager. Membership of users in these groups determines

the level of access that they are permitted in the application.

MSDOperators are allowed access to features required for routine use; MSDAnalysts, to a higher level for review and method development; and MSDManagers, to the full set of capabilities including administrative tasks. The application checks for membership of the active user in these groups to determine the appropriate level of access. Membership of an active user in multiple groups automatically confers the privileges of the highest-level group to which the user belongs. The MSDmanager role is reserved mainly for administrative use. Standard operations should only be performed by MSDOperators or MSDAnalysts. Table 2 summarizes the user privileges granted to the different user groups.

Table 2. MSD Security ChemStation User Privileges

User privileges	Operator	Analyst	Manager	Windows administrator
Data acquisition	X	X	X	
Data reprocessing	X	X	X	
Spectra manipulation		X	X	
Library searching		X	X	
Modify and save method		X	X	
Modify and save sequence		X	X	
Data archival		X	X	
Command line access			X	
General configuration			X	
User management				X
Security policies				X

The System Administrator

The system administrator is a user with Windows administrator privileges who manages the users, security policies, system audits, etc. Typically, he will be an IT representative and not a system user. The system administrator is not a user level inside the MSD Security ChemStation.

MSCFR Local User

To protect it from unauthorized access the application and its file system is entirely managed by an internal user called MSCFR. This user is created at installation time and has sole ownership of the entire file system belonging to the application, which is created during installation (default directory name: MSDCHEM). This MSCFR user manages the whole file system of the application. The password of this user is set to a value known only within the MSD Security ChemStation application. It is Agilent-confidential and is not disclosed to other parties.

The MSD Security ChemStation makes use of Windows' "Run As" capability, to switch from the Windows Session user to the MSCFR user before starting the application. Thus, the running application has access to the file tree protected by the local system user's permissions. The currently logged on Windows Session user has no access to the file tree.

Password Policies

Password Security is ensured by making use of the local Windows password policies as defined on an operating system level. Here, rules such as minimum password length, password history, password expiration and number

of unsuccessful attempts until an account lockout event occurs are defined (Figure 2).

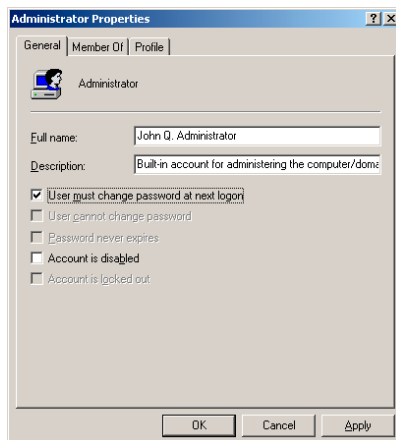


Figure 2. Setting up users.

The Security Monitor

The Security Monitor, which appears as a small window in the bottom right portion of the screen (by default), is always on top and displays the full name of the current user, allows you to change your password, and provides a quick way to change users. You can also lock the ChemStation to keep unauthorized users from accessing the system. See Figure 3.



Figure 3. MSD Security Monitor.

Session Locking

The application provides for two lock functions to protect the system from unauthorized access during unattended operation, such as during sequence acquisition. There is an explicit lock function that allows the user

to lock the application when leaving the system, and a time-based session lock that automatically locks the application after a specified time of inactivity as configured in Windows as part of the Windows display properties. The application lock replaces the Windows screen saver, thus allowing the user to still monitor the analysis while the lock is enabled.

When locked, the system does not allow any access to the computer, unless it is unlocked by an authorized MSD Security ChemStation user.

For periods of unattended operation the software provides for:

- Explicit lock function for private session locking when leaving the system unattended (for example, during a break)
- Non-private session locking (for example, for shift changes)
- Configurable inactivity timeout (unlocking requires reauthentication with both user-ID and password). See Figure 4.

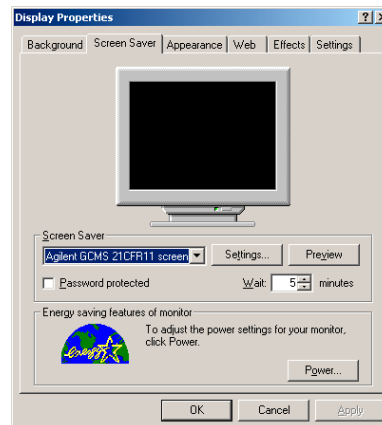


Figure 4. Configuring the inactivity timeout.

Record Protection

Raw, meta, and result data are at the operating system level protected by Windows NTFS file system security. The NTFS permissions used by the software ensure that no data can be deleted nor altered. Only an application-internal user has access to the file system and executables (Figure 5). No other user has access to the file system unless explicitly taking ownership of the whole file tree of the application (default name: MSDCHEM). Archived data is

compressed and protected with a security file hash to ensure that it cannot be modified. The file hash is generated during archival and checked for correctness during dearchival. Data that was archived or exported from the secured file system needs to be further protected through procedural control such as standard operating procedures covering these tasks.

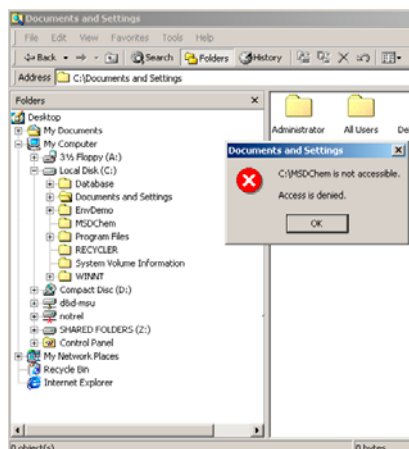


Figure 5. Access to the file system is denied.

Data Integrity

A key requirement is to maintain data integrity. This involves a secure storage of data, as well as the unbreakable linkage of raw, meta, and result data and the versioning of result data. The MSD Security ChemStation stores all modifications of an electronic record as versions. Versioning applies for result data, methods, and sequences. No result data is ever overwritten. When data is archived the built-in archive/restore tool always archives the complete electronic record including all result versions.

File Structure

The MSD Security ChemStation creates a single results file that contains raw, meta, and result data for a version. A version file is a snapshot of the state of data recorded in the method, data, or sequence. It is stored in a compressed format, protected with a hash value. Besides result data the MSD Security ChemStation also provides versioning of methods and

Version File Name Syntax

<prefix>-<version>.<suffix>

<prefix> = METHmethod version
SEQsequence version
ACQacquisition data version
PROCresults data version

<version> = <year>-<month>-<day>-<hour>-<minute>-<second>-<msec>UTC

<year> = 4 -digit year

<month> = 2-digit zero left padded month

<day> = 2-digit zero left padded day of month

<hour> = 2-digit zero left padded 24-hour clock hour

<minute> = 2-digit zero left padded minutes

<second> = 2-digit zero left padded seconds

<msec> = 3-digit zero left padded milliseconds

UTC = a constant

<suffix> = a combination of r, v, and s, indicating the kind of hash blocks appended to the file

r =reference block, links to other files

v =validation block, system-applied signature of user of record, no explicit authentication

s = signature block, interactively applied electronic signature

There is no space or other separator in the time field: 152903005 is 15:29:03.005 in 24-hour clock format. The names are unique on a MSD Security ChemStation.

Run Directories

Run directories are where the results from single runs or sequences as well as imported data are stored. The data path to the run directory is configurable.

Run Directory Name Syntax

<prefix>-<version>

A **Run-<version>** directory contains the data file and a copy of the method version run on that data.

A **Seq-<version>** directory contains all data files, a copy of the sequence that generated the data files, and a copy of each method used in the sequence.

An **Imp-<version>** directory contains an imported data file.

<prefix> = Run results of Run Method
Seq results of Run Sequence
Imp results of Import Data File

<version> = As described above

sequences in separate method and sequence file trees.

Data and methods consist of a directory with the extension *.D or *.M, respectively and contain a set of files representing the raw

and meta data. Version files reside in Versions subdirectories of method (.M) and data (.D) directories. Each version carries a time stamp in UTC format (UTC means Universal Coordinated Time and corresponds to

Greenwich Mean Time GMT). Sequences are stored in single files with the extension *.S. Versions are stored in a sequence directory, which has the same name as the associated sequence file but without the .S suffix.

Data Traceability

Viewing Result Versions

For full traceability the MSD Security ChemStation retains all result versions by applying strict revision control of all records maintained by the system. Its time stamp, as described in the previous section, uniquely identifies a version. Reports that were generated during the review are stored as electronic copies with the record.

reports that were created for a specific version.

Electronic Signatures

Electronic signatures must be applied whenever a new result version is created. The user has to re-authenticate himself with both signature components - user ID and password. A short comment with a minimum length of six characters is mandatory

for signing records electronically for approval.

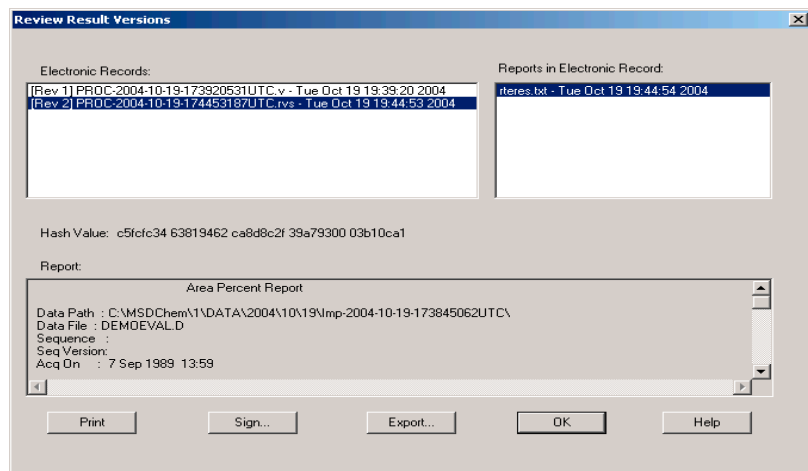


Figure 6. Result version viewer.

All result versions and the reports associated with specific results can be easily reviewed in the Report Viewer (see Figure 6). The viewer provides a list of all result versions of an electronic record in chronological order. It can display as well print all result

(Figure 7). Electronic signatures are documented in the record audit trail attached to the electronic record.

While certain tasks in the MSD Security ChemStation require an electronic signature before they can be completed (for example data archival or saving a method), the report viewer provides means

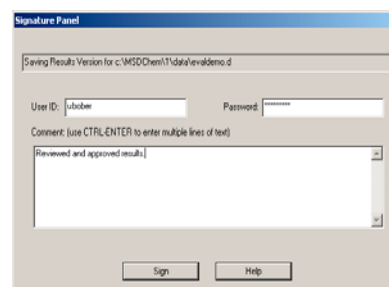


Figure 7. Electronic signing of a record.

Linking of Signatures to Electronic Record

The FDA mandates "Electronic signatures...shall be linked to their respective electronics records to ensure that (they) cannot be excised, copied, ...to falsify an electronic record by ordinary means". The design of the MSD Security ChemStation ensures referential integrity between raw and meta data and result versions. The record audit trail and signature information cannot be manipulated or deleted. Electronic signatures are documented in the record audit trail with signature meaning, full name of the signer and date and time stamp (Figure 8). It is directly attached to the result version it was applied on as outlined in "Data Integrity" on page 11.

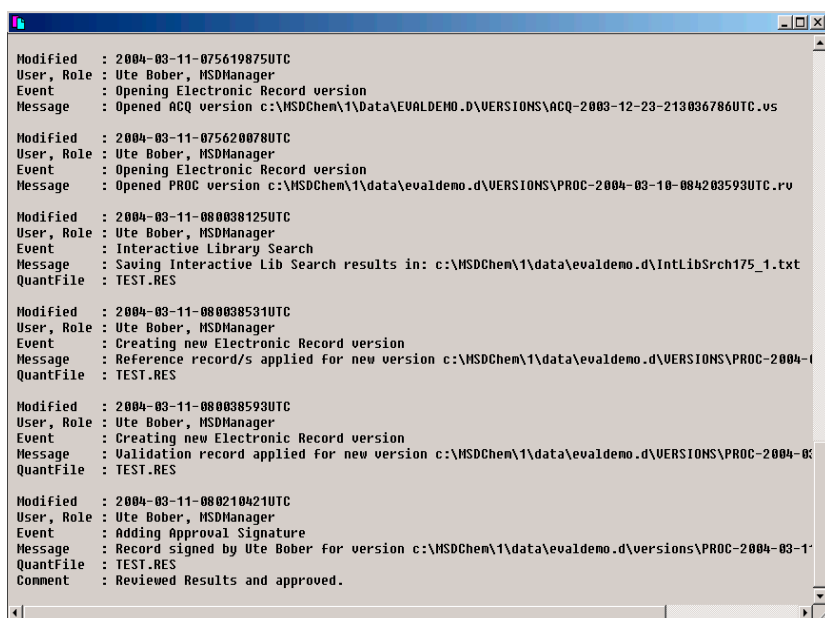


Figure 8. Record audit trail.

System Configuration

The configuration of the GC/MS system is done through the system configuration program. It allows users to define their instruments and GPIB addresses or LAN IP addresses. System configuration requires MSD Manager privileges.

Offline Operation

In the system configuration program it is also possible to configure a system to operate the software in an offline mode. In this mode, the system is not actually connected to the GC/MS system and cannot acquire data

Uniqueness of Electronic Signature Components

"Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else." The application makes use of the built-in Windows user management and security policies. This requires procedural controls in the organization, typically handled by HR and IT departments. IT policies ensure that combinations of user-ID and passwords are unique and periodically revised. For example, when setting up new users a password change during first login can be forced.

or access some of the features that require online operation. This mode is useful, however, for learning the software, data review, or method development.

Workflow

Routine use of the MSD Security ChemStation typically involves:

1. Data acquisition
2. Data reprocessing and/or manual integration (first pass review)
3. Peer review
4. Final review and approval
5. Data archival

The MSD Security ChemStation user interface is designed into

Views that group software functionality according to typical analytical tasks. Each view consists of a set of standard user elements including menus and toolbars. The toolbars provide rapid access to the common system tasks such as loading a method or sequence.

Data acquisition (step 1) is done from Instrument Control View. Data review (steps 2–4) involves Data Analysis View. Data is

archived from the Configuration View (step 5).

Instrument Control View

Instrument Control is where most of your work will originate. You can edit a method, set up and start a single run, and perform an autotune of the MSD. You can also fine-tune and monitor discrete parts of the GC and/or MSD control and display various status monitors.

Data Analysis View

Data Analysis is an offline "view" that runs independently of the other views. This view is used for integrating, quantifying and identifying your data.

The View menu lets you access the following productivity tools:

- **EasyID** – Lets you update expected retention times and ion ratios for MS data in an existing quantitation database on a compound-by-compound basis.
- **QEdit** – Lets you review and edit quantitation results once a data file has been quantitated. QEdit allows storage of manual integration events with the result ensuring full traceability of results generated by manual integration.
- **Parametric Retrieval** – Lets you access the Parametric Retrieval view which helps you locate compounds in a mass spectral library.
- **RTL Lock Setup** – Accesses the RTL Lock Setup view which is used for retention time locking (RTL) tasks.

Tune and Vacuum Control View

This view provides tools for tuning and maintaining your MSD. The user can select from several autotuning options, use the tune wizard for target tuning, or access the software's manual tuning capabilities. The access to the tune view is restricted to MSD Analysts and MSD Managers.

Tuning is a process for optimizing the performance of the MSD. The goal of tuning is to maximize

sensitivity while maintaining acceptable resolution, ensuring accurate mass assignment, and providing the desired relative abundances across the mass spectrum. As electron impact mass spectrometry provides a fingerprint for a compound, the relative abundances of a mass spectrum will affect the quality of a library search.

Configuration View

The configuration view is dedicated to MSD Security ChemStation managers. It provides access to administrative functions such as configuring the instrument and archival or dearchival of data.

Methods and Sequences

The MSD Security ChemStation analytical method fully describes how a particular analysis is performed. It contains all the parameters for instrument control, data acquisition, and data analysis, including integration, quantitation, and reporting.

A sequence allows you to automate the analysis of one or more samples using one or more methods. When an autosampler is installed, the entire analysis, from injection of the sample through reporting of results, can be automated. A bar code reader can be used for further automation.

Example methods and sequences are supplied with the MSD Security ChemStation software. The example methods can be imported, edited, and used as a starting point for a particular application (such as drug analysis). It is also possible to create RTL methods.

eMethods is short for electronic methods - a quick and easy way to obtain packaged application solutions from Agilent or to share your own personal applications.

This is a process that can greatly improve your laboratory's productivity. eMethod enables you to:

- Electronically export existing methodologies to new instrumentation—Agilent's eMethod process allows you to package any 5973 series MSD method and export it to an Agilent 5975 inert MSD, thus enabling you to bring a new GC/MS instrument online in the shortest possible time.
- Maximize instrument productivity—Whether you have multiple GC/MS systems in the same laboratory or across the world, the Agilent eMethod process makes sharing and standardizing methodologies across your organization as easy as e-mailing an attachment. Analytical separation can be easily duplicated on multiple systems thus maximizing the productivity of each GC/MS.

- Electronically import new Agilent application solutions—No more manual entering of method parameters. Agilent's integrated eMethod process allows you to download any new Agilent eMethod application solution from the Agilent Web site and import that method to your Agilent 5975 inert MSD or 5973 series MSD and receive the entire method without any manual editing errors.

For a complete list of available Agilent eMethods, please visit the eMethod homepage on the Agilent Web site.

<http://www.chem.agilent.com/scripts/generic.asp?lpage=33687&indcol=N&prodcol=Y>

Acquisition and Instrument Control

The Instrument Control view has an easy to use graphical user interface. Each instrument control option is represented by buttons on the icon bar of the Instrument Control screen. These buttons let you control, set, and monitor parameters for the:

- 6850, 6890A, 6890 Plus, and 6890N GCs
- 5973A, 5973N, 5973, and 5975 inert MSDs
- 7683 Autosampler
- G2612A ALS controllers
- G1888A, G1289B, and G1290B HeadSpace samplers (requires G2923AA A.01.04 software package)

Acquisition

The ChemStation allows the control of and data acquisition from multiple GC and MSD detectors. Up to two detectors can be controlled by one MSD Security ChemStation (a maximum of one MS detector).

Data may be acquired in scan or selected ion monitoring modes.

Combined Signals

Combined GC and MS signals can be acquired from a single sample. Signals from GC and MS detectors can be calibrated, quantified, and the results reported in a combined report.

Select and Display Monitors

The Instrument Control panel lets you select which system monitors you want to be displayed. These monitors include GC and MSD [TIC, extracted ion chromatogram (EIC), spectra] detector signals,

system temperatures, and flow and pressure set points.

Easy Tuning

Tuning the MSD is easy; you can select from several existing Autotune algorithms or tune manually. All tune results can be viewed, printed, and saved for review and later evaluation.

Early Maintenance Feedback

The EMF (early maintenance feedback) utilities in the Instrument Control view are used to select or reset various limits and counters. These values are used to alert you when a limit is reached and a maintenance task needs to be performed, such as changing the GC septum. These utilities are only available in an online configuration.

Each time a method is run, the limits will be checked. An alert box is displayed if the EMF check indicates a limit has been reached. If the system is running a sequence, any EMF alerts will be logged into the sequence logbook.

Items monitored that may affect performance include mechanical pump fluid change, number of injections exceeded, detector change based on electron multiplier (EM) counts, septum injections, inlet liner injections, and tune time limits.

Synchronous SIM/Scan

Synchronous SIM/Scan is an acquisition mode that enables collection of both SIM data and full scan data in a single run. In many laboratories, full scan is the

most common form of data collection due to the ease of setup and the availability of spectral libraries for compound confirmation. SIM mode, on the other hand, offers significant improvement in sensitivity over full-scan. The Agilent SIM/Scan mode combines the best of both SIM and full scan from a single sample injection to improve productivity. Agilent MSD Security ChemStation's AutoSIM feature allows you to create a SIM method automatically from ANY existing full scan method. Once you create the SIM method you can run synchronous SIM/Scan. The Agilent Synchronous SIM/Scan offers the following benefits:

- Confirmatory information - fullscan data for library search capability
- Maximum sensitivity - SIM data enables trace analysis
- Automated setup conversion - The AutoSIM feature automatically processes fullscan data of chemical standards into SIM acquisition parameters for use in the SIM/Scan method. This feature is only supported on 5973N and all inert instruments, not on 5973A.

Data Analysis - Integration

The MSD Security ChemStation provides two different modes for automatic integration:

- Integration based on fixed integration parameters
- AutoIntegrate

The integration mode as well as the integration parameters are an integral part of the ChemStation method. All automatic integration is based on a single integration algorithm, the ChemStation integrator.

Integration is controlled by integration parameters which can be reviewed and edited. These parameters can be saved in an integration parameter (.P) file which can be used to integrate

the target or qualifier ions for a particular compound or as the default integration for an entire method.

The ChemStation integrator can satisfactorily integrate all types of chromatograms, including those with difficult baselines and negative peaks. You can control the integration process by setting integration parameters, usually referred to as "integration events."

The ChemStation integrator allows you to AutoIntegrate using initial integration events. If the results are not suitable, you can make changes to the integration parameters and then reintegrate

manually or automatically.

The RTE integrator is not supported. Methods imported from the MSD Productivity ChemStation need to be converted to the ChemStation integrator prior to importing.

Data Analysis - Quantification

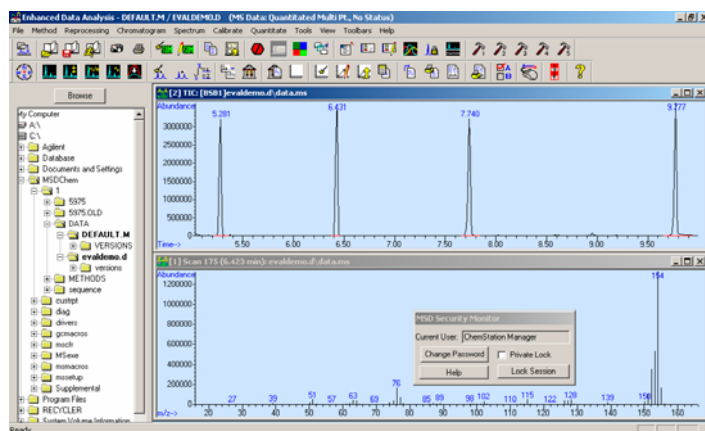


Figure 9. The new user interface with Explorer-style window

The new Explorer-style window (Figure 9) provides easy navigation of method and data files. You have the ability to show or hide the Explorer window, and right-click menus are provided for quick data and method file actions.

Right mouse-click actions are available in the Chromatogram/Spectrum windows and can be easily accessed via a toolbar button. (The classic mouse actions are still possible.)

The Reprocessing Top was removed and its functions were integrated in the Data Analysis menu.

- A spreadsheet-like SIM Parameters Table is provided for easy editing using right mouse-click actions and can be easily accessed via a toolbar button.
- QEdit functionality is improved to allow generating custom and quantitation reports from QEdit, custom configuring X-axis to be shorter so that user does not have to zoom all the time, and quick review of the integration.

Quantification is based on external standard or internal standard (ISTD) calculations calculated on either peak area or height. Calibrations may be multilevel and include multiple ISTD definitions. Calibration histories are automatically saved and can be used to weight the recalibration calculations based on running averages.

Calibration curves are constructed for each compound by using the calibration levels to define the curve. The algorithm used to generate the calibration curve may be selected as:

- Linear – a linear regression fit of the data points
- Linear, force – a linear regression fit forcing origin
- Quadratic – a quadratic fit of the data points
- Quadratic, force – a quadratic fit forcing origin
- Average response/amount

In addition, for linear and quadratic curves, point weighting can be applied as equal, inverse of concentration, or inverse square of concentration.

Compound identification may be refined by defining individual

retention time window parameter limits and qualifier peaks.

Qualifier peaks are usually the same compound detected on a different signal with a predictable response ratio. They are used as a further check on peak identification rather than just relying on retention times.

The MSD Security ChemStation allows 20 individual levels of calibration for each target compound your analytical method requires. While actual and practical limits are different, the quantitation database can handle compound lists in excess of 2000 entries.

Data Analysis - Quantitative Analysis

Two stages are involved in quantitative analysis:

- Calibration, in which you set up a quantitation database from the analysis of calibration standards. This analysis is used to generate a calibration curve for every compound you plan to quantitate.
- Quantitation, in which you run unknown samples and generate reports on how much of a particular compound is present in a sample.

The MSD Security ChemStation software produces a quantitative report in two stages: first the quantitation calculation and then the report generation.

Quantitation Database

A quantitation database is a collection of information and data needed to perform quantitative

analysis. For each compound, the database includes the calibration table and the information required to extract and integrate the ion chromatograms. Calibration curves from the calibration tables are used to quantitate target compounds.

Quantitation Calculations

Two sets of parameters are used to maximize the effectiveness of the quantitation calculations: peak integration parameters and peak identification parameters.

The steps the software performs during quantitation are shown in *Quantitation Flow*.

At each stage of the calculations, the two steps the quantitation process uses to determine the presence or absence of a compound are **Integrate** and **Analyze**.

The quantitation procedure creates a **<methodname>.res** results file in the data file directory. Report generation software reads the results file and formats a report.

AutoQuant Setup

Setting up a GC/MS calibration table often requires knowledge of the sample and software. For new users, or occasional or routine operators who are not familiar with the software, setting up the MS calibration may be difficult and time-consuming.

The AutoQuant Setup feature allows the user to quickly establish a GC/MS calibration with minimal knowledge of either the sample or the software.

When AutoQuant Setup is selected, it steps through each integrated compound in the total ion chromatogram, searches the selected MS spectral database compound name, and provides the first four hits as possible names. The user selects the compound name of interest or enters a user-defined name, and the software automatically selects the target ion and three qualifier ions. Additional compounds and calibration edits are also easily performed.

Quantitation Flow

Process external standards

1. Retrieve information about first compound from the quantitation database. If not an ISTD, process as an external standard.
2. Extract the quantitation (target) and qualifier ions signals over the expected RT range.
3. **Integrate** the extracted ion chromatograms.
4. **Analyze** the integrated peaks.
5. Repeat steps 1–4 until an ISTD is encountered.

Process ISTDs and target compounds

6. Retrieve information about first ISTD from the quantitation database.

7. Extract the quantitation (target) and qualifier ion signals over the corrected expected RT range. If the compound is an ISTD, then the correction factor is 1 (value not corrected).
8. **Integrate** extracted ion chromatograms.
9. **Analyze** the integrated peaks.
10. Calculate RT correction factor if the compound is a time-reference ISTD.
11. Repeat steps 7–9 for each target compound until the next ISTD is retrieved.
12. Repeat steps 7–11 until the end of the quantitation database is reached.
13. Generate quantitation report.

Data Analysis - Reporting

The MSD Security ChemStation comes with a set of predefined report types that are listed below. The report types are described in more detail in the online help. In addition, methods originating from the MSD Productivity ChemStation and containing further report customization can be imported into the MSD Security ChemStation.

The following reports are available from the Data Analysis:

- Area Percent Report
- Library Search Report
- Quantitation Report
- Non Target Peaks Report
- Integration Results Report
- Calibration Report
- Compound List Report
- Quant Database Report
- The Review Peak Purity function is now available in data analysis-This function helps you detect overlapping peaks (multiple-component peaks) in your chromatogram.

Custom Reports

The MSD Security ChemStation software includes the ability to let you create custom report formats. The Custom Reports software lets you transfer quantitative results from Data Analysis into the Custom Reports spreadsheet program where you can create your own custom report templates. You can also set up databases of quantitative results from multiple samples, then view and print charts of the data. The Custom Reports software uses a Report Wizard which lets the user select the content they want to

use for their custom reports. The user can define which elements to include in the header: general information about the data file (such as date acquired and method name), single-compound information and calibration information. Next you can select the compound-specific information (such as compound name or number) for all compounds in the quantitation database. Once the report content is selected, the software formats the report automatically into the spreadsheet program. You can then further customize the report using the formatting features available from the menus and toolbar. Up to 240 graphic elements can be added to the report template. Any formatting changes you make are saved with the report template.

Once a report template or database is created and linked to a method, you can print the report or update the database automatically whenever the method is run.

Data Analysis - Spectral Data Evaluation

Data Processing Tools

The Data Analysis software is a complete mass spectral data processing application. Mass spectra can be viewed, tabulated, added, subtracted, and printed with just a click of the mouse. See Figure 9.

Spectral Background Subtraction

The spectral background subtraction feature (BSB) allows correction to the background masses. It automatically subtracts a spectrum of choice from the complete chromatogram. The spectrum is interactively taken from the same chromatogram. It can be a single spectrum as well as averaged over a specific time range.

Mass Spectral Libraries

Commercial mass spectral libraries can be searched using the probability-based matching algorithm (PBM) included with the software.

You can also create your own custom library. These can be created and edited using acquired mass spectra.

In addition, libraries created on other MSD ChemStations (MSD Security ChemStation or MSD Productivity ChemStation) can be imported and further extended by adding newly acquired mass spectra.

Up to three libraries may be selected for sequential searching of unknown spectra. Default search criteria provide quality search results for most applications. However, in those

cases where default values are not applicable, the MSD Security ChemStation software allows the operator to define the parameters used in the search.

The mass spectral PBM search result list returns the "hits" with the highest quality as defined by the search criteria.

All interactive as well as automatic library search results are stored with the electronic record and can be viewed in the report viewer. See "Data Traceability" on page 12 for more information.

About PBM

The PBM algorithm uses a reverse search to verify that peaks in the reference spectrum are present in the unknown spectrum. Extra peaks in the unknown are ignored, thus allowing the analysis of a spectrum resulting from a mixture of compounds.

Since not all mass-to-charge (m/z) values of a mass spectrum are equally likely to occur, the PBM algorithm uses both the mass and abundance values to identify the most significant peaks in the reference spectrum. When a spectrum is added to a library, these peaks are used to generate a condensed reference spectrum that is used by the PBM search routine.

A prefilter within the search routine then assigns a significance to each of the peaks in the unknown spectrum and uses these to find the most probable matches in the condensed reference library. The

selected condensed spectra are then compared, using the reverse search described above, with the complete unknown spectrum. The prefilter immediately eliminates approximately 95% of the compounds in the database and greatly speeds up the search (when using the default strategy parameters).

Chemical Structures

Chemical structures provide additional information that helps in detailed evaluation of the mass spectrum. The MSD Security ChemStation software supports chemical structure libraries in the .MOL format. Chemical structures with valid CAS numbers are automatically recalled and displayed with each searched spectrum.

Parametric Retrieval

The Parametric Retrieval feature in Data Analysis allows you to locate compounds in a spectral library based on specific criteria. The retrieval produces a list of compounds in the library that satisfy the specified criteria. You may then view the spectra of these compounds and compare them with the spectra from your samples.

Automation

Methods

With the MSD Security ChemStation, you can edit or create methods that completely automate tuning the MSD, sample introduction, signal acquisition, data processing, searching mass spectral databases, and creating/printing reports.

ChemStation methods are actually directories containing a set of files with these setpoints. A method is saved to disk and is automatically designated by .M at the end of the directory name. Once a method has been created and saved, it may be recalled again automatically as part of a sequence or interactively for example when running in single sample.

Pausing Sequence to Edit Method

When pausing a sequence to edit the method, verify that the method edited is from the Seq-directory and not the Method from the Methods directory.

If the paused sequence is edited, the sequence has to be resaved before running it. This will start the sequence from the beginning. The sequence can be paused (to add samples to the Tray for example) and restarted but there is no way to modify the sequence after it has started running.

Sequences

The ChemStation uses sequences to run batches of samples automatically, using one or more methods. The sequence

information is entered into the Sample Log Table where there must be a line for each injection to be made.

A sequence is saved on disk and is automatically designated by .S at the end of the file name. Once a sequence has been created and saved, it may be recalled again as a starting point for running another batch of samples.

The sequence may be defined to use automatically generated or user-defined file names. The user may select to run full analyses or just reprocess sequences.

The Sample Log Table, or list of analyses to run, is built in a spreadsheet-like user interface that allows users to specify vial numbers and sample names, analysis methods, and sample quantification parameters.

While entering information, the user can jump between individual cells in the table and copy, cut or paste individual cells or entire rows or series of rows in order to build sequences efficiently and quickly.

Before running a sequence the MSD Security ChemStation can process (simulate) the sequence. Simulating the sequence will allow the user to check the sequence for errors before running the samples. The simulation checks only for common errors of syntax, not logical errors.

Once started, the sequence will proceed with the analysis of all the samples until completed or paused for priority samples. If paused, changes can be made to the sample list and the sequence restarted.

Retention Time Locking (RTL)

The retention time is the fundamental qualitative measurement of chromatography. Most peak identification is performed by comparing the retention time of the unknown peak to that of a standard. It is much easier to identify peaks and validate methods if there is no variation in the retention time of each analyte.

However, shifts in retention time occur frequently. Routine maintenance procedures such as column trimming alter retention times. In a multi-instrument laboratory running duplicate methods, the retention times for each instrument will differ from each other, even when run under nominally identical conditions. These differences in retention times mean that each instrument must have a separate calibration and integration event table, making it time-consuming to transfer methods from one instrument to another. Differences in retention time also complicate comparison of data between instruments over time.

The ChemStation's RTL feature allows to automatically correct for those retention time shifts and gives you the ability to very closely match retention times on one system to those on another system with the same nominal column. By making an adjustment in the inlet pressure, the retention times on a given system can be closely matched to those on another system.

The process of RTL is to determine what adjustment in

inlet pressure is necessary to achieve the desired match in retention times.

To establish and maintain a locked method, RTL should be performed whenever:

- The column is changed or trimmed
- The method is installed on a new instrument
- A detector of different outlet pressure is used
- System performance is validated
- Troubleshooting chromatographic problems

To lock a given method for the first time or for the reasons below, you must first develop a retention time versus pressure (RT versus P) calibration. Even when using columns with the same part number (same id, stationary phase type, phase ratio, and same nominal length), separate/different locking calibration curves are needed when using:

- Systems with different column outlet pressures
- Columns differing from the "nominal" length by more than 15% (for example, due to trimming)
- Systems where the predicted locking pressure falls outside the range of the current calibration

A specific solute (usually one found in the normal method calibration standard) must be

chosen and then used for both developing the locking calibration and locking all future systems. The solute, or target peak, should be easily identifiable, symmetrical, and should elute in the most critical part of the chromatogram. Solutes that are very polar or subject to degradation should be avoided.

Once the target solute has been chosen and all other chromatographic parameters of the method have been determined, five calibration runs are performed. The runs are made at conditions identical to the nominal method except that four of the runs are made at different pressures. The pressures used are typically:

- Target pressure -20%
- Target pressure -10%
- Target pressure (nominal method pressure)
- Target pressure +10%
- Target pressure +20%

The retention time of the target compound is determined for each run. The resulting five pairs of inlet pressures and corresponding retention times are generated by the MSD Security ChemStation software and an RTL calibration is generated.

This calibration only needs to be generated once. Subsequent users of the method can use this calibration when running the method on a similar instrument setup, regardless of location.

Audit Trails

The FDA rule requires that audit trails be generated automatically and independently of the operator. The audit trail documents all relevant activities with date and time stamp information and the full user name of the current application user. Audit trails cannot not be turned off, nor modified or deleted. Audit trail information is stored electronically and is available in human-readable format for viewing as well as printing.

The system provides for three levels of Audit Trail:

System Audit Trails

General system events such as Logging on to the MSD Security ChemStation, unsuccessful logon attempts, setup of new users and so on are written to the system audit trail.

Record Audit Trails

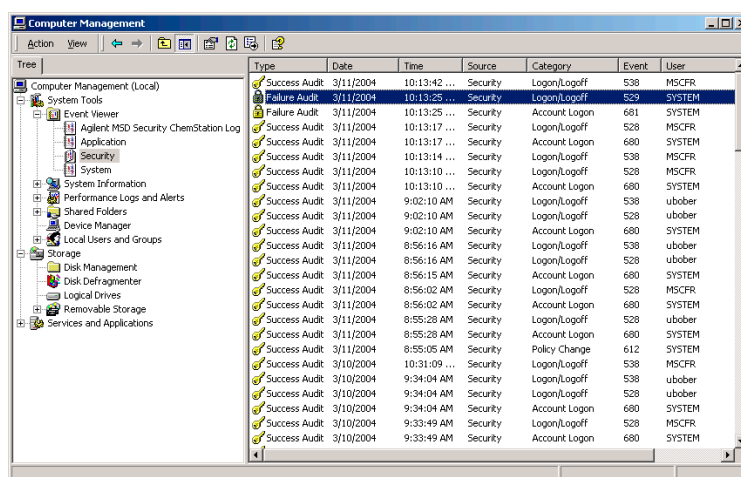
Documents all events related to a specific electronic record. It contains information on versioning of records, applied electronic signatures, and related approval comments.

Acquisition Logbooks

Contains events related to the acquisition of data as well as the instrument, for example, errors or turning it on or off.

System Audit Trail

The MSD Security ChemStation uses Windows Event Logging for documenting security-specific events as well as for capturing system events. For example, user logon/logoff as well as failed logon attempts are recorded in the Windows Security Event log (with success auditing enabled for that event). See Figure 10. The record contains information on the name of the affected user as well as date and timestamp of the event.



Type	Date	Time	Source	Category	Event	User
Success Audit	3/11/2004	10:13:42 ...	Security	Login/Logout	538	MSCFR
Failure Audit	3/11/2004	10:13:25 ...	Security	Login/Logout	529	SYSTEM
Failure Audit	3/11/2004	10:13:25 ...	Security	Account Logon	681	SYSTEM
Success Audit	3/11/2004	10:13:17 ...	Security	Login/Logout	528	MSCFR
Success Audit	3/11/2004	10:13:17 ...	Security	Account Logon	680	SYSTEM
Success Audit	3/11/2004	10:13:14 ...	Security	Login/Logout	538	MSCFR
Success Audit	3/11/2004	10:13:10 ...	Security	Login/Logout	528	MSCFR
Success Audit	3/11/2004	10:13:10 ...	Security	Account Logon	680	SYSTEM
Success Audit	3/11/2004	9:02:10 AM	Security	Login/Logout	538	ubober
Success Audit	3/11/2004	9:02:10 AM	Security	Account Logon	680	SYSTEM
Success Audit	3/11/2004	8:56:16 AM	Security	Login/Logout	538	ubober
Success Audit	3/11/2004	8:56:16 AM	Security	Account Logon	680	SYSTEM
Success Audit	3/11/2004	8:56:15 AM	Security	Account Logon	680	SYSTEM
Success Audit	3/11/2004	8:56:02 AM	Security	Login/Logout	528	MSCFR
Success Audit	3/11/2004	8:56:02 AM	Security	Account Logon	680	SYSTEM
Success Audit	3/11/2004	8:55:28 AM	Security	Login/Logout	528	ubober
Success Audit	3/11/2004	8:55:28 AM	Security	Account Logon	680	SYSTEM
Success Audit	3/11/2004	8:55:05 AM	Security	Policy Change	612	SYSTEM
Success Audit	3/10/2004	10:31:09 ...	Security	Login/Logout	538	MSCFR
Success Audit	3/10/2004	9:34:04 AM	Security	Login/Logout	538	ubober
Success Audit	3/10/2004	9:34:04 AM	Security	Account Logon	680	SYSTEM
Success Audit	3/10/2004	9:33:49 AM	Security	Login/Logout	528	MSCFR
Success Audit	3/10/2004	9:33:49 AM	Security	Account Logon	680	SYSTEM

Figure 10. Security Event Log.

The event details reveal additional information such as an unknown user-ID logged during an unsuccessful logon attempt (Figure 11). This can give administrators an indication of an attempt to gain access to the system by an unauthorized individual.

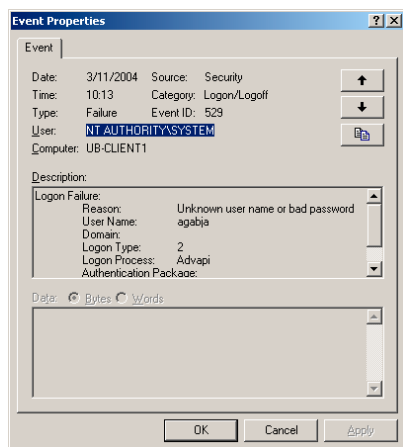


Figure 11. Event details showing an unsuccessful logon attempt.

The Agilent MSD Security ChemStation log, an application-specific event log that is created during installation, captures all events that are specific to the application, for example, the archival of data or a change of the application user. Figure 12 gives an example of an event detail logged by the Agilent MSD Security ChemStation log. Like the Windows Security log, the content can be viewed with the standard Windows Event Log Viewer. The log files are stored in the Windows standard location. The same policies for event log size limits and archival should be applied as for other systems to allow an archival of the log files in reasonable intervals, based on the local standard operating procedures for backup and recovery, and data archival.

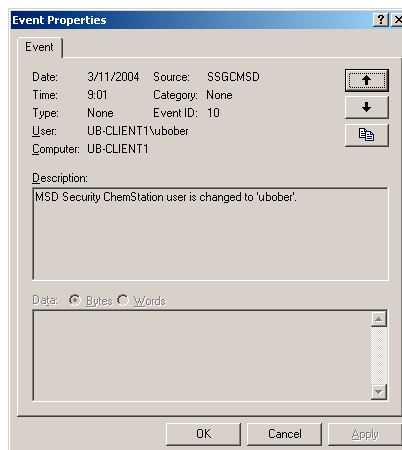


Figure 12. Event detail logged in the MSD Security ChemStation log.

Record Audit Trail

Record audit trails are maintained for results, methods and sequences. They are inherent parts of the records and document all changes applied to the record. Each new version of a result, method, or sequence requires an electronic signature, which is written to the audit trail with information on the change. The audit trail contains a complete change history of every record, for example, the result audit trail will carry information on all integration iterations that generated new results - regardless whether automatic or manual integration - or library searching activities, automatic as well as interactive. It also documents any kind of spectral manipulation, such as adding or subtracting spectra. Figure 8 on page 13 gives an example of a result audit trail, where the user approved it with an electronic signature after reviewing it and inspecting a library search result.

Acquisition Logbooks

During data acquisition, all events are documented in the sequence logbook with date and time stamp (Figure 13). The sequence and run logbooks document data acquisition events such as:

- Execution of a sequence
- Sample and data file name of the acquired data
- Name of the method that was run
- File location of the acquired data
- Any errors encountered during the sequence

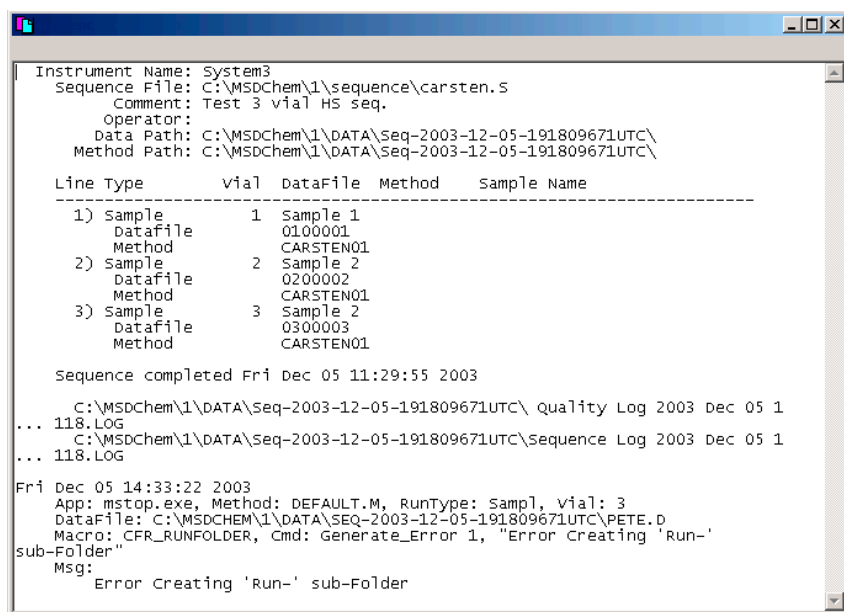


Figure 13. Sequence logbook.

The instrument logbook contains all events related to the instrument. As shown in Figure 14, this includes:

- Turn-on or turn-off events and power failures
- Information on the 'ready' status of the instrument
- Loading and saving of methods
- When a run is started, stopped or aborted

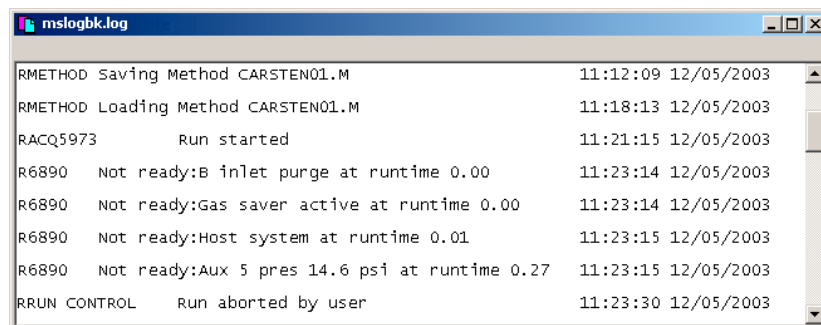


Figure 14. Instrument logbook.

Checks

As controls for a closed system, the FDA rule mandates the following checks:

- “operational system checks to enforce permitted sequencing of steps”
- “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”
- “device (for example, terminal) checks to determine... the validity of the source of data input”

The MSD Security ChemStation addresses these requirements as described in the following paragraphs:

- Operational system checks are used to enforce permitted sequencing of steps. For example, processes that require sequenced steps are the archive/delete procedure - records must be archived before they are allowed for deletion - or electronic signing - a record cannot be electronically signed without specifying a reason for the signature.
- Authority checks are used to ensure that only authorized individuals can use the system. This is achieved using standard Windows functionality as well as application-specific security controls. For example, a mandatory logon to the MSD

Security ChemStation further protects the system from unauthorized access. See “Data Security” on page 8 for more information.

- Device checks are standard consistency checks in the software. During startup as well as when sending a command (such as starting a run) to the instrument a bidirectional connectivity check is done. The instrument is clearly identified by its GPIB address or IP address, which has to be configured by the administrator when setting up the system. See also “System Configuration” on page 13.

Import/Export Function

The MSD Security ChemStation provides a controlled import/export mechanism for data (.D), methods (.M), sequences (.S) and libraries (.L) as shown in Figure 15. These two functions provide a bridge between the MSD Security ChemStation and other MSD ChemStations.

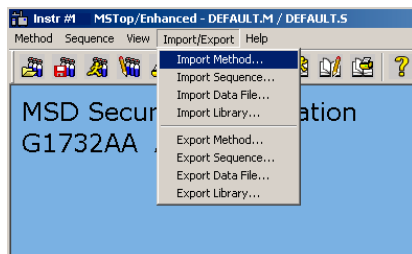


Figure 15. Import/Export of data.

Import

Import copied files from the hard disk or external medium, such as

a CD-ROM or floppy disk, into the MSD Security ChemStation. Import should be used to migrate data from an MSD Productivity ChemStation to the MSD Security ChemStation.

Export

Export writes files from the secure file system either to the hard disk or to an external device. Security restrictions are removed from the exported copies. The original files are not changed.

In order to use this function, a user must have Analyst or Manager permissions. Operators are not allowed to import or export any data. The user is required to give an electronic signature and a reason when

importing data. The activity is documented in the audit trail.

The export/import does not transfer the complete electronic record with all versions, raw and meta data, and audit trail. Import only migrates data (raw data, single methods or sequences, and libraries) to the MSD Security ChemStation. Export only retrieves these records from the secured environment. For exchange of complete records between MSD Security ChemStations, the Data Archival function should be used.

Data Archival, Backup, and Recovery

As outlined in “Data Integrity” on page 11, electronic records generated by the application are always stored along with all related raw, meta, and result data (including all result versions). The data written to the hard disk can be stored to durable media by using the built-in tool for data archival. Data is archived in the system configuration editor as shown in Figure 16. The data archival tool allows creating archives with or without deletion of the local data stored in the MSD Security ChemStation. The delete mechanism should be used when data is no longer required online and is archived for long-term storage. An archive without deletion corresponds to the complete copy of an electronic record in electronic format, for example for provision of the data for inspection as mandated by the FDA, while printouts on paper or to file may serve as a human-readable copy of the same data.

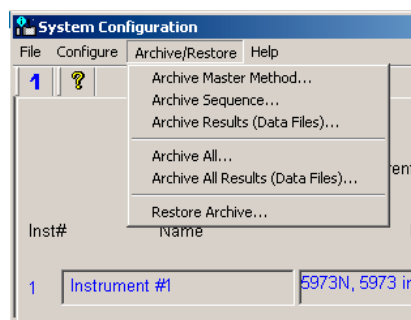


Figure 16. Options for data archival.

The built-in archive/restore tool provides for archival of:

- Methods (including all versions and audit trail)
- Sequences (including all versions and audit trail)
- Result data, including
 - raw data
 - all related meta data (including methods and sequences)
 - all result versions
 - audit trail information (including electronic signatures)

The user can decide to archive single records, all result records or all records, with or without deletion.

Archiving is a sensitive process. The user is required to authenticate himself with user ID and password before being able to archive any data. The archival of data is logged in the Agilent MSD Security ChemStation Log as shown in Figure 17. For more details on the system audit trails see “Audit Trails” on page 24.

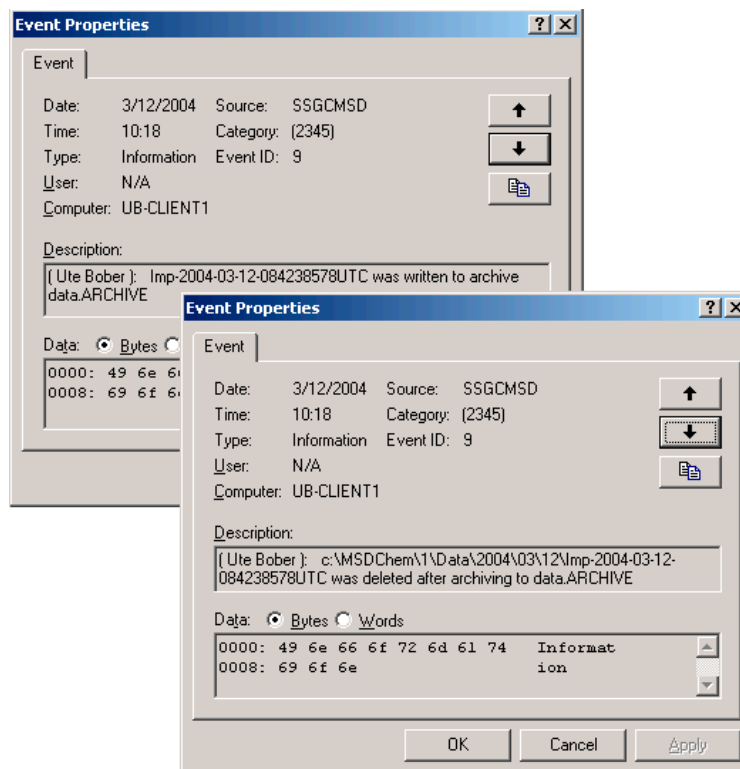


Figure 17. Logging of the archival in the system audit trail.

The built-in archive/restore tool provides for:

- User-configurable archive name and destination on the local hard disk
- Automatic deletion of archived data after successful archival
- Optional archival without delete for backup purposes or provision of data to a regulatory agency for inspection

- A catalog file (`<archive name>.MANIFEST`) in XML format for each archive unit describing its content (for example, for data handling in archive management or knowledge engineering systems). See Figure 18.
- Single archive file (`<archivename>.ARCHIVE`)
- Secure and easy restore of archived data
- Archives can be stored on any online or offline archive media

Archival generates a single, compressed archive file, secured with a file hash that is calculated during the process and attached to the archive unit. A data integrity check during dearchival ensures that the archive was not altered by comparing the stored hash value to a newly calculated one. If this check fails, the archive will fail to restore. An archive unit can be restored to any MSD Security ChemStation.

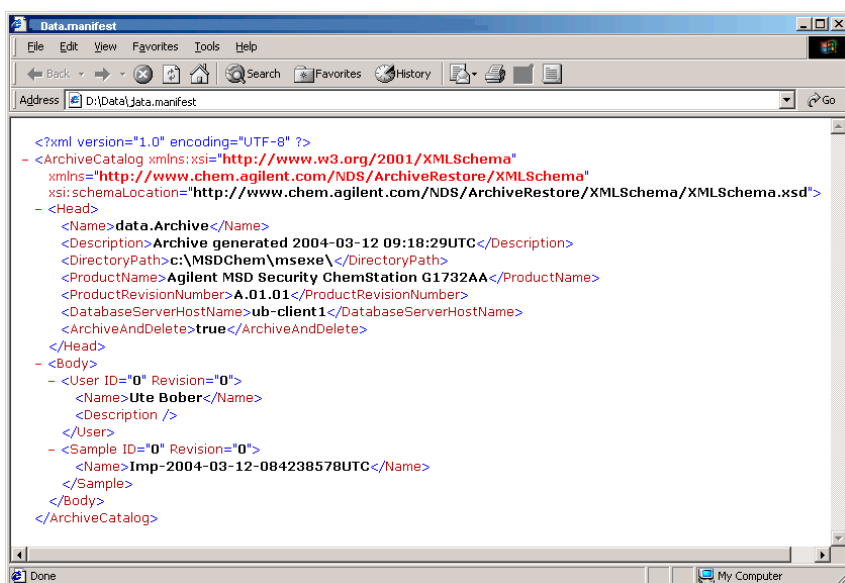


Figure 18. Example of XML file.

Automatic Backup of Data

The only Windows group whose members have access to the MSD Security ChemStation file system are Windows BackupOperators (Figure 19). With this design it is possible to implement advanced backup strategies, for example, with "incremental backup" where already archived files get flagged. Since 21 CFR Part 11 requires that procedures have to be in place to ensure data integrity it is important to notice that with this design BackupOperators can modify the MSD Security ChemStation data without logon to MSD Security ChemStation and generating audit trails. Thus, there should be an SOP in place stating that all MSD Security ChemStation operators should not be a member of the BackupOperators group. This is because an operator could have an interest to modify data to match some specification. The SOP could, for example, read "The system administrator should restrict regular MSD Security ChemStation operators and their managers from modifying data through technical controls".

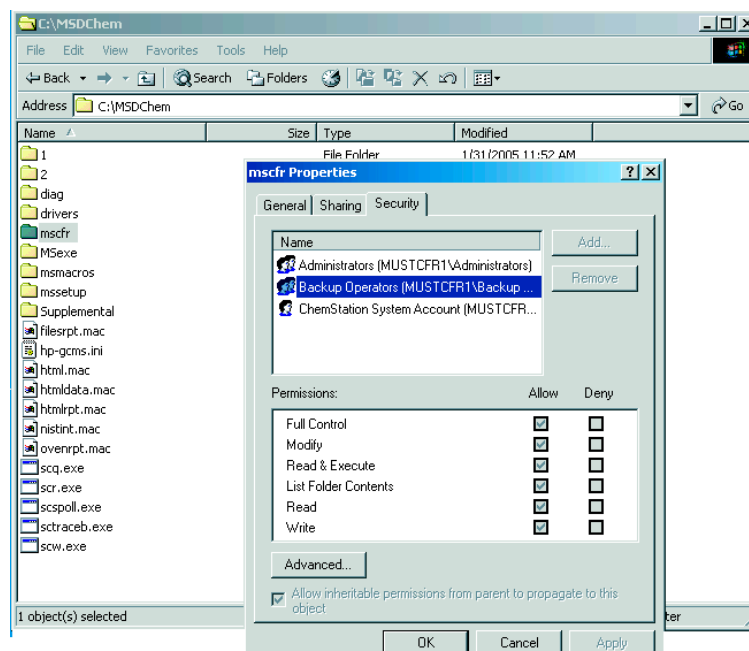


Figure 19. Backup-operator set up in Windows User Management.

Product Structure and Ordering

The complete Agilent MSD Security ChemStation is provided on a single CD-ROM. For existing MSD ChemStations, Agilent provides an upgrade product for upgrading to the latest revision of the MSD Security ChemStation as described below in Table 3.

Table 3. Ordering Information

Description	Product no.
MSD Security ChemStations	
Require but do not include Windows 2000 (SP4) or XP (SP2)	
MSD Security ChemStation Software	G1732AA
Migrates the G1701DA MSD Productivity ChemStation to G1732AA MSD Security ChemStation	G1742AA
Upgrades MSD Security ChemStation G1732AA Rev A.01.xx to Rev A.02.00	G1652AA
MSD Security ChemStation Bundles	
Include PC, monitor, printer, LAN communications, LAN cable, LAN hub, and Windows XP	
High-performance MSD Security ChemStation Includes G1732AA MSD Security ChemStation, Pentium PC with 512 MB RAM, DVD/CD-RW, 17-inch LCD monitor, printer equivalent to HP 2300 LaserJet, installation, and familiarization	G1729DA Option 210
MSD Libraries	
All require a PC with CD-ROM drive	
NIST05 MS Library Bundle Includes NIST05 Library, NIST05 Mass Spectral Search and Deconvolution programs, and NIST05 Chemical Structure Library (G1036A). Requires 145 MB of free disk space.	G1033A
NIST Chemical Structures Library	G1036A
NIST MS Library Bundle Upgrade	G1041A
Wiley Library, 7th Edition Requires 143 MB and 91 MB of free disk space for full and condensed CD-ROMs.	G1035B

Validation Services

The MSD Security ChemStation is validated during design and ships with a declaration of system validation based on the internal quality processes at Agilent.

On the other hand, formal acceptance testing is expected from the user. The objective of this test is to ensure that the system supports the work-practices of the laboratory based on the established operating procedures.

Note: Functionality not covered by the system itself may be covered by a procedural control SOP.

Users may perform the validation tasks themselves or may decide to purchase the validation services from a qualified party (typically the vendor).

Agilent delivers a fully qualified data handling system together with all necessary services which are needed to implement such a system to meet the requirements of the FDA regarding

21 CFR Part 11. Agilent offers additional validation services for installation qualification (IQ), operational qualification (OQ) and ongoing performance verification (PV) for hardware and software. As part of this service a document is compiled that describes the installed configuration and documents the results of the executed IQ and OQ procedures.

Installation Qualification

IQ ensures that new Agilent hardware and software is installed correctly from the moment it is unpacked to the point it is ready for operation -

documenting the completeness of the shipment, the operating environment and the components of the system.

Operational Qualification

OQ ensures basic accuracy from the beginning. OQ is performed to verify and document an Agilent instrument's ability to meet specified performance criteria after it is installed. OQ involves a comprehensive test of the complete system using established conditions and known sample characteristics. A key benefit to this procedure is to ensure the basic accuracy and precision of the instrument or system and to uncover any potential problems before they occur.

Agilent Technologies helps you qualify your analytical instruments for correct installation and operation in your laboratory. We provide:

- Software that automatically verifies correct installation and operation of your hardware and computer software.
- IQ and OQ/PV delivery services for instruments, standalone computer systems and networked data systems (NDS). This consistent and efficient delivery by Agilent's certified engineers will produce uniform documentation from laboratory to laboratory, assuring consistent and traceable test results amongst all your operations.

- Documentation of SOPs for equipment testing.
- Audit-ready documentation of qualification results, collated in system binders. This provides evidence to help satisfy the requirements from the regulatory agencies, and ensures confidence in the integrity of your measurements.

Documentation

Using the Online Help

The MSD Security ChemStation software comes with extensive online help which includes both task and reference information about the system.

The online help for each analysis mode is comprehensive and context-sensitive, with full text-search capabilities. There is a Help menu in every view of the software which gives you access to the help topics.

The information in the online help can be viewed on the screen, printed as an individual topic, printed as a set of topics, or copied to the Windows clipboard for incorporation into the user's documentation.

Learning the Software

The online help is the primary source of information on how to use the MSD Security ChemStation software. It provides information about instrument control, data acquisition, data analysis, methods, sequencing, tuning, troubleshooting the MSD, and system commands.

The example methods and data files supplied with the software can be used to practice and learn the MSD Security ChemStation software features described in the online help.

Software User Information CD

A Software User Information CD-ROM is supplied with the MSD Security ChemStation software. This CD can be used to learn more about your GC/MS system.

The Software User Information CD contains the following information:

- An MS Fundamentals tutorial.
This tutorial explains the basics of GC/MS principals, and includes graphics, animations, and video files.
- A glossary that defines common MS terms.
- A collection of manuals in PDF format:
 - G1732AA MSD Security ChemStation Software Installation Manual
 - G1732AA MSD Security ChemStation MSD Manager's Guide
 - G1732AA MSD Security ChemStation Software User's Guide

For More Information

For more information about ChemStation products and services, go to our Web site at: www.agilent.com/chem/nds

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