Agilent ChemStation Plus

January 2003

Specifications

General Description

This document provides specifications for Agilent ChemStore C/S, Agilent ChemStation Plus Security Pack, Agilent ChemAccess C/S Agilent ChemStation Plus Method Validation Pack, which are part of the Agilent ChemStation Plus family. With the Agilent ChemStation Plus family you need only purchase the features needed. This can be the fully featured software package for the most advanced capabilities, or you can exclude features that you may not want now, and add them later as your needs change.

The Agilent ChemStation Plus software package currently consists of the modules below.

Agilent ChemStation for GC, LC, LC/MSD, CE, UV-visible and A/D systems—instrument control, data evaluation systems. Detailed specifications are available in the Agilent ChemStation Specifications (Agilent publication number 5988-5314EN).

Agilent ChemStore C/S—data organizing and storage module that provides a scalable in-process chromatographic data organization system for Agilent ChemStations (pages 2–16).

Agilent ChemAccess C/S—remote access module that provides a laboratory-wide remote status and control client/server data system for networked Agilent ChemStations (pages 17–19).

Agilent ChemStation Plus Security Pack—designed to support the requirements of 21 CFR Part 11. It uses a relational database based on the ChemStore C/S database for secure result data storage, data review and electronically signing off runs (pages 20–31).

Agilent ChemStation Plus Method Validation Pack—advanced statistics module to calculate the quality of analytical results including configuration, design and execution of method development and method validation experiments. It provides an automated printout of a complete method validation report as requested by ICH and Pharmacopoeia guidelines. All validation data are stored with versions in a built-in relational database for full data security and data integrity and to support FDA's 21 CFR Part 11 (pages 32–59).

Agilent Technologies

1. Agilent ChemStore C/S

Product Description

Agilent ChemStore C/S is a scalable in-process chromatographic database for Agilent ChemStations. It provides a means to easily organize, review and approve analytical data based on study and sample information. Agilent ChemStore C/S supports the users' data review process offering statistically result summaries, flexible control charts, cross-sample reports and documented data archiving and restoring. These services also aid users in doing on-going system suitability testing. The Agilent ChemStore C/S server database can be used as a single place for data storage for all analytical data including methods, sequences and the raw data. This data storage also satisfies the requirements for data handling in a regulated environment including the detailed requirements of the U.S. food and drug administration for electronic records and electronic signatures, known as 21 CFR Part 11.

Agilent ChemStore C/S is available in two different configurations:

- **Agilent ChemStore C/S standalone database**
  This provides a low cost, easy-to-use, entry-level database module which integrates with a single Agilent ChemStation workstation.Very limited maintenance support is required and any user with advanced knowledge of the Windows NT or Windows 2000 operation system functionality for backup and administration can maintain it. This entry-level database module allows for storage of all raw and meta data in single database file to ensure full data integrity. The file format adheres to a common standard, which is used by many other applications, for example, MS Access.

- **Agilent ChemStore C/S server Oracle® database client/server system**
  This client/server system is based on an Oracle database running on a Windows NT or Windows 2000 server together with multiple Agilent ChemStations and/or Agilent ChemStore C/S review clients. It provides enhanced data security and data integrity, distributed processing, as well as the ability to store raw data, methods and sequence files within the database. This configuration reflects best the regulatory needs for electronic records and ensures full data integrity and traceability.

Based on standard database features, Agilent ChemStore C/S offers functionality which focuses on the user's needs for fast, secure and traceable handling of chromatographic data:

- User-defined or automated transfer of selected data from the Agilent ChemStation into the Agilent ChemStore C/S database.
- Define, edit and manage "studies" as the underlying data storage format.
- Manage or restrict data access in studies by assigning study access only to authorized users.
- Create database queries graphically without the need for any knowledge of the SQL language.
- Review entire sets of data across instruments and studies, that several sequences in a fast and easy manner.
- Create additional filters and selection criteria to produce adequate subsets of the study in order to best sort the data and optimize the performance.
- Complete audit traceability by individual log-ins and complete documentation within the database including authorization failures.
- Security check of all files that have been transferred over the network from the ChemStation application to the ChemStore database application and back. Whenever a corruption of the datafile is detected, the user receives an error message and the file is no longer available for modifications.
- Approve or reject runs after reviewing, following the rules for electronic signature.
- Ability to flag an arbitary set of samples for reprocessing, and to initiate batch reprocessing of those samples on any Agilent ChemStation in a C/S network.
- Custom fields—User specified additional information fields with each set of results ("run") to hold values not measured by the Agilent ChemStation (for example, weights, pH, etc.) that can be used for later queries, reports or charts.
- Flexibility in scaling and labeling control chart data.
- Simple user-defined calculations for control charts and reports.
- User-controlled fast and easy data export to other applications such as MS Excel®.
- Powerful and intuitive report generator based on MS Access runtime including most commonly used report templates.
- Architecture allows for off-line review. Can be installed as a data review client running on a separate PC without needing the Agilent ChemStation software.
- Data from non-Agilent chromatography systems may be included via the Agilent ChemStation AIA import capability.
- Agilent ChemStore C/S offers the possibility to start with an entry level solution, and to then upgrade when the data processing needs increase. Laboratories can easily upgrade from one or more entry-level standalone systems to an Agilent ChemStore C/S server Oracle database client/server system. Previously stored data in the entry-level databases can be easily migrated to the new server database. The user interface does not change, except that some additional items are available for administrators.
- A built-in archive/delete tool allows for easy data transfer to other disks and or media to free up database space while keeping a complete audit-trail of all archiving and delete operations.
- Automatic archiving based on a set of configurable archive queries for easy database maintenance and administration.
- Open system connectivity using XML (Extensible Markup Language) for easy data exchange with other applications.

1. Agilent ChemStore C/S standalone

Hardware requirements

The following list shows the minimum hardware requirements for this application:

- 400-MHz Pentium II (Pentium IV recommend)
- 4 GByte of free hard disk space
- 96 MB RAM for single ChemStation instrument. 128 MB is recommended for best performance, for Windows 2000 the minimum requirement is 128 MB.
- 128 MB RAM for two ChemStation instruments (256 MB or more is recommended for best performance)
- Display: 1024 × 768, small fonts, 65-thousand colors

Software requirements

The following list shows the minimum software requirements for this application:

- Windows NT Workstation 4.0 with Service Pack 6a, or Windows 2000 Professional with Service Pack 2
- Agilent ChemStation revision A.09.03 or later
- Microsoft Internet Explorer 4.01 or later
- Microsoft data access components (MDAC) 2.5 will be installed on your system. If you already use a later version of MDAC, or for compatibility reasons require a previous ver sion, please contact your Agilent support representative for compatibility information.
- A local or network printer must be installed and configured.

Hardware considerations

Disk space requirements depend on several factors, such as:

- number of runs and compounds,
- technique (3D data requires more disk space than 2D data)
- Agilent ChemStation report style
- the “Store in Addition” settings of the study to which the run is assigned, (see table 4 on page 7), and
- use of custom fields
- database backup requirements

Typical runs use approximately 10 KB for a short report with four peaks, and use up to 300 KB per run for an extended performance report with 20 peaks. Table 1 helps calculate the amount of hard disk space requirements. Additional information on this topic may be found in the *Agilent ChemStore C/S Installation* manual and the *Concepts Guide*.

Note:
The standalone database size is limited to 800 MB due to some strict size limitations in the underlying file format. To ensure optimum performance for later data review Agilent strongly recommends not to exceed this database size limit. If a larger single database is required, Agilent recommends that the client/server version of the product be purchased. The client/server database uses Oracle, which allows for a much larger database. Additional standalone databases can be created via the Agilent ChemStore C/S utility.

Number of peaks	Agilent ChemStation report style	Run length (minutes)	Approximate size per run (KB)
4	short	6	10
4	short	30	40
4	extended performance	6	80
20	short	6	190
20	extended performance	6	300

Table 1
Client storage requirements for result only data storage

2. Agilent ChemStore C/S server Oracle® database system

Client hardware requirements

The following list shows the minimum requirements for the ***client*** in a client/server installation.

- 400-MHz Pentium II (Pentium IV recommend)
- 4 GByte of free hard disk space
- 96 MB RAM for single ChemStation instrument. 128 MB is recommended for best performance, for Windows 2000 the minimum requirement is 128 MB.
- 128 MB RAM for two ChemStation instruments (256 MB or more is recommended for best performance)
- Display: 1024 × 768; small fonts; 65-thousand colors

Client software requirements

- Windows NT Workstation 4.0 with Service Pack 6a or Windows 2000 Professional with Service Pack 2
- Microsoft TCP/IP protocol
- Microsoft Internet Explorer 4.01 or later
- Microsoft data access components (MDAC) 2.5 will be installed on your system. If you already use a later version of MDAC, or require for compatibility reasons a previous version, please contact your Agilent support representative for compatibility information.
- Oracle 8i client version 8.1.7 (included with the ChemStore C/S server software)
- Agilent ChemStation version A.09.03 or higher (optional)
- A local or network printer must be installed and configured.

Server hardware requirements

Agilent has optimized the performance of a ChemStation Plus client/server system to an average of 30 "concurrent" Agilent ChemStation/Agilent ChemStore Review clients, where concurrent clients are defined as clients connected to the central ChemStore C/S data organization system, that actively either spool data to the database or perform interactive queries (review client). Due to the nature of the application the impact of data retrieval is higher as this requires direct access to the database, while during acquisition the spooler is able to buffer data, thus ensuring a secure transfer in case of a network failure, for example. So the optimum number of concurrent clients might vary depending on the work practice in the laboratory. Depending on the combination of 2D/3D instruments, a typical high-end configuration can thus grow to approximately 30 acquisition clients with a maximum of 90 instruments. It is therefore recommended to use a high speed dual processor system with sufficient RAM.

The minimum requirements for the ***server*** in a Client/Server installation are the following:

- 600-MHz Pentium III processor
- 512 MB RAM
- RAID SCSI controller
- 6 disk drives - 9 GB or larger– 2 drives configured as a mirror set and 4 drives configured as a RAID-5 array
- Tape Device
- Uninterruptable Powersupply (UPS)

Note:
The drive configuration yields one mirrored partition for the operating system and application software, and one large array for the database files.

Server hardware considerations

The hardware requirements of the Agilent ChemStore C/S server will

	Entry level	Standard level	Highend level
No. of concurrent review clients	1-5	1-15	> 15
Processor speed (GHz)	1	1	1
Number of processors	1	1	2
RAM (MB)	512	1024	2048
Number of RAID controllers	1	2	2
Disks for operating system	2 × 18 GB RAID 1	2 × 18 GB RAID 1 (Controller 1)	2 × 18 GB RAID 1 (Controller 1)
Disks for Oracle database	3 × 18 GB RAID 5 RAID 5	5 × 18 GB RAID 5 (Controller 2)	5 × 36 GB RAID 5, (Oracle Data, Contoller 2) 2 × 18 GB RAID 1 (Index Log Files, Rollback Segments, Controller 1)
Hot swappable drives	yes	yes	yes
Backup device	DAT/DLT tape drive	DAT/DLT tape drive	DAT/DLT tape drive
UPS	yes	yes	yes

Table 2
Recommended server configurations for Agilent ChemStore C/S

vary based on the size of the database selected at installation time and the number of concurrent connections (the number of active instruments acquiring samples to the database and Agilent ChemStore C/S review clients) and the backup requirements for the server database. Table 2 shows three recommended server configurations. In a very small networked installation with less than three clients and no need for advanced security using RAID, the Chemstore C/S Oracle database can also run on a high-end PC using Microsoft Windows NT server software as operating system.

Note:
Planning the server disk configuration is very important:
12 GByte (for small database) to 54 GByte (for large database) hard disk, RAID 5 configuration is recommended. Using a RAID 5 hard disk configuration (redundancy and striping) yields less free hard disk space than RAID 0 (no redundancy). For example, 3 disks of 9 GByte each using RAID 5 yields 18 GBytes while using RAID 0 yields 27 GByte. RAID 5 is recommended for maximum performance and protection of your data. For backup operation of the database, the required disk space must be duplicated, that is a 54 GByte RAID 5 configuration should have an additional 54 GByte of disk space available for database backup. When calculating server memory requirements, calculate 8 MB of additional memory for each Agilent ChemStore C/S client. For more details on setup and configuration of the server, please refer to the *Agilent ChemStore C/S Installation* manual.

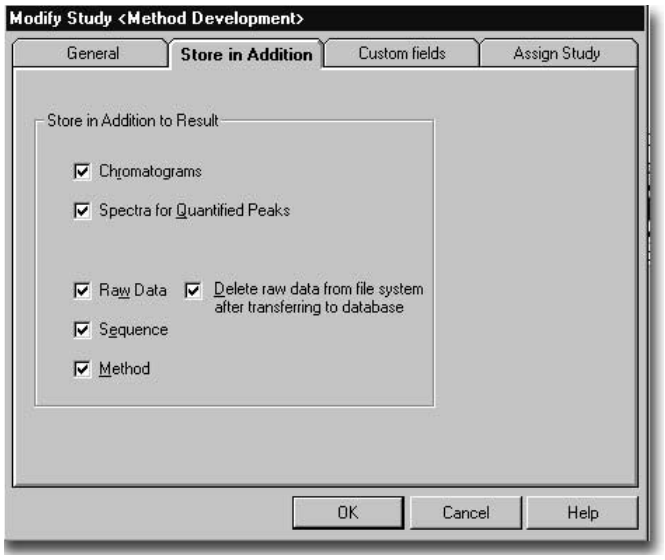

Figure 1
Study setup for full data integrity in the server database

Server software requirements

- Windows NT Server 4.0 with Service Pack 6a or
- Windows 2000 Server with Service Pack 2
- Microsoft TCP/IP network protocol
- Microsoft Internet Explorer 4.01 or later (for admin client only)
- Internet Information Server version 3 or greater (IIS is integrated into Windows 2000 Server but has to be installed separately for Windows NT)
- Oracle 8i Standard Edition version 8.1.7 (included with ChemStore C/S server software)

Database size

The database size is selected at installation time and should be given careful consideration as this will affect the total number of runs which can be accessed online and the frequency of archive/dearchive operations. Archive with delete (to recover run space in the database) or dearchive operations (to access run data online). At installation time you can either select from the preconfigured databases configurations listed in table 3, or have a customized configuration.

Database configuration	Approx. no. of runs	Database size
small	≤ 7500	4 GByte
medium	≤ 25000	10 GByte
large	> 25000	40 GByte

Table 3
Database configurations

Note: The custom database configuration must be planned as a project with Agilent database consulting specialists prior to system installation. The size of the Agilent ChemStore C/S database is based on an Agilent ChemStore C/S system which has an average distribution of all Agilent ChemStation 2D and 3D techniques. Also, all *Store in Addition* checkboxes are enabled for all studies, as shown in figure 1. The space requirements for runs stored in the Agilent ChemStore C/S database will vary depending on your environment. A run is defined as a single set of results produced from a single sample acquisition or reprocessed by an Agilent ChemStation which has been transferred and stored in the Agilent ChemStore C/S database.

The actual amount of space consumed by each run in an Agilent ChemStore C/S database will vary depending on:

- the *Store in Addition to Result* settings of the study to which the run is assigned (table 4), and
- the technique and complexity (numbers of peaks, Agilent ChemStation reports, custom fields, and so on) of your chromatography for that run.
- For details on the size of raw data files by technique, please refer to table 5.

Technique	Average file size (kB)
GC/LC	2D – 50
LC	3D – 60
LC/MS	3D – 750
CE	3D – 600

Table 5
Average raw data file size by technique

Supported Agilent ChemStation software

Agilent ChemStore C/S can be used with the following Agilent ChemStation software:

- Agilent ChemStation for gas chromatography, revision A.09.03 or later,
- Retention time locking software, add-on module for Agilent ChemStation for gas chromatography,
- Agilent ChemStation for liquid chromatography, revision A.09.03. or later,
- Gel permeation chromatography software add-on module for the Agilent ChemStation for LC,
- Agilent ChemStation for capillary electrophoresis, revision A.09.03. or later,
- Agilent ChemStation for liquid chromatography mass selective detection, revision A.09.03 or later.
- Agilent ChemStation for analog signal acquisition, revision A.09.03. or later,
- Agilent ChemStation for capillary electrophoresis mass selective detection, revision A.09.03. or later,
- Agilent ChemAccess C/S remote instrument control, and
- Agilent ChemStation Plus Method Validation Pack A.01.02.

Store in Addition	Description
Chromatograms	Stores all available chromatograms (from each detector and/or signal)
Spectra for quantified peaks	Stores spectra from all peaks that have been identified and quanti fied as compounds in the calibration table.
Raw data	Stores the acquired data in addition to the calculated result. *Note:* This setting has a significant effect on the amount of storage space required for each run in the ChemStore C/S database. For example ChemStation data which is created from 3D techniques such as a liquid chromatography diode array detector will require more storage space than a 2D technique such as gas chromatography.
Sequence	Stores the ChemStation sequence.
Method	Stores the ChemStation method

Table 4
***Store in Addition* study settings**

1. Data transfer

The Agilent ChemStation Plus concept consists of different software components designed for the various tasks in the chromatographic laboratory. The Agilent ChemStation manages data acquisition and data analysis, and the Agilent ChemStore C/S database offers advanced data and result management along with additional sample information management such as data organization, result approval, and archiving. This concept allows a clear separation of result rework and result review and offers unmatched data integrity and traceability by tracking the data history — Results in ChemStore can only be under review or after review completion, results in ChemStation are under rework. It is therefore very important to have a secure and documented data transfer between the software application. The specifications will offer a detailed outline of the data transfer including security measures for both directions.

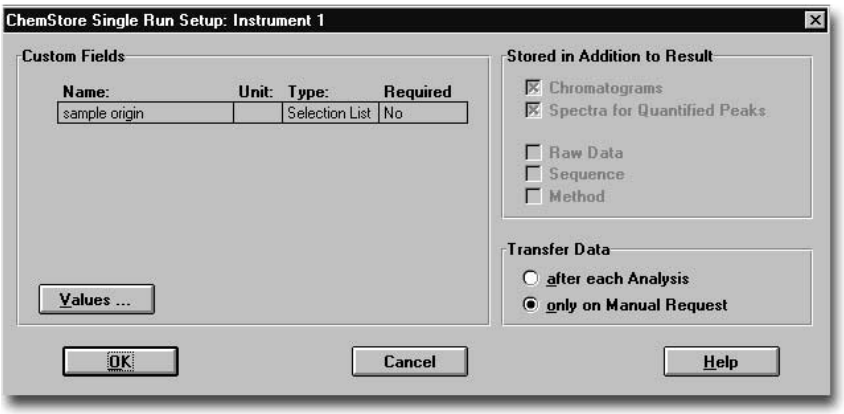

Figure 2
Data transfer setup screen in the Agilent ChemStation

From Agilent ChemStation to database

Agilent ChemStore C/S offers two modes of data transfer from the Agilent ChemStation into the Agilent ChemStore C/S database – interactive mode and automated mode. Figure 2 shows the interactive mode.

Interactive mode
Users perform the transfer manually from the Agilent ChemStation menu item in "Data Analysis View" or use the batch review interface of the Agilent ChemStation. This mode of operation is useful for analysts who wish to perform a first pass data review from the Agilent ChemStation data analysis view before transferring the approved results to the database.

Automated mode
Results are transferred automatically to the database at the end of each run. This mode ensures that all analytical data are transferred into the Agilent ChemStore C/S server database and are protected from unattended modification. If the same sample injection is reanalyzed and then transferred, a new version of the result data is created, together with an entry in the audit trail of the Agilent ChemStore C/S database, thus ensuring a full history of the injection.

File security during data transfer
Each file that is transferred over the network from the ChemStation to the ChemStore database or back is protected with a hash value. The application software automatically calculates the hash value prior to any data transfer using a 24 character value based on the RSA Data Security, Inc, MD 5™ message digest algorithm. The hash value is stored with the data file. Whenever this data file is transferred over the network, e.g. for a reanalysis cycle, the same message algorithm calculates the hash value of the current file and compares it with the stored value. Any difference is reported as error and the data transfer is interrupted.

Assignment of studies and custom field information
Runs are stored in studies which form the top level hierarchy of the Agilent ChemStore C/S database. Study access is restricted to users

that are assigned to the study. Users must be assigned to a study in order to review study data or spool data into the study. The amount of result and meta data that is stored in the Agilent ChemStore C/S database is defined on a per study basis. For example, the transfer of a set of results may also include the raw data, methods and sequence file used to produce those results.

Custom fields allow additional information fields to be linked to each set of results ("run"). They are used to store additional information that is not accessible from the Agilent ChemStation method or results, that is, information which may reflect other measurements (for example, sample pH, patient weight, dosage, and so on) or may be used to organize the data (for example, the identification code of the test subject from whom a serum sample was obtained). These custom fields may be configured as "required" or "optional". For the former, a value must be specified before results can be transferred to the database or a sequence can be executed. Custom fields can also be used in later queries for reports or charts.

Study and custom field configuration

- Single sample/manual operation: Study and custom field values are entered by a "single run"' Agilent ChemStation menu item (figure 3).
- Sequence operation: Study and custom field values are specified per sequence line and and stored with the sequence.

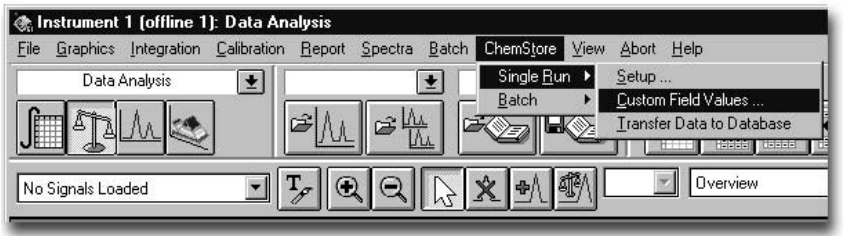

Figure 3
Data transfer setup screen in the Agilent ChemStation

Using Agilent ChemStore C/S data review capabilities, the lab manager or a quality control person can review data generated on multiple instruments throughout the lab.

Samples can be approved, rejected, excluded or assigned for rework by the Agilent ChemStation (see below *From database to the Agilent ChemStation*).

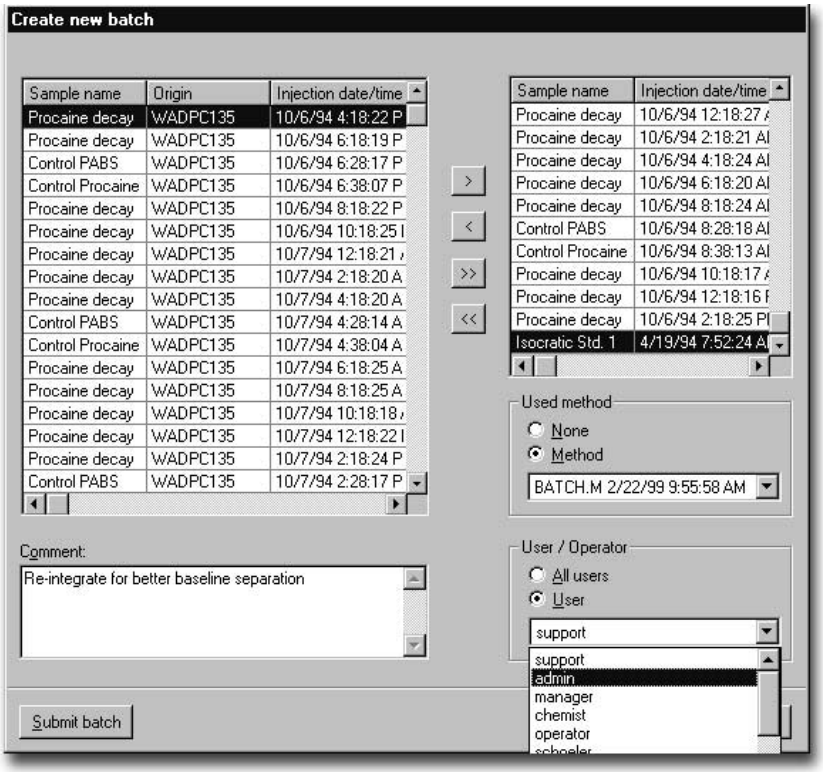

Figure 4
Batch setup for data transfer from database to the Agilent ChemStation

ChemStore spooler – Managing data transfer from Agilent ChemStation to Agilent ChemStore C/S
To ensure optimum performance of the Agilent ChemStation, a background spooler takes care of a secure result transfer from the Agilent ChemStation data into the Agilent ChemStore C/S database. This approach has several advantages, including

- releasing the Agilent ChemStation to go on with other tasks quickly while the transfer continues in the background and
- guarding against data loss in case the database insert operation fails or the network is down.

From database to the Agilent ChemStation

Runs which require further rework or further investigation can be transferred from the database to the Agilent ChemStation.
Agilent ChemStore C/S creates an Agilent ChemStation batch to ensure a consistent ease of operation. The setup for this batch resubmittal is a two-step approach:

1. Create the batch request from the Agilent ChemStore C/S review client by marking the runs for transfer in the user interface. The operator configures the transfer details in an interactive pop-up window (figure 4). These include
- assigning the run data to one or, in case of several runs, to more than one user for reanalysis on a per run basis,
- optionally transferring the method with the data (including the choice between all versions of the method), and
- entering a comment with each run transfer that will be displayed to the Agilent ChemStation operator.

2. Use the Agilent ChemStation *Load Batch from ChemStore* menu point to select the desired batch from the pool of Agilent ChemStore C/S batches to download the runs to the Agilent ChemStation.

2. Task flow in the review client

Retrieve and review sample data

The task flow of Agilent ChemStore C/S is designed to support the laboratory's workflow and can be outlined as follows:

1. Select the database that contains the data you want to work with.
2. Extract the set of results you will work with. This is done via a database query and the results become the "current set of data".
3. Perform any of the following tasks, in any order:
- Review the results "by sample" or "by compound". While reviewing the results, you may switch between any of several different data presentations (for example, a table, a chart, or plots of the chromatograms and/or spectra). In addition, you may specify additional statistical computations to be done on the results and included in the tabular or graphical presentations.
- Generate a report on the data in the set of data. Any of a set of report templates may be used, and you may customize those templates according to your needs.
- Export selected data. Data may be sent to an Excel 5.0 "*.xls" file or to an application that supports cut-and-paste of the appropriate format.
- Set up a "batch" by marking runs whose data and method are to be transferred back to the Agilent ChemStation for reanalysis.
- Filter or exclude any run in the current data set.
- Approve or reject runs based on your result review. Both steps follow the FDA requirements for electronic signatures.

Performing statistics calculations

The user may optionally select to have statistical calculations performed on the (numerical) data which is being reviewed, as shown in figure 5. This can be achieved using summary statistics that calculates statistical values based on a single column of numerical values. The calculated values are:

- number
- minimum
- maximum
- sum
- mean
- variance
- standard deviation
- relative standard deviation

In addition, *Regression Statistics* can also be used to calculate curves and statistics of two numerical columns. Curve types include:

- linear
- quadratic
- cubic
- logarithmic
- exponential
- power

The curve parameters for the curves and the residuals will be calculated and displayed. Residual and curves can also be displayed in a chart.

Custom expressions

Mathematical calculations may be performed on results using the built-in expression definition interface (figure 6).

This offers the basic expression functions (addition, subtraction, division and multiplication) plus the following functions:

- exponential
- natural logarithm
- logarithm
- square
- square root

	Biphenyl			
Statistics	Amount	RT	Area	Height
Count	15	15	15	15
Sum	0.14	38.57	4074.03	559.70
Minimum	0.00536	2.56547	142.49	25.44
Maximum	0.01701	2.58024	452.50	58.34
Mean	0.00955	2.57133	271.60	37.31
Standard Deviation	0.0045	0.0051	127.4384	13.9228
Rel. Std. Dev. (%)	47.2374	0.1968	46.9210	37.3131
Variance	0.0000	0.0000	16240.5492	193.8437

Figure 5
Summary statistics

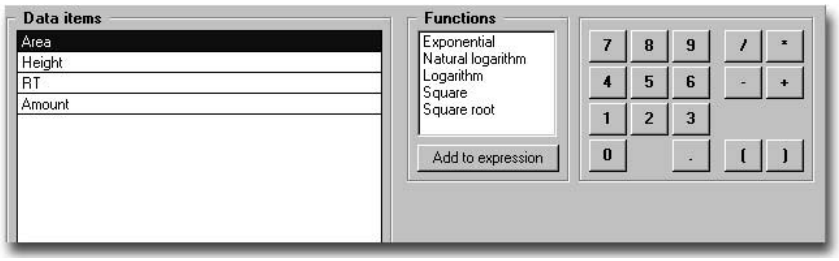

Figure 6
Setup of custom expressions

Agilent ChemStore C/S — Reporting

Agilent ChemStore C/S offers a powerful report generator enabling users to easily create and generate final summary reports. The preview function helps to interactively develop the desired report without requiring test printouts. Agilent ChemStore C/S comes with a set of built-in templates to cover the most common needs for summary reporting. These templates can be used as a starting point to build your own customized reports.

Following is a list of built-in reports
- *Analysis Results* reports.
- *Compound Amounts* reports for individual results.
- *Instrument and Run* reports
- *Peak Details* reports
- *Sample* reports with numeric tables of the result information.
- *Kinetic Decay* reports.
- *System Suitability* summary reports including statistics over replicate injections.
- Sequence summary report—a complete report for GMP requirements including summary statistics, graphics of chromatograms and spectra and result charts with control limits for each compound type grouped by the sample type.

The following are key customizable features of the reporting
- display of the selection criteria of the query,
- display of all custom calculations that have been used in the data section of the report
- an overall report header displayed on each page that allows to include graphic items such as a company logo,
- table information,
- fonts and font attributes,
- individual sections with additional individual headers containing data tables, chromatogram and spectra (if available from a diode array detector) or data charts,
- individual page breaks,
- additional sorting criteria within one data section to group data logically, for example, around a vial number, a sample type or any other item that the user requires,
- restriction capabilities to focus on an adequate subset of the data, that is, one peak within a chromatogram, and
- statistical calculations selected interactively at any time during the data review from the ChemStore C/S user interface.

The ChemStore C/S application offers an additional functionality to print the current view. This function gives access to an immediate printout of the actual screen including all graphics without any formatting or configuration tasks.

Agilent ChemStore C/S — Data Export into Other Applications

Agilent ChemStore C/S allows an easy export of selected database information (selection by records and data fields) to third party applications (notably MS Excel). The user has control over which fields are included and in which order. This can be done based on queries or reports exporting data into the native file format. Agilent ChemStore C/S also offers clipboard cut-and-paste for both tabular and graphical data (figure 7). Report outputs can be in a file format allowing convenient publishing of reports, for example, HTML for internet and intranet publishing. ChemStore C/S allows printing in the following file formats:
- HTML format for review with an Internet browser (excluding graphics).
- CSV format for spreadsheet applications
- XML format as generic file-interface

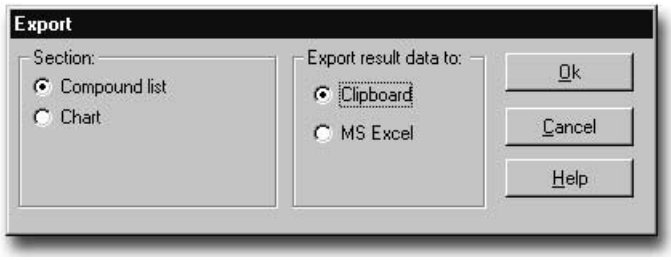

Figure 7
Interactive data export from Agilent ChemStore C/S into other applications

Agilent ChemStore C/S — User Interface

The Agilent ChemStore C/S review client offers the user two main "toolkits": data review and database administration.

Sample and compound review

Within the data review toolkit, the user has a choice of whether to see data organized by analysis (also referred to as "run" or "sample") or by compound.

Chromatogram/spectrum presentation

Here, the display area can contain both graphics and a table. The details differ for sample and compound review.

General chart presentation

The chart presentation is available only if no summary or regression statistics are in use. If regression statistics are being calculated, the regression chart and residual chart presentations replace it.

Figure 8 is an example of a chart contained in the display area.

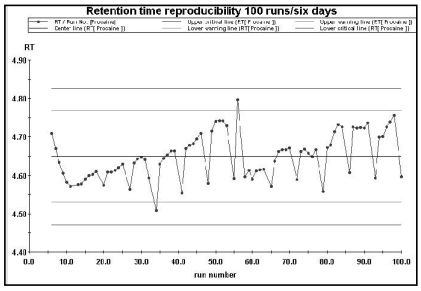

Figure 8
Chart for retention time reproducibility with warning and critical limits

Agilent ChemStore C/S — Security

Data acquisition, data analysis and data review are password-protected. Each user must have a valid user-id and a password to log on to the application, as shown in figure 9. To be able to transfer data to the database the user must be logged on to the database. User validation is done on a per database level and always requires to enter a user name and a password. Permissions for several tasks like approval or archival of runs, creation of custom fields or studies can be assigned to each individual user. Four user group templates for permission rights are supplied with the review client. They can be used as a starting point for the assignment of the permissions. Note that users and their security permissions are configured separately for each Agilent ChemStore C/S database. Users and their permissions can be imported from an existing database during creation of a new standalone database. In a client/server environment users are centrally managed in the Oracle database.

Electronic signatures and password security

Agilent ChemStore C/S uses electronic signatures based on the application User-ID/password combination to uniquely identify the users and their signatures. In order to keep the password unique to the individual user an additional security function is implemented to periodically check and revise passwords, and apply the company's password policy. *Minimum length* is the minimum acceptable length (in characters) of a password. *Password validity* is the length of time (in days) over which the password remains valid. *Minimum password recycle* is the minimum number of new, unique passwords that a user must use before a password can be used again.

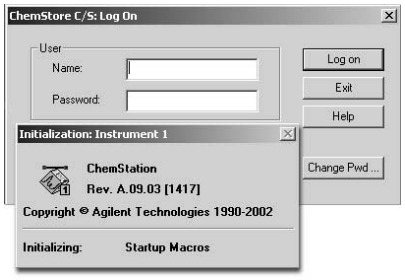

Figure 9
Password protection of the application software

Agilent ChemStore C/S — Database Administration, Backup and Recovery

Database administration

The review client provides the graphical user interface (GUI) through which the user can accomplish the following administrative tasks. Although the capabilities of the entry-level and client/server versions are to some extent different, the GUI is identical.

- Create a new database–(entry level database only),
- Compact (defragment) a data base–(entry level database only),
- Create or modify a study or custom fields,
- Administer system settings,
- Administer users and security,
- Manual or automatic archive, delete and de-archive data (server-only),
- Assign studies to users,
- Email notification on security violations (server-only).

The client/server version offers supplementary tools for administrators in the *Admin Client* to perform proper maintenance of the server database, archive/ dearchive or archive/delete functions and other setup tasks. The Agilent ChemStore C/S *Admin Client* is a web-based application that can be run from any PC on the network. The *Admin Client* performs the following main tasks on the server database using a service running on the server.

- Schedule archive, dearchive and delete operations.
- Modify scheduled operations.
- View reports detailing pending operations.
- Review archive and dearchive history.
- View information about archives, runs and other objects, including a list of all runs in the archive unit.
- Execute archive, dearchive and delete operations immediately.
- Keep an audit trail of all archive and archive delete operations.
- Add and modify database connections to offer connection to a second Oracle database.

Database backup and recovery

One of the most important IT routines is the implementation of a Backup and Restore concept. Backups and – equally as important – the ability to restore a backup are important tasks in order to protect business data and laboratory investments.

Agilent Technologies can provide assistance in creating, implementing and testing a ChemStore C/S Server Backup and Restore strategy. This strategy should ideally be planned before the implementation but Agilent offers both, a service prior to the installation as well as a post implementation service.

For this purpose a ChemStore C/S Backup & Recovery strategy paper has been developed. With this strategy paper and by working with a customer's ChemStore C/S administrator Agilent provides a consulting service to plan and implement the right backup and recovery strategy for your business.

With a working knowledge of implementing solutions Agilent uses software from Veritas called Veritas Backup Exec™ for Windows NT and Windows 2000, Backup Exec Agent for Oracle™ and Backup Exec Intelligent Disaster Recovery.

Agilent ChemStore C/S — Archiving Data

The client-server version provides for manual or automatic archiving to a separate file on disk or tape of runs present in the database.

Manual archiving is done from the "Archive/Delete" view in the ChemStore C/S review client and is based on the selected data set.

An administrator with archival permission can set up a list of individual archive queries for automatic archiving, which are executed at predefined time intervals. Each custom query is put together from a set of criteria, including for example, injection time, sample name, instrument name, operator name, sequence name, method name, study name, custom field values, approval status and so on (figure 9a). The available operands depend on the data category (text, numeric values, date) including wildcards and relative values (for example, runs "older than x days"). For performance reasons the number of clauses that can be defined for

automated archival is restricted to 10. Each archive query is stored under a unique user-defined name and can be executed based on a configurable time interval (per query), for example, daily, weekly, monthly or in conjunction with a counter such as every x days. A test functions allows the user to obtain information on the number of runs that the query returns at the moment with the given query condition. For each archive query the name and path for the archive unit have to be specified. The filename for the automatic archive file is appended with the archival date, resulting in a file name format "<filename>-yyyy-mm-dd". Each archive query can be disabled when not required permanently. After successful completion of the archive the data can be automatically deleted to create free space in the database.
Both manual and automatic archival require re-identification with user-ID and password.

A checksum-protected archive catalog file in XML format is generated with each archive unit, which contains detailed information about the content of the binary archive file. A generic archive interface provides a closer linkage to other applications for enhanced archive management (for example, archive management or hierarchical storage management systems).

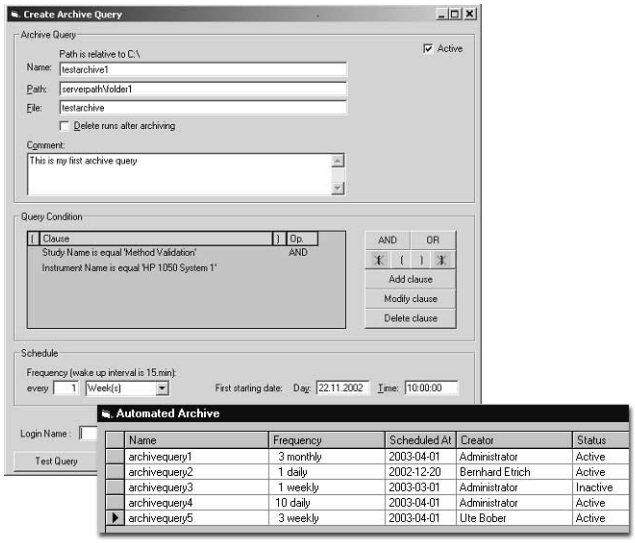

Figure 9a
Setup of automatic archive queries

Agilent ChemStore C/S — Installation and Upgrading

The standalone version of Agilent ChemStore C/S is user-installable from the ChemStore C/S CD-ROM and can be added to an existing ChemStation installation (Agilent ChemStation software family CD-ROM version A.09.03 or higher).

The Agilent ChemStore C/S Oracle client/server version includes :

- ChemStore C/S server software (included on the ChemStation Plus CD-ROM),
- Oracle 8i standard edition version 8.1.7 (included in ChemStore C/S server software on a separate CD-ROM),
- ChemStation Plus CD-ROM, and
- ChemStore C/S client software (on ChemStation Plus CD-ROM).

Agilent ChemStore C/S database migration

The Agilent ChemStore C/S system includes a migration utility which enables you to migrate your Agilent ChemStore C/S data in the following ways:

- Migrate Agilent ChemStore A.01.03 or B.0x.0x data (standalone) to Agilent ChemStore C/S B.02.02 (standalone).
- Migrate Agilent ChemStore C/S B.02.02 data to Agilent ChemStore C/S server data.

If you are currently running Agilent ChemStore A.01.03 on your system, and you wish to migrate your data to the Agilent ChemStore C/S server Oracle database, you will need to migrate in two steps. First migrate to the B.02.02 Agilent ChemStore C/S standalone database, then migrate from there to the Oracle database.

Agilent ChemStore C/S — Product Options and Configurations

Standalone version

The complete Agilent ChemStore C/S standalone software is provided on the Agilent ChemStation Plus CD-ROM as described in table 6a.

Agilent ChemStore C/S server

The Agilent ChemStore C/S server product includes the ChemStation Plus CD-ROM and Oracle 8i revision 8.17 software on a separate CD-ROM offering one Oracle standard edition license. In addition an application-specific full user license is required and sold from Agilent for each additional user running a ChemStore review client. Five application-specific named user licenses are already included with the Agilent ChemStore C/S server software. Refer to table 6b for details.

Description	Product No.
Software module to add Agilent ChemStore C/S to an existing ChemStation for GC, LC, LC/MSD, CE, CE/MSD or A/D.	G2181BA
License to use the ChemStore C/S database module on another computer. Must either be on the same order as G2181BA or the customer must supply the license number for the original software. Does not require ChemStation.	G2186BA
ChemStation Plus client upgrade software, upgrades a single ChemStation Plus client to the latest software revision. Requires valid software licenses and ChemStation upgrade software G1656A.	G1657A

Table 6a
Agilent ChemStore C/S standalone version

Description	Product No.
ChemStore C/S client/server version. Includes ChemStore C/S server software Oracle standard editions, 5 Oracle application-specific named user licenses.	G1410A Qty: 1 per server
Oracle connectivity license. Required for each additional named user of the ChemStore C/S server database.	G1411A Qty: (number of named users) –5
Licence to use the ChemStore C/S review client on another computer. Includes one online ChemStore license for use with an online data acquisition ChemStation plus an additional offline ChemStore license for offline data review	G2186BA Qty: (number of clients connected to the server)
ChemStation Plus client upgrade software, upgrades a single ChemStation Plus client to the latest software revision. Requires valid software licenses and ChemStation upgrade software G1656A.	G1657A
ChemStation Plus server upgrade software Upgrades ChemStation Plus server software to the latest revision. Includes G1656A ChemStation software upgrade. Requires valid software license.	G1655BA

Table 6b
Agilent ChemStore C/S client/server version

2. Agilent ChemAccess C/S

Product description

Agilent ChemAccess C/S is a client/server application which facilitates the secure and controlled integration of Agilent ChemStations into a networked environment by enabling users to:

- monitor and control instruments from any client on the network, for the following instrument modules:

  HP 1090 Series and 1050 Series, Agilent 1100 Series, Agilent CE system, Agilent 5890, 6850, 6890 GC systems, Agilent 5972, 5973A and 5973N GC/MSD system, Agilent 1100 LC/MSD system, Agilent 35900 A/D converter
- provides flexible centralized data organization features which allows Agilent ChemStation files to be automatically and securely stored onto the Agilent ChemAccess C/S server. This functionality is largely superceded when combining or adding Agilent ChemStore C/S to a Agilent ChemAccess C/S system.

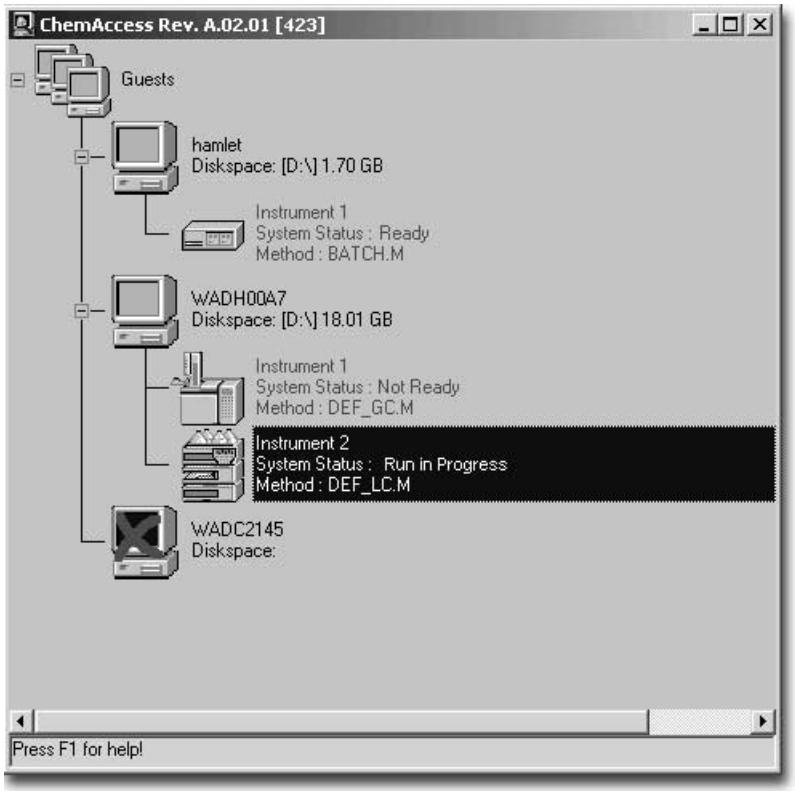

Figure 10
Agilent ChemAccess C/S remote status and control user interface

An Agilent ChemAccess C/S data system contains Agilent ChemStation clients, the Agilent ChemAccess C/S software and a Microsoft Windows NT server. Agilent ChemAccess C/S is compatible with both the multi-technique Agilent ChemStation and data analysis versions, enabling flexible and cost effective remote status monitoring control and review from locations which are situated away from the laboratories instrumentation.

Remote status and monitoring and control

From any Agilent ChemAccess C/S client an authorized user can remotely perform the following tasks on a remote instrument:

- Start and stop the method or sequence currently running.
- Assign a method or sequence
- Real time plot of the instrument signals.
- Execute a remote Agilent ChemStation command.
- Monitor the status of the remote PC's resources (disk space, memory and software revisions).
- Monitor the status of the Agilent ChemStation and instrument modules. Details are shown in figure 10.

Working with Agilent ChemAccess C/S

Data storage and organization

Agilent ChemAccess C/S enables the Agilent ChemStation results (raw data, methods and sequences) to be securely stored on the Agilent ChemAccess Windows NT server. The results can be transferred automatically at the end of each run or interactively through the data analysis view of the Agilent ChemStation. If the same results are retransferred to the server, Agilent ChemAccess C/S employs data versioning to ensure that an entire record of the analysis is recorded.

Agilent ChemAccess C/S — System Requirements

Client hardware requirements

Agilent ChemStation and ChemAccess C/S

The PC client should conform to the requirements as specified in *Agilent ChemStation Specifications* (Agilent publication number 5988-5314EN). In addition to these requirements further 8 MB memory is required for network connectivity software and Agilent ChemAccess C/S software.

Agilent ChemStation, ChemAccess and ChemStore C/S

Configure the client using the Agilent ChemStore C/S client hardware requirements specified in this document.

Client software requirements

The ChemAccess C/S client module can be added to the Agilent ChemStation. The ChemAccess C/S module is supported with the following ChemStation software packages:

- Agilent ChemStaion for gas chromatograhpy mass selective detection revision C.00.xx,
- Agilent ChemStation for gas chromatography, revision A.08.04. or later,
- Retention time locking software, add-on module for Agilent ChemStation for gas chromatography,
- Agilent ChemStation for liquid chromatography, revision A.08.04. or later,
- Gel permeation chromatography software add-on module for the Agilent ChemStation for LC
- Agilent ChemStation for capillary electrophoresis, revision A.08.04. or later,
- Agilent ChemStation for liquid chromatography mass selective detection, revision A.08.04.or later,
- Agilent ChemStation for analog signal acquisition, revision A.08.04. or later, and
- Agilent ChemStation for capil lary electrophoresis mass selec tive detection, revision A.08.04. or later.

Each Agilent ChemStation that is integrated in an Agilent ChemAccess C/S system should conform to the following Agilent ChemStation and Windows software revisions:

- ChemStation for GC, LC, LC/MSD, CE and A/D revision A.08.04 or higher on Windows NT 4.0 Service Pack 6a or Windows 2000 Service Pack 2
- GC/MSD ChemStation revision C.00.xx on Windows NT 4.0 Service Pack 6a.
- GC/MSD ChemStation revision D.00.xx on Windows NT 4.0 Service Pack 6a or Windows 2000 Service Pack 2.

Note:
Agilent ChemAccess C/S currently does not support the Agilent ChemStation for UV-visible systems.

Server hardware requirements

Agilent ChemAccess C/S supports up to 15 “concurrent” Agilent ChemAccess clients, where concurrent is defined as a client connected to the Agilent ChemAccess C/S server which either transfers result data from the Agilent ChemStation to the server for data storage or performs remote real time plot. Recommended server configurations are listed in table 7.

Note:
For a ChemStation Plus server system which has both Agilent ChemAccess and Agilent ChemStore modules, use the Agilent ChemStore C/S server requirements. Disk configurations may need to be customized to fit to your laboratories online and to long term storage needs.

Server software requirements

- Windows NT 4.0 with Service Pack 6a or Windows 2000 Service Pack 2
- Microsoft TCP/IP networking (supplied with Windows NT and Windows 2000).

	Entry level	Hi-end
Number of clients supported	1-10	1-15
Agilent NetServer model or equivalient	LC2000	LH3000
Processor speed (MHz)	933	1 GHz
Number of processors	1	1
RAM	384 MB	512 MB
Disk (number and size)	3 x 18 GB	2 x 18 GB, 3 × 18 GB
Raid level	five	one and five
Hot swappable drives	yes	yes
Network interface card	1	1

Table 7
Recommended server configurations for Agilent ChemAccess C/S

Agilent ChemAccess C/S — Product Options and Configurations

The complete Agilent ChemAccess C/S software is provided on the Agilent ChemStation Plus CD-ROM. This includes the software listed in table 8.

Description	Product No.
ChemAccess server software for remote status, monitoring and control of ChemStation. Includes 10-user licenses for 3D data analysis software and a 2-user license for the GC/MS data analysis software	G1494A
ChemAccess client software, 5-user license remote status, monitoring and control client software for ChemStation.	G1495A
ChemStation Plus server upgrade software. Upgrades ChemStation Plus server software to the latest revision. Includes G1656A ChemStation software upgrade. Requires valid software license.	G1655BA

Table 8
Agilent ChemAccess C/S software

3. Agilent ChemStation Plus Security Pack

Product Description

The ChemStation Plus Security Pack is a module of the Agilent ChemStation Plus Series designed to support the requirements of 21 CFR Part 11. In the Agilent ChemStation the ChemStation Plus Security Pack modifies data analysis and provides advanced data management with regard to supporting the requirements for electronic records. It also offers a procedure to sign off runs with an electronic signature. It offers an easy upgrade for an existing ChemStation installation.

The Agilent ChemStation Plus Security Pack is compatible with the following ChemStation modules:

- Agilent ChemStation for GC, LC, A/D, CE, CE/MS and LC/MS for instrument control and data analysis
- Agilent ChemAccess C/S remote instrument control
- Agilent ChemStore C/S data organization and data storage module
- Agilent ChemStation Plus Method Validation Pack

The UV-Vis ChemStation offers a separate solution for 21 CFR Part 11. Please refer to the specifications of the UV ChemStation Security Pack included in publication number 5980-0678E.

The ChemStation Plus Security Pack is available as a standalone solution or in a fully integrated client server network connected to the ChemStore C/S server Oracle database. It provides full support of 21 CFR Part 11 by offering advanced data security, data integrity and full change documentation in audit-trails. Specifications of the ChemStore C/S database module are available in the ChemStore C/S section of this document.

To achieve data security, the ChemStation Security Pack utilizes a combination of Windows user accounts and file permissions and auditing. In addition, it utilizes an application-related second layer of data security based on standard database security features. The application-related security requires a valid ChemStation Plus user account allowing the log-on to the application. A user with administrative priviledges can assign appropriate user permissions to other users within the Chemstation Plus software.

The ChemStation Plus Security Pack software allows to match user tasks in the laboratory with user roles in the software. It modifies the ChemStation operator rights, allowing to routinely operate the ChemStation application in the operator mode. For proper use and to achieve the best data security capabilities of Security Pack, all users except those with administrative functions should utilize the ChemStation operator mode.

To achieve data integrity, all users are required to log on to a single database. This database (determination of the database connection requires the log-on to the Windows operating system with an administrator account) will store all raw and meta data. In addition, any recalculation of results in the ChemStation will automatically be recognized as a new result version and will be transferred to the database as a new version. This versioning assures that no data is ever lost or overwritten and that a complete chain of events is documented.

To achieve data traceability, the ChemStation Plus Security Pack utilizes logbooks and audit trails that document who did what, when and why. These logbooks and audit trails are user-independent and cannot be modified or deleted.

All data is in electronic format and capable of long-term storage/recall and printing in human readable format.

Key product features of the ChemStation Plus Security Pack include storage of all chromatographic data in a relational database, such as

- password protection to access the data,
- full data protection using Windows security and database security tools,
- application protection with a mandatory log-in,
- user management with individual user profiles and privileges for the application–independent of the operating system,
- an application-specific session lock allowing to lock one ChemStation session while leaving a second instance running on the same PC, and
- an automated time-based appli-

cation lock to lock the current ChemStation session and avoid any unauthorized access to the ChemStation application.
- A completely revised ChemStation operator access level which allows operating the entire application as ChemStation operator.
- A modified batch review interface providing an automated user-independent data versioning with detailed audit-trails for all modifications.
- Complete change control documentation for methods and manual events.
- Four levels of audit-trails for data acquisition, data analysis application tasks and security violations.
- Electronic signatures for each result version following the guidelines of 21 CFR Part 11.

ChemStation Plus Security Pack — System Requirements

Client hardware requirements

The following list shows the minimum hardware requirements for this application:

- 400-MHz Pentium II (Pentium IV recommend)
- 4 GByte of free hard disk space
- 96 MB RAM for single ChemStation instrument. 128 MB is recommended for best performance, for Windows 2000 minimum requirement is 128 MB.
- 128 MB RAM for two ChemStation instruments (256 MB or more is recommended for best performance)
- Display: 1024 × 768; small fonts; 65-thousand colors

Client software requirements

The following list shows the minimum software requirements for this application:

- Windows NT Workstation 4.0 with Service Pack 6a or Windows 2000 Professional with Service Pack 2
- Agilent ChemStation revision A.09.03 or later
- Microsoft Internet Explorer 4.01 or later
- Microsoft data access components (MDAC) 2.5 will be installed on your system. If you already use a later version of MDAC, or require for compatibility reasons a previous version, please contact your Agilent support representative for compatibility information.
- A local or network printer must be installed and configured.
- The hard disk partition that is used for installation of Method Validation Pack must be formatted with NTFS.

The standalone database size is limited to 800 MB due to some strict size limitations in the underlying file format. To ensure optimum performance for later data review Agilent strongly recommends not to exceed this database size limit. A configurable size-checking tool automatically launches a warning message when the specified size limit is reached.

If a larger single database is required, Agilent recommends that the client/server version of the product be purchased. The client/server database uses Oracle, which allows for a much larger database. Table 9 gives some data on the time of downloading data from the standalone database into the active memory of the client. The time mainly depends on the size of the standalone database and the number of runs marked for download. All runs were stored with raw data, methods and sequences. The PC used for the test was below the recommended configuration (Kayak PIII, 450 MHz, 128 MB, and no data acquisition running).

Database Size	No. of peaks	No. of runs	No. of runs loaded from database	Time [s]
93986	2137	240	100	17
192048	4642	410	100	17
445826	22621	868	100	13
			683	76
1048472	36710	2203	100	13
			683	59

Table 9
Run download time depending on the number of runs selected for download and the database size.

Result management

The ChemStation Plus Security Pack is designed to store ChemStation data in a relational database by transferring it as a post-data analysis spooling job to the database. The ChemStore C/S ODBC spooler is a proprietary tool managing the transfer and protecting data against loss, modification or damage in case of transfer problems or network errors.

Data protection

Using the Security Pack in the standalone version, all data is stored in a single database file. The subdirectory storing the database files is protected with Windows file security permission rights and only allows write access for members of the Windows user group.

The application denies access to data without a valid ChemStation Plus user-id and password. Any attempt to access the data in the standalone database directly with another application such as MS Access fails as it requires a password/user-id combination that is strictly confidential and only known by Agilent. It is not known by or given to any customer with this product.

Accessing data directly in the Oracle database without using the ChemStore user interface is impossible because users must have valid user-ID/password combination and they must have access to the data dictionary describing the meaning of the table columns. The dictionary is only available from Agilent Technologies against a written Confidentiality Agreement and should not be available for application users.

Data storage

By default the the database stores the following data:

- calculation results of the ChemStation,
- contents of the ChemStation data directories; the *.d directories including the chromatographic raw data files,
- current method used for data acquisition and data analysis,
- current sequence, if a sequence was run to acquire or reprocess data,
- sequence, run and method logbooks,
- detector channel chromatograms as images according to the report configuration of the method, and
- apex spectra of all identified peaks in a chromatogram, when using a 3D detector.

Protection of temporary data files

The ChemStation uses a given data directory structure to store acquisition and result data. The ChemStation Plus Security Pack also protects this data. After completion of data acquisition and a first result calculation, by default the data transfer is immediately initialized through the ChemStore spooler and the *.d directory with all its contents is deleted from the local hard disk (these default settings can only be modified by a user with administrative rights in the database). From then on, the data security mechanisms of the database itself secure the data. The temporary directory where the database spooler stores intermediate data is protected using Windows NTFS file security.

Reanalyzing data after a first pass result review in the ChemStation Plus requires restoring data files to a temporary subdirectory. The Security Pack protects this subdirectory hpchem/x/data/chemstor where x is the instrument session number with read-only access for members of the Windows users group thus denying unauthorized access for operators.

Configuration and data protection using Windows security features

For security reasons, a user must be a member of the Windows user group *Administrators* to access the configuration of the ChemStation Plus Security Pack. It restricts access to all data directories on the local PC with important information using the Windows users group privileges. The default configuration automatically sets all directory permissions and access limitations as part of the installation using the Windows groups “Users” or “Administrators”. Each ChemStation user has to be member of either one of the groups.

For custom configuration of the Windows user group and user rights, local IT can use this documentation to copy the default security settings and file permissions that are set automatically during installation to an individual user administration. It allows setting up either additional predefined NT user groups or new user groups configured individually in the company's Windows user management. Table 10 gives an overview of the permission rights that are limited to members of the Windows administrator's group.

Local directories storing relevant chromatographic data are also protected with Windows file and directory permissions. Table 11 gives an overview of the Windows permission rights on the data directories on the local hard disk. The first item in brackets displays the permission rights on the folder; the second item displays the individual file permission rights.

Note:
Windows file security does not give any access to a folder or directory for users that do not have access rights to the folder, even if the user has control over the files in the folder.

User task	Granted to members of Windows NT/2000 user group	Granted to member of NT administrator group
Create a new MS Access database	no	yes
Configure database Alias	no	yes
Access the ChemStore ODBC spooler to resume interrupted data transfer	yes	yes
Access to the selection list of available databases	no	yes

Table 10
Tasks requiring membership in the NT administrator's group

File path	Permission right NT user	Permission right NT administrator	Directory/file owner	Data directory contents
\hpchem\chemstor \database	(W)(full)	(full)(RWXD),	All members of local NT administrator group	Contains database *.mdb file storing all raw and meta data
\hpchem\chemstor \spool	(WX)(full)	(full)(RWXD)	All members of local NT administrator group	Spooler jobs and data files
\hpchem\chemstor \hputil00.exe	none	(full)	All members of local NT administrator group	Access to ChemStore utility tool to create/ copy and manage local database files
\hpchem\X (instrument session number)\data\chemstor	(WX)(Full)	(full)(RWXD)	All members of local NT administrator group	Stores data files reloaded from ChemStore database to ChemStation batch review

Table 11
Directory and file permissions [(directory)(file)] set by the ChemStation Plus Security Pack

User management and ChemStation Plus Security Pack user access rights

Security Pack provides a fully integrated user management that is independent of the Windows operating system. The user management covers both the ChemStation Plus data acquisition and data analysis tasks and the ChemStore C/S database data review privileges. The entire user administration itself is a user-privilege granted to administrators in the ChemStore C/S database. The ChemStation Plus Security Pack includes a modified ChemStation operator level allowing operators to perform all important acquisition and data analysis tasks for daily operations. Table 12 shows the most important changes in user privileges compared to the standard ChemStation for data acquisition. The ChemStation Manager always has access to all tasks within the ChemStation. A detailed documentation of the data review user privileges in the ChemStore C/S database is in the ChemStore C/S concept guide.

Application security

The Security Pack only allows users with a given user-ID to log on to the ChemStation Plus application, as shown in figure 9. Users need to be set up by the administrator to gain access. At initial login, users must specify their initial password in order to keep it unique to each user. Protecting the application software from unauthorized access during operation is possible with a separate session lock (figure 11). This lock function offers

- an interactive session lock which should be enabled manually before leaving the PC unattended, e.g. during a break or shift change, and
- for enhanced security a time-based automated lock of the session for other periods of short-term absence from the PC.

The time-based session lock is configured centrally through users with administrative rights in the ChemStore C/S database, and is automatically applied on all connected ChemStation Plus applications. The session lock allows to lock each instrument session individually, so users sharing computers with two or more instruments connected to one computer can operate with a clear and unique user identification. The name of the current user and the instrument session are always shown in the title bar. The instrument sessions can be locked either

- privately, allowing only the user who locked the session or an administrator to unlock it, or
- non-privately allowing all users with a valid user-ID in the data base to unlock the session, for example during shift changes (figure 11). If a dialog is still open the application will automatically lock privately.

User privilege	Security pack operator	ChemStation operator
Save acquisition method	no	no
Save data analysis method	yes	no
Load/run/save sequence	yes	yes
Modify acquisition parameter	yes	yes
Re-Integrate chromatograms manually	only in batch review	no
Change integration events	only in batch review	no
Recalibrate overview and peak summing	only in batch review	no
Recalibrate other	no	no
Apply method to data and print report	yes	yes
User-independent automated result versioning	yes	no
Access to tasks with manual result versioning	no	no

Table 12
Comparison of user privileges in the ChemStation Plus Security Pack and the standalone ChemStation

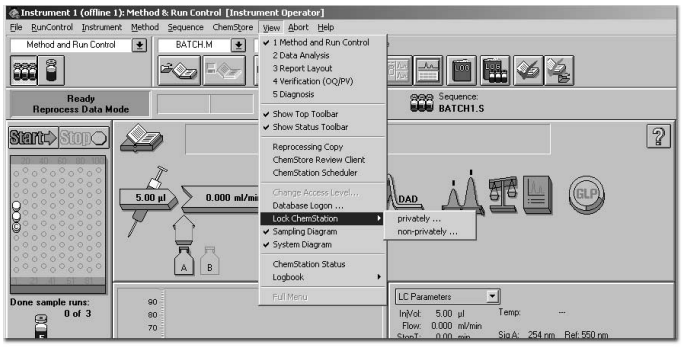

Figure 11
Instrument session lock

Data integrity

The Security Pack maintains full data integrity by storing all results along with the raw and meta data in a relational database as shown in figure 12.

Result revision management

Daily work in the analytical laboratory often requires sample reanalysis. The ChemStation Plus Security Pack includes a result versioning that stores all recalculation results from one original injection as result versions. In addition, the application software includes a tool that automatically detects new results during the reanalysis process. This application-controlled automated process does not require any user interaction such as *Save Results* or a similar action. It is completely user-independent and covers the following reanalysis steps:

- All functions in the batch review that calculate results such as reintegration, recalibration, execution of predefined methods including manual reintegration
- In the data analysis view: Integrating, printing reports and recalibration excluding manual reintegration

A sequence reprocessing and all initial review tasks (loading a batch from disk, initial loading of a run into the interactive data analysis view) always create new result versions. These reanalysis tasks cover all activities of the ChemStation operator thus ensuring that all reanalysis steps at the ChemStation operator level include a user-independent versioning.

In addition, ChemStation Plus managers can perform manual result manipulation interactively in the *Data Analysis* view without using the batch review window. The user-independent revision management does not cover the manual reanalysis of results in the standard ChemStation data analysis view. The user creates new result versions in this review function using the manual *Transfer Data to Database* command (figure 13).

The following manual tasks in the data analysis view require a user selected *Transfer Data to Database* command to create a new result version, such as

- drawing a manual baseline,
- deleting a peak,
- tangent skimming of one peak,
- splitting a peak, and
- integrating manually with a negative baseline.

Access to tasks with a user-dependent creation of new results is the only difference in the result management between the ChemStation Security Pack manager level and the ChemStation Security Pack operator level. The new result version in the database is the same for both automated and user-dependent data transfer.

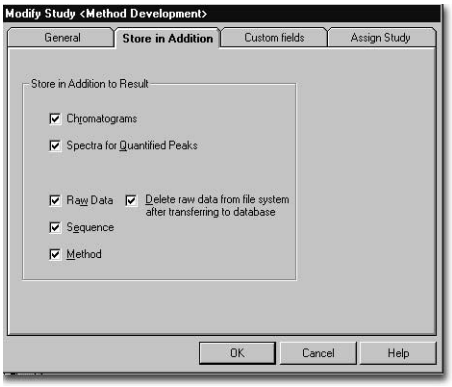

Figure 12
Default configuration of data storage in database

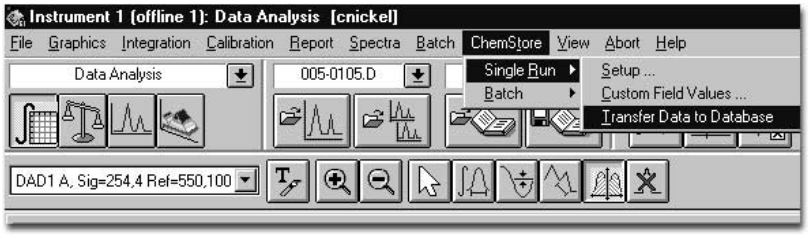

Figure 13
Manual revision management

User-independent, automated result version management

The data storage includes an application controlled version management that is based on the creation of a result reference file. Prior to reprocessing, the application software creates a binary result registry file called *save_sec.reg* for each file. This *save_sec* register is stored along with the raw data. It includes all numeric results of the current result revision in a binary format, such as amount, compound retention time and so on. Whenever a new result is calculated, the software automatically compares the new run result with the original result in the register file. If the results changed, the software detects the difference between the most recent and the current result and creates a new result version.

For proper documentation of the changes, the application software creates a second file in a human readable format that stores the results of the comparison and documents the changes. The file is named *sec_trac.txt* and is stored along with the raw data in the *.d subdirectory, as shown in figure 14. Both the registry and the text file are also stored in the database along with the raw data and they can be restored in order to regenerate the result from raw and meta data at any time, for example, in an audit situation. Manual integration events are also documented in the Manual Integration Events section of the ChemStore audit-trail as shown in figure 14a

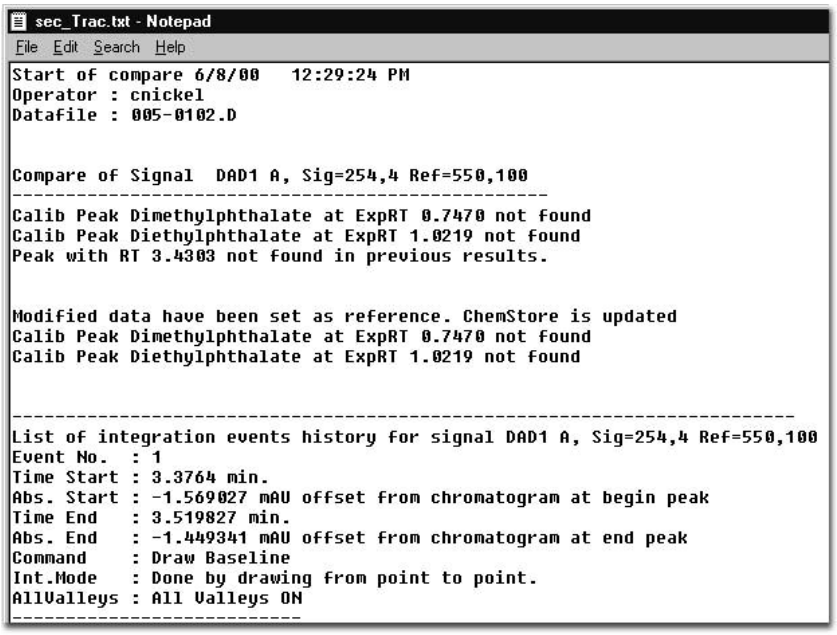

Figure 14
Text file documenting result changes for the actual run revision

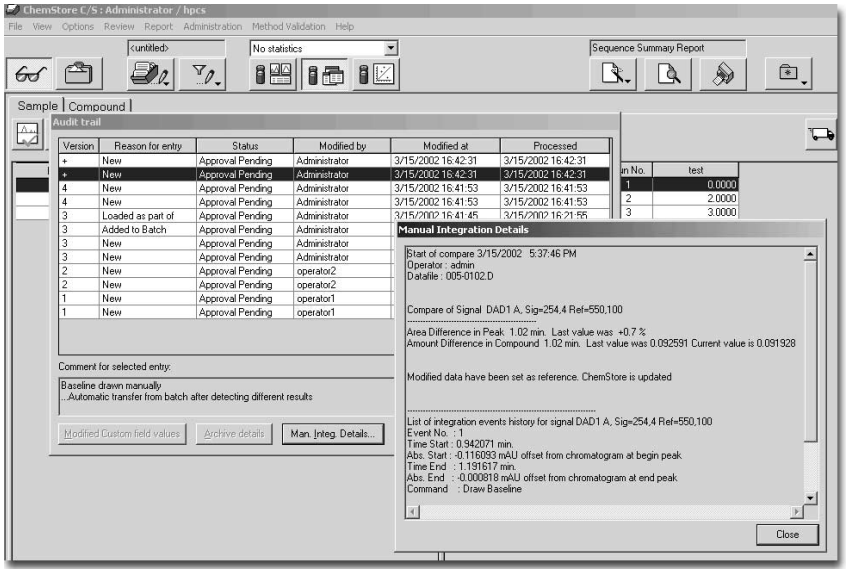

Figure 14a
Manual integration events documented in ChemStore run audit-trail

Summary of version management in the ChemStation Plus Security Pack

Each time a new result is calculated in the ChemStation, the application compares the values with the result values of the last reprocessed result copy. If it detects a difference, it automatically initializes the data storage in the database. Each data transfer of new results creates a new version entry in the database so that no data is ever overwritten. The versioning also assures that no "data" is lost and that a complete "chain of events" is documented. This ensures full data integrity and traceability.

Agilent ChemStation Plus Security Pack—Graphical Result Review and Result

All data reanalysis cycles require a restore of the data to the ChemStation batch review interface. The batch review interface in the ChemStation Plus Security Pack allows splitting the review into a working and a calculation section. The ChemStation Plus Security Pack allows a graphical rework of the chromatogram for each run. This is done by setting new integration events and applying manual events such as baseline drawings and others without an immediate transfer to the database. The transfer takes place after the user decides to calculate the results with the new settings (figure 15). As soon as new results are created, the result transfer to the database is performed either for the single run, or if starting an automated result recalculation, for all reprocessed runs. After finishing the data review in the batch interface and closing the batch, the temporary files will be deleted from the local hard disk.

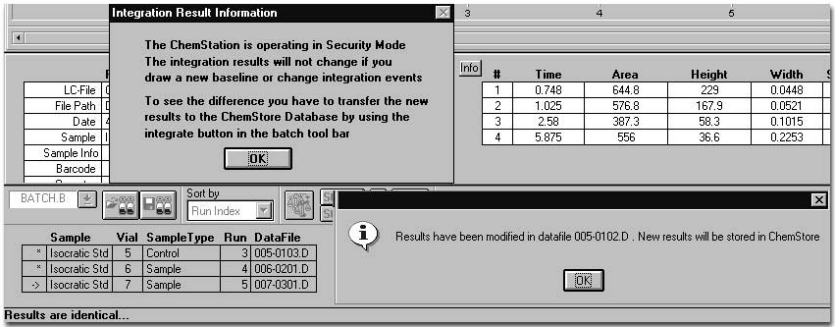

Figure 15
Result calculation and automated versioning

21 CFR Part 11 permits the use of electronic signatures if the application ensures data integrity, data security and full audit-trail documentation. If an electronic signature is supposed to be equivalent to a handwritten signature it must contain at least two distinct identification components such as an identification code and a password.

The ChemStation Plus Security Pack protects all activities that create, modify or delete electronic records with user privileges and electronic signatures. Signing for approval is a privilege that must be configured and granted by the system administrator and is therefore limited to certain users. Signing runs for approval and rejection always prompts for a re-identification and password confirmation of the signing and currently logged-on user for each run, plus a mandatory comment for the sign off, as shown in figure 16.

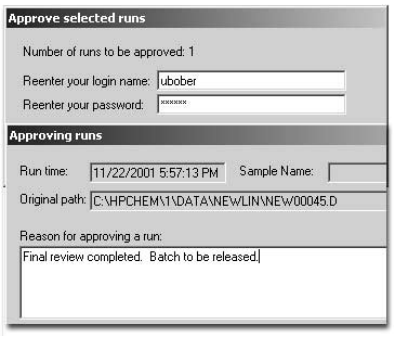

Figure 16
Signing off results requires reentry of user ID with password confirmation and a mandatory comment

All other sensitive actions (for example, changing run-related custom field values such as the batch ID) and the archival or deletion of runs follow the same process as described above. All electronic signatures are noted in the individual sample audit-trail and in the database logbook.

The ChemStation Security Pack uses electronic signatures based on the application User-ID/password combination to uniquely identify the user and their signature. In order to keep the password unique to the individual user an additional security function is implemented to periodically check and revise passwords, and apply the company's password policy (figure 17). The administrator can specify the values for these conditions.

- Minimum length is the minimum acceptable length (in characters) of a password. Passwords shorter than the minimum length are invalid and rejected by ChemStore C/S. The default is eight characters with a valid range between 0 and 30.
- Password expiry date is the number of days over which the password remains valid. The password expires after the specified validity, and a new password must be provided. The default is 90 days with a valid range between 1 and 32000.
- Password uniqueness is the minimum number of new, unique passwords that a user must use before a password can be re-used. The default is 12, which means that a user must change the password at least 12 times before re-using the original password. The range is between 0 and 32000.
- Account lockout after 'x' attempts (where 'x' is the number of failed log-on attempts) is the maximum number of consecutive unsuccessful attempts that a user can enter before ChemStore rejects the user. The default is three with a valid range between 0 and 32000. If the maximum number of re-entries is reached, the current user is invalidated and must be reactivated by a user with the required permission.

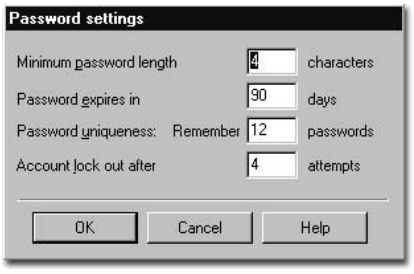

Figure 17
Password policy

The Agilent ChemStation Plus Security Pack includes four audit-trails:

- run logbooks,
- method revision history data,
- sample audit-trail, and
- database logbook.

Sequence and logbook

During data acquisition, all events are documented in the sequence and run logbook with date and time stamp (figure 18). The sequence and run logbook documents all data acquisition events such as

- start and execution of methods
- the actual sequence line in the sequence table,
- any failure during method execution, and
- initialization of data spooling to the ChemStore C/S database.

Method changes

The method changes are stored with each current method version including a mandatory user comment for the change (figure 19). The method audit-trail stores

- the time of change and the operator who performed the change
- the current method revision in the database, and
- a mandatory comment of at least five characters each time the method was changed.

Sample audit trail

The sample related audit-trail, shown in figure 20 documents

- all changes and modifications, on one sample,
- all run versions,
- all user comments during reanalysis cycles, and
- a detailed change documentation of manual integration events.

All reanalysis events and result versions are documented in the sample audit-trail. The sample audit-trail creates for each result change one new line in the audit-trail table. It displays both the interactive manual changes and the system generated entries each in a separate line. Examples for

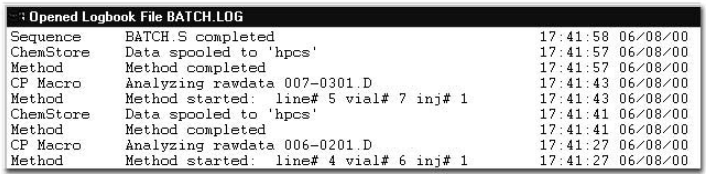

Figure 18
Run and sequence logbook

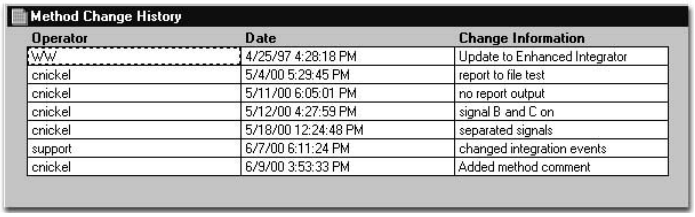

Figure 19
Method change audit-trail

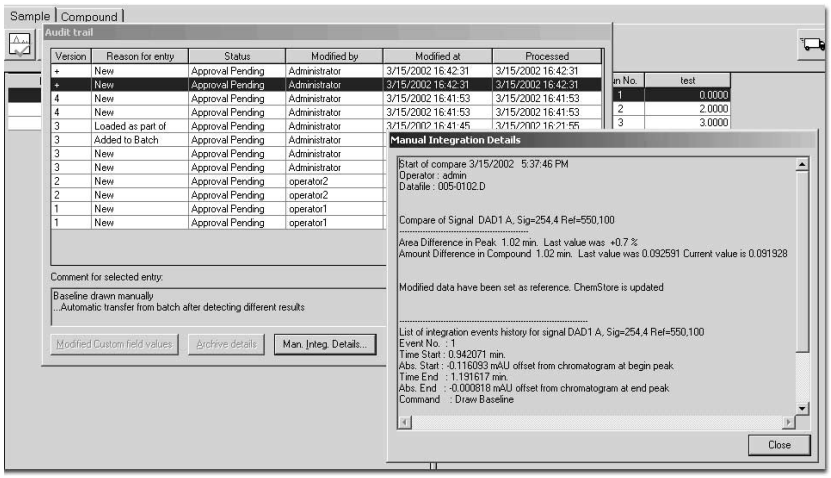

Figure 20
Audit-trail table with manual change documentation in the comment field

manual interactive changes are:

- change of custom field values
- manual reintegration during reanalysis,
- approval, rejection and retransfer to batch,
- reloading data to disk,
- archiving and dearchiving, and
- re-opening of read-only runs.

The automated entries in the sample audit-trail are created when

- a run is transferred to the database
- a new result version is created
- a run is reloaded in the ChemStation batch review interface for reanalysis.

Database logbook

The database logbook (figure 21) stores all application related activities such as:

- log-on/log-off events and failed logon attempts,
- archive/delete/reopen activities,
- session locks and unlocks,
- approval and rejection of runs,
- modification of custom fields and custom field values,
- changes in user administration,
- modification of user permissions,
- password resets and password clearance, and
- database migration from Access to Oracle.
- Account lockout events.

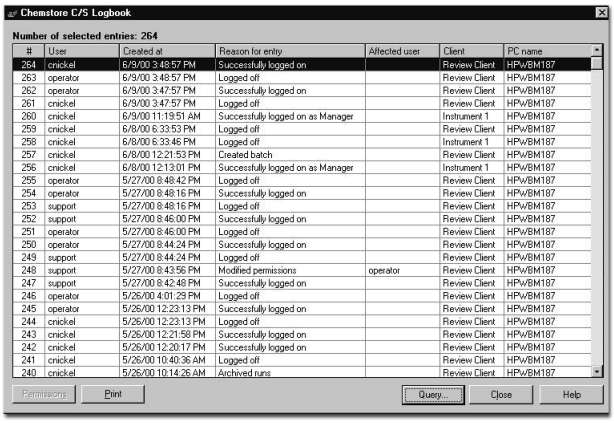

Figure 21
Database logbook

Agilent ChemStation Plus Security Pack—E-Mail Notification

For instant notification of unauthorized attempts to access the database, an e-mail message can be triggered by account lockout events in the ChemStore C/S database logbook (client-server only). The e-mail message can be sent to a configurable list of recipients with user-defined message text (figure 21a). This function requires an e-Mail server to be running in the network. The e-mail message can be transferred to the e-mail server through Simple Mail Transfer Protocol (SMTP).

Figure 21a
Setup of e-mail notification

ChemStation Plus Security Pack—Product Options and Configuration

Standalone version

The standalone version provides the ChemStation CD-ROM revision A.09.03 or higher and the ChemStation Plus CD-ROM revision B.02.02 or higher as described below.

Description	Product No.
ChemStation Plus Security Pack. Adds the secure ChemStore C/S relational database add-on software module to the ChemStation Plus SW for A/D, GC, CE, LC and CE/LC-MSD. Supports 21 CFR Part 11. Includes user documentation, licenses and media.	**G2183AA** 1 per PC 1 per laboratory
License to use G2183AA on another PC. Includes license and user information only. Supports 21 CFR Part 11. Must be on same order as G2183AA or requires a valid license for G2183AA.	**G2187AA** 1 per PC be in the same laboratory
ChemStation Plus client upgrade software. Upgrades a single ChemStation Plus client to the latest software revision. Requires valid software licenses and ChemStation upgrade software G1656A.	**G1657A**

Client/server version

The client server/version of the product consists of a set of components that are required to implement ChemStation Plus Security Pack in a client/server version. The product number are listed below along with the required quantities.

Description	Product No.
ChemStore C/S server application software. Includes:1 x ChemStore C/S and Oracle 8i standard edition software, 5 Oracle application-specific named user licenses are included.	**G1410A** Qty: 1 per server
Oracle connectivity license. Required for each named user of the ChemStore C/S server database.	**G1411A** Qty: (number of clients connected to server) – 5
ChemStation Plus Security Pack. Adds the secure ChemStore relational database add-on software module to the ChemStation Plus client server SW for A/D, GC, CE, LC and CE/LC-MSD. Supports 21 CFR Part 11.	**G2183AA** Qty: 1 per server
ChemStation Plus ChemStore client license. Includes one online ChemStation Plus license for online data acquisition and one ChemStore C/S offline data review license. Includes license and user information only. Requires but does not include ChemStore Plus software media.	**G2186BA** Qty: (number of clients connected to server – 1
License to use G2183AA on another PC. Can be used as additonal copy for standalone installations or as additional Security Pack client in ChemStation Plus Security Pack C/S installations. Includes manual, 1 license for either online or offline use and media. Supports 21 CFR Part 11 Must be on the same order as G2183AA or requires a valid license for G2183AA.	**G2187AA** 1 per PC in the same laboratory.
ChemStation Plus client upgrade software. Upgrades a single ChemStation Plus client to the latest software revision. Requires valid software licenses and ChemStation upgrade software G1656A.	**G1657A**
ChemStation Plus server upgrade software. upgrades ChemStation Plus server software to the latest revision. Includes G1656A ChemStation software upgrade. Requires valid software license.	**G1655BA**

4. Agilent ChemStation Plus Method Validation Pack

Introduction

A comprehensive understanding of the functionality of Agilent ChemStation Plus Method Validation Pack requires a brief introduction to the general aspects of method validation.

The goal of method validation is “to provide documented evidence that a specific process will consistently provide results meeting the predetermined specifications.” This definition is taken from one of the FDA's method validation guidance documents. The analytical purpose of the method validation experiments is to provide a master method with a master chromatogram for all consecutive separations of this particular sample. Method validation testing must compare results of multiple runs (it is inter-chromatographic) in order to answer the question "is this method suitable for the separation task?" The comparison must give a qualitative and quantitative answer to this question based on the analytical results. A comparison typically involves a human judgement, so how can a comparison provide a user-independent and quantitative result? This is the most difficult task in the method validation process, because proper execution requires:
1. The definition of general good quality criteria for a method to address the qualitative requirements, and
2. The definition of specific requirements for the individual analytical problem to address the quantitative question.
Eventually it requires an answer to the question "does this method provide good results based on independent requirements?"

For step 1, ICH and FDA used the definition of general good quality criteria (along with many other contributors). These organizations defined a number of criteria that a separation method must fulfill to be classified as "good quality." These criteria are
- accuracy
- precision
- robustness
- selectivity
- limit of detection/quantification
- linearity
- calibration function

Based on the compound type, all or a subset of these criteria must be met. Most common compound types are
- main compound
- side compound
- known impurities
- unknown impurities

It is obvious that it is not necessary to determine the limit of detection for the main compound as the amount of the main compound will always be closer to saturation than to limit of detection. A detailed list of compound types and appropriate test criteria can be found in ICH and USP literature. Method validation pack uses built-in templates to automatically configure the method validation according to the guideline under consideration.

Based on these test criteria, step 2 can be executed. This is an individual definition by the responsible validation person of requirements (quantitative limits) for the statistical results of the tests. This step must be repeated for each new validation and will provide different limits for each validation experiment. Method validation pack maps this step with a set of advanced statistical calculations. The calculations offer simple summary statistics (RSD, %RSD and linear regression statistics) as well as a set of advanced calculations for outlier detection, trend tests and many more. For each criterion, a different set of statistical calculations on the result values is performed based on the checkpoint requirement. The administrative user defines the calculation limits, transferring analytical requirements into quantitative result criteria. Method validation pack offers tests such as Neumann trend tests and Outlier tests (e.g. according to Dixon) and many more to provide and document an assessment of the quality of analytical separations.

Product description

Agilent ChemStation Plus Method Validation Pack is a data management system for all method validation data. It includes advanced statistical calculations and result management in a relational database.

Method Validation Pack offers a compound-centric design. For each compound it allows to define a set of tests (checkpoints) according to ICH, Pharmacopoeia or DIN guidelines. By default each test requires results of at least six repetitive injections in order to use statistics for a quantitative result evaluation. The statistical results display whether the results meet their specifications or if there is any deviation. When all tests are passed, the compound meets the requirements. When all compounds meet the requirements the method can be seen as applicable or "validated" according to its well-defined purpose. At this stage, the validation can be locked, the full validation is printed and the validation database for this method can be archived.

Method Validation Pack provides all required statistical calculations, stores all results with their raw and meta data, displays the statistics graphically, and captures all actions in user-independent audit-trails. Further, it allows to map the key steps in validation experiments - planning and definition of expected results, experiment execution and result evaluation - as separate tasks. All steps are documented in audit-trails and are fully traceable.

Agilent ChemStation Plus Method Validation Pack—Work Flow

Configuration

The configuration of validation experiments is hierarchical. The top level represents the complete validation experiment, including the method in text form, calculation documentation and SOP file documents. The next level introduces a compound-centric view of the validation in the form of components. This enables individual calculations and validations for each compound or peak in an analytical separation. For each component, additional sub-levels offer a list of checkpoints such as robustness, linearity and others as defined in the various regulation guidelines. The planning of checkpoints is the lowest level because each checkpoint can have a different planning configuration. Within the planning dialog, data is configured such as the applicability of multiple injections, multiple determinations for one result data point as well as the number of result values and calculation tests.

Test execution

Having completed the validation configuration, the experiments can be executed on an Agilent ChemStation Plus system. Method validation pack transfers the theoretical validation planning into a list of analytical runs by creating one or multiple ChemStation method validation sequences (MVS). The user has two options during sequence generation:

- The validation can be transferred into one sequence for the complete validation or in multiple validations experiments where each component creates an individual sequence as shown in figure 22.
- Some checkpoints can use the same result data. Method Validation Pack provides a wizard to define multiple usage of analytical results as shown in figure 23.

Method Validation Pack also transfers these sequences to the ChemStation for data acquisition and data analysis. The sequences can load into an Agilent Method Validation Pack ChemStation system and run similar to other sequences in the Agilent ChemStation. The results of the method validation sequences are stored automatically in the ChemStore database. Each validation corresponds to a separate ChemStore study.

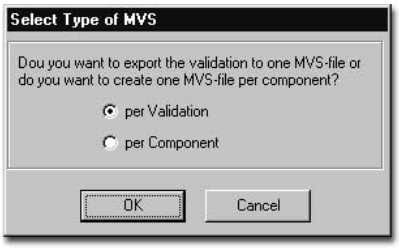

Figure 22
Options for generation of Method Validation sequence: One sequence for each component or one sequence for the entire validation

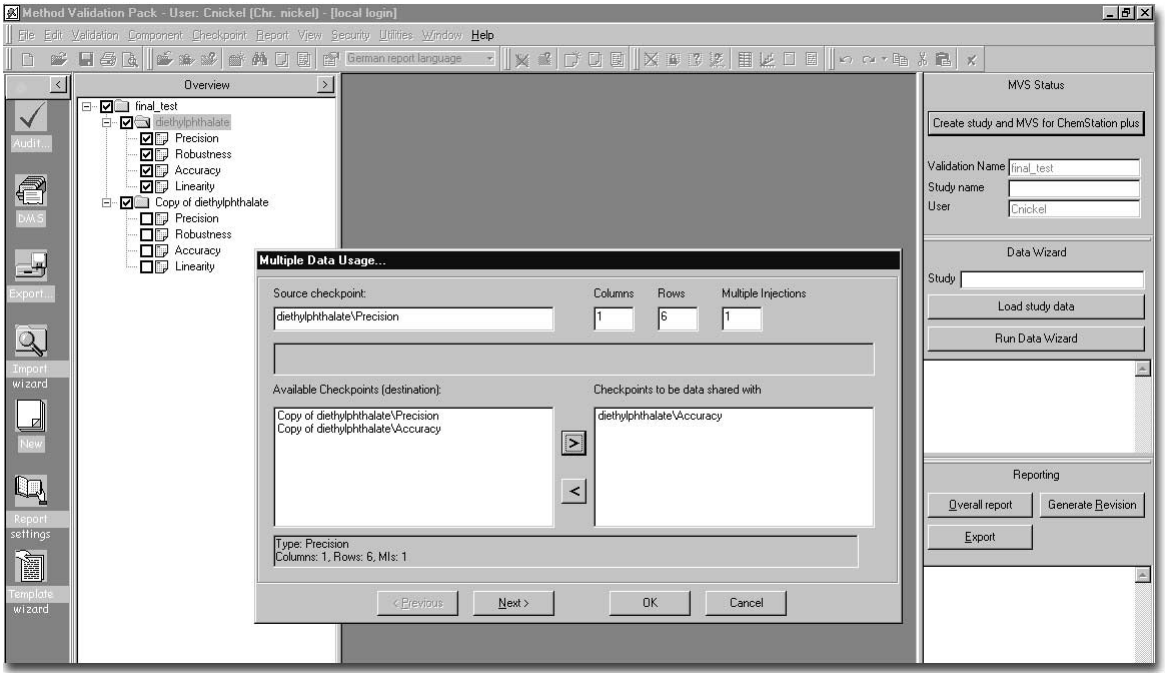

Figure 23
Wizard for multiple usage of checkpoint results

Result data entry and statistical calculations

After completion of the analytical experiments the results can be uploaded from the ChemStore database into Method Validation Pack. The upload from ChemStore is an active and automated direct database data access. The transfer is executed as defined in the planning of the validation experiments. The analytical results are contained in the ChemStore database whereas the validation results are contained in Method Validation Pack. Traceability of results is achieved with unique run-IDs in ChemStore for each result version. The ChemStore run-IDs are also transferred and displayed along with the analytical results in the Method Validation Pack.

When all result data is imported, the validation report can be printed. This report displays all data related to the validation as defined in the top-level validation configuration. This includes the components, their planning and result data as well as the calculation results and conclusions, for example, "outliers [not] detected" along with result representation in charts.

Data management and audit-trails

All configuration and result data along with the MVS files and validation reports form the "validation database". Each validation has its own database. It is stored in a relational database for full data integrity and to ensure data security. Every validation modification or configuration change is stored in the database as a new version of the existing validation. All changes and modifications are documented either in the program audit-trail (for program related events such as logon) or in the validation audit-trail.

Compatibility with ChemStation Plus modules

Agilent ChemStation Plus Method Validation Pack A.01.02 is compatible with the following ChemStation Plus modules:

- Agilent ChemStation for GC, LC, A/D, CE, CE/MS and LC/MS for instrument control and data analysis
- Agilent ChemAccess remote access and module
- Agilent ChemStore data organization and data storage module

For result management in a relational database, Method Validation Pack requires the ChemStore database or ChemStation Plus Security Pack. Method Validation Pack is available in a standalone PC-based version or as full client-server application. The standalone database file format adheres to a common standard, which is used by many other applications, for example, MS Access. The client-server version is based on an Oracle relational database.

Hardware requirements

The following list shows the minimum hardware requirements for the client application:

- 400-MHz Pentium II (Pentium IV recommend)
- 4 GByte of free hard disk space
- 96 MB RAM for single ChemStation instrument. 128 MB is recommended for best performance, for Windows 2000 the minimum requirement is 128 MB.
- 128 MB RAM for two ChemStation instruments (256 MB or more is recommended for best performance)
- Display: 1024 × 768, small fonts, 65-thousand colors

Method Validation Pack installs and runs on the same instance of the Oracle database as ChemStore C/S and thus does not require a separate Oracle licence. For server hardware requirements, please refer to the server hardware requirements for ChemStore on page 5.

Software requirements

- Windows NT Workstation 4.0 with Service Pack 6a or
- Windows 2000 Professional with Service Pack 2
  Agilent ChemStation revision A.09.03 or later
- Agilent ChemStore C/S B.02.02 or higher
- Microsoft Internet Explorer 4.01 or later
- Microsoft data access components (MDAC) 2.5 will be installed on your system. If you already use a later version of MDAC, or require for compatibility reasons a previous version, please contact your Agilent support representative for compatibility information.
- A printer must be installed and configured in Windows.
- The hard disk partition that is used for installation of Method Validation Pack must be formatted with NTFS.

Hard disk space

Standalone installation using Microsoft Access database

Method Validation Pack needs approximately 40 MB hard disk space for installation. The validation files typically need 250–1000 KB per file. This depends on the size of embedded graphics. If possible, use vector graphics (WMF-format) rather than bitmap graphics (BMP) to reduce validation file size. Using large bitmap graphics in validation comments also has an impact on the DMS size. Hard disk requirements for the Oracle database are discussed later.

Database size for Client-Server installation using Oracle database

Method Validation Pack supplies three pre-defined schemes for database installation: small, medium and large. The databases are separated into multiple tablespaces for better performance and administration. In particular, the validation/comment-table and the DMS/BLOB (binary large objects) tables reside in special (large) tablespaces. Table 13 shows the database sizes according to the configuration. VDB files are actual validation data files, the DMS stores all VDB files; changes to one VDB file are stored as versions, new VDB files create a new entry in the DMS system.

Database parameter have been chosen for unattended operation; tablespaces and datafiles extend automatically until their maximum file size has been reached. Nevertheless, you should keep in mind that frequent DB administration might be necessary for correct and secure operation (backup tasks, size checks etc.). Your database administrator may manually expand your database if necessary. There is no limitation of DB sizes in Method Validation Pack.

	Small		Medium		Large	
VDB data	**Database**	**MB**	**Database**	**MB**	**Database**	**MB**
	Initial size	30	Initial size	600	Initial size	1200
	Maximal size	300	Maximal size	1200	Maximal size	2400
	File growth	15	File growth	30	File growth	60
	Comments		**Comments**		**Comments**	
	Initial size	100	Initial size	1400	Initial size	2800
	Maximal size	700	Maximal size	2800	Maximal size	5600
	File growth	40	File growth	70	File growth	140
DMS data	**Database**	**MB**	**Database**	**MB**	**Database**	**MB**
	Initial size	20	Initial size	500	Initial size	2000
	Maximal size	200	Maximal size	1000	Maximal size	4000
	File growth	5	File growth	25	File growth	100
	BLOBS		**BLOBS**			
	Initial size	180	Initial size	4500	Initial size	18000
	Maximal size	1800	Maximal size	9000	Maximal size	36000
	File growth	45	File growth	225	File growth	900

Table 13
Database configuration during installation

General software operation

Compatibility with Microsoft functionality

Method Validation Pack is a Microsoft Windows program and can be operated via mouse clicks and keyboard in accordance with the Microsoft Windows standard. Users of Microsoft Windows programs should easily become familiar with operating Method Validation Pack.

Context menu

During operation of Method Validation Pack, the right mouse button opens the context menu of your current program option. The context menu can consist of functions concerning a selected component, or the attributes of a graphic or a report. All functions of the context menu are also accessible via the main menu bar.

Adjustment to user

All settings that you change in the menus or tool bars are recorded for you at the end of a session. They are automatically loaded during your next login.

Navigation bar

On the left of the screen, the navigation bar presents the most important top-level functions of Method Validation Pack. You can use this bar for directly selecting

- audit program, default, validation and validation audit
- DMS Document Management System,
- export dialog,
- import wizard for templates,
- new validation wizard,
- planning wizard,
- report settings (output formats, etc.), and
- security settings

Easy operation

Validation assistant

Method Validation Pack comes with an additional validation assistant that helps to configure and setup method validation functionality. An administrative user can configure the assistant to automatically start after initial user logon. In addition, the wizard can be started interactively during software operation. If configured the assistant is displayed at the start of method validation. The assistant helps you by speeding up operation of the software, and offers a quick and easy way to resume your work. The assistant offers the following options at startup:

- Creation of a new Validation
- Opening an existing Validation
- Opening the last Validation (per user)

The validation assistant guides the user through all configuration and planning steps in Method Validation Pack. It can be used either to add a complete validation or to add a new component to an existing validation. It is accessible from the validation or help menu or with the context-sensitive menu started with the right mouse button. During program start, the assistant can be used only to create a new validation.

Data completion wizard

Some checkpoint information (such as concentration for linearity results) can only be added after data acquisition. It is not available during checkpoint planning. Method Validation Pack therefore has an integrated data completion wizard. As long as a checkpoint is not complete, the related report cannot be generated (or is incomplete) and you see an invalid-data entry in the table of contents. The Data Wizard displays all incomplete checkpoints. Double-clicking on it opens the data input grids. Input fields with a dark background are locked and intended for automatic fill from a study. Input fields with normal background are for manual completion.

Method Validation Pack software structure

ChemStation Plus with Method Validation Pack maps the validation requirement within the application software. It requires the user to configure and execute validation tests in a stepwise approach. By design it forces the user to separate method validation testing into
a) planning and design,
b) test execution (run samples), and
c) result calculation based on the experimental result data.

All tasks are managed within the ChemStation Plus system. All ChemStation Plus modules support data security, data integrity and audit-trails for comprehensive support of FDA's requirements of electronic records and electronic signatures. The combinations of audit-trails in all ChemStation Plus modules with advanced database data security offers full traceability and complete documentation of all steps during user's method validation experiments.

Method Validation Pack hierarchy

The Method Validation Pack software structure is strictly hierarchical with 5 levels. These levels also correspond to user-access levels. The list below outlines the step-by-step execution of the method validation experiments with the hierarchical structure and the user access levels.

Prior to test execution

1) Setup and configuration (Levels 5 and 4)
Validation planning and component configuration in the Method Validation Pack software

2) Checkpoint planning (Level 3)
Each checkpoint can use different calculation techniques depending on the various guidelines. The checkpoint configuration step is either repeated for each checkpoint or it is copied from another component using drag and drop functionality.

From planning to execution

3) Experiment setup and data management configuration (Level 3)
a) Creation or update of ChemStore study for all Method Validation Pack analytical result data
b) Automated system generated creation of ChemStation method validation sequence based on the validation configuration and
c) Transfer of the sequence to the ChemStation analytical system for data acquisition and first pass analysis

After data acquisition

4) Data entry and result calculation (Level 2)
a) Data storage in ChemStore database method validation study and
b) Data upload by database transfer to Method Validation Pack application

5) Method validation reporting (Level 1)
After data completion, creation of method validation report document with result calculation and statistics

Figure 24 illustrates all data transfer steps. All configuration and transfer steps are fully automated and are integrated in the ChemStation Plus software. All export and import jobs are documented in audit trails avoiding any accidental transfer or transcription error.

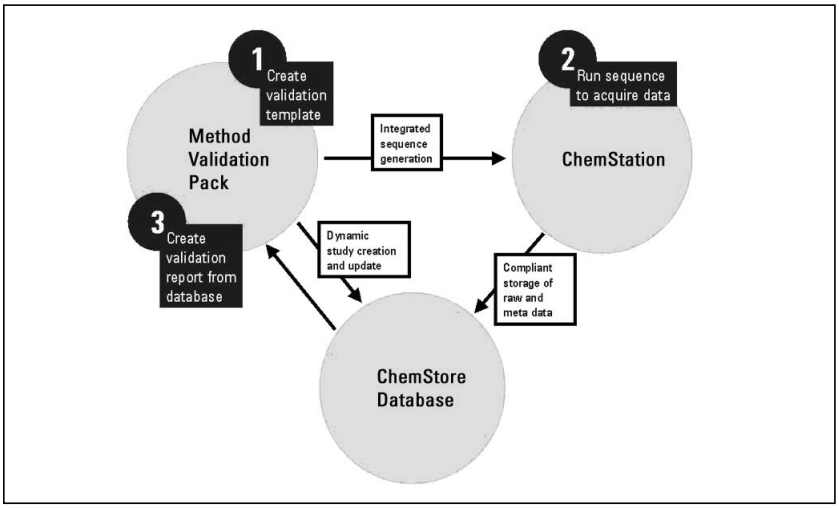

Figure 24
Interaction of ChemStation Plus software modules and their mapping of the key steps of method validation experiments

User levels

Top-level (Level 4 and 5): Validation setup and configuration

Setup
Method Validation Pack organizes data in method validation databases. A method validation database is the top-level container for all data that relate to one validation. All settings are linked to one validation database. For new validation files the software offers a master validation template that allows building new validations on the template. The following settings or properties are configured for each validation:

- validation configuration,
- output settings,
- default reporting header data,
- storage of external documents and,
- storage of method in text format.

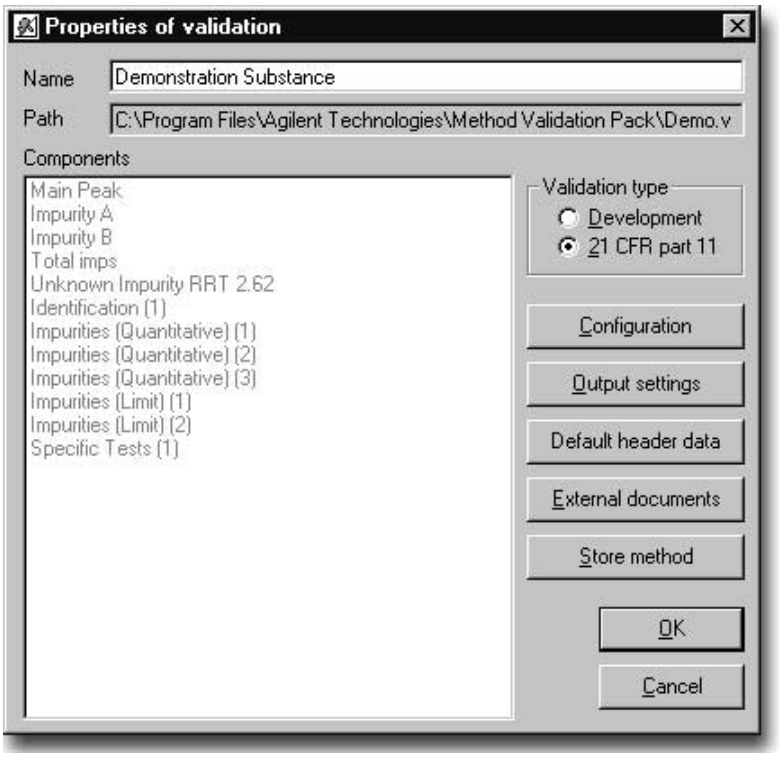

Figure 25
Validation properties menu for validation setup and configuration

Validation configuration
Validation configuration defines the statistical calculations in the report. Each checkpoint offers different calculation options and is configured individually. In addition, the configuration task defines overall calculations that are common for all checkpoints. These are outlier tests, trend test, homogeneity tests and systematic error detection calculations. Other settings allow specifying the standard sample number for each test, handling of 0 as input and handling of missing values. For non-Part 11 validations, you can specify the audit-level in the configuration as well.

Output settings
The method validation output settings define contents of the checkpoint calculations and the report content for each checkpoint. For details on the checkpoint content, please see the checkpoint section later. Output settings also define overall report configuration items for text and graphics section and the documentation of configuration values in the report.

Text output settings define:

- the report title page,
- an additional general report comment page,
- the report header and,
- default comments for validation planning and validation configuration

In addition, the text configuration defines the checkpoint table headers (such as method name, instrument type etc). Each checkpoint can have up to ten header data lines with different content. The header information is used to describe general validation information that is necessary to uniquely identify and characterize the method validation experiment. Examples for useful table header are the product name, the analytical equipment, QS or internal ID number, test method and

others. Default entries for these headers can be defined when selecting the default header data button in the validation properties. Figure 25a shows table headers and default header data. Table

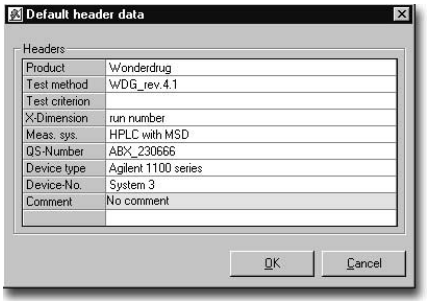

Figure 25a
Default header (grey) and header data

header can only be changed or overwritten by changing the complete validation configuration while the default header data can be overwritten for every checkpoint.

The graphics section defines the checkpoints that will have graphic result visualization in the final report.

Default (checkpoint) header data
This section defines the header data section of the checkpoint report table header data as defined in output settings. It allows to enter common data for all checkpoints in this central location e.g. the method name or an internal code for the tests. All data that are entered as default reporting header data are copied to all checkpoint headers. The default checkpoint header data can be overwritten for each individual checkpoint if the actual results are different from the preconfigured header data. Using default header data speeds up the checkpoint configuration as it allows skipping data entry for the checkpoint header. One example that might outline the usage of default data for the checkpoint header is the definition of the analytical system as checkpoint header. The system will remain the same for all checkpoints except for the robustness testing where another system from a different vendor might be used. The user now enters the analytical system by default in the default header data and applies this to all checkpoints. For the robustness checkpoint the default header data for the instrument will be manually overwritten, for all other checkpoints the default header data are copied and do not need a manual entry.

Storage of external documents
Users can store any external document with the validation database. The document must be available as a file with an extension that allows direct read-out and data display. This is particularly useful for adding master methods, sample preparation information and other method related information to the validation. All external documents can be printed in the final validation report. The storage capability of external documents in the method validation database allows using the Method Validation Pack software as database for all method validation related data.

Store method
Store method allows adding the method text file to the validation database. The method must be in file format and can not be a folder or anything else that can not be opened with a standard program.

Level 4: Component configuration and checkpoint configuration

The next level under the top-level is the component level. The component typically correlates to a peak (or in ChemStation terminology to a compound) in a separation but it allows having multiple components for one peak e.g. to perform result comparison or result copies. Usage of multiple components per peak is mainly used during method development. The component configuration configures the name of the component along with the checkpoints that will be executed for this component. Checkpoints are either created according to a user selection or they use predefined templates. The templates include:

- Complete range (all check points will be selected),
- Trace method (selecting precision, calibration function and limit of detection/quantification),
- Trace method with demand (above plus lab capability)
- Non-trace method (precision only), and
- Non-trace method with demand (above plus lab capability)

Each component typically includes one or multiple checkpoints from the list below:

- Precision - used to monitor random errors

- Robustness
- Lab capability (mainly used in non-pharmaceutical applications)
- Calibration function
- Limit of detection/quantification
- Accuracy
- Selectivity
- Ring experiment (used to compare results among multiple laboratories)
- Linearity

The checkpoint configuration will typically depend on the compound type, and hardly any component requires execution of all checkpoints. The system therefore requires running the checkpoint configuration for each component individually.

Level 3: Checkpoint planning

Each checkpoint must be configured. The configuration defines the test and calculation methods, data sources and data types for x- and y values (e.g. for linearity x-value is amount in mg/mL and the y-value is peak height). The following sections are configurable for all checkpoints:

- **Checkpoint headers**
  Data sections will show default data if configured in the validation properties and allow individual data entry for each header line
- **Test planning data**
  Selects the calculation method from a pool of possible calculations used for this checkpoint
- **Number of result values and y-unit**
  Defines the number of samples used for calculations (*Note:* By default, minimum number must be six and the system will show missing values either as Zero or as MV in case the configuration allows 0 as valid data input)
- **Multiple injection and multiple determination of data point.**
  Multiple injections uses repetitive injections from the same vial and averages the results before applying statistics; the number can be between 2 and 10. Multiple determinations allows using data from two different vials for the same checkpoint. Number of multiple determinations allows for values from 2 to 10
- **Method Validation Pack – Planning**
  Configures the data type that is imported from the ChemStore database as result value plus additional header information that is imported from ChemStore along with the result values. Available result values are peak area, peak height, peak width, retention time, and amount. Additional header information can be:
  - method name and method text,
  - instrument name,
  - instrument module with serial numbers,
  - run Ids (database Ids),
  - run Ids and approval status,
  - run Ids and raw data file path, and
  - all custom fields with data entries.

  The system allows a maximum of 5 additional header items.

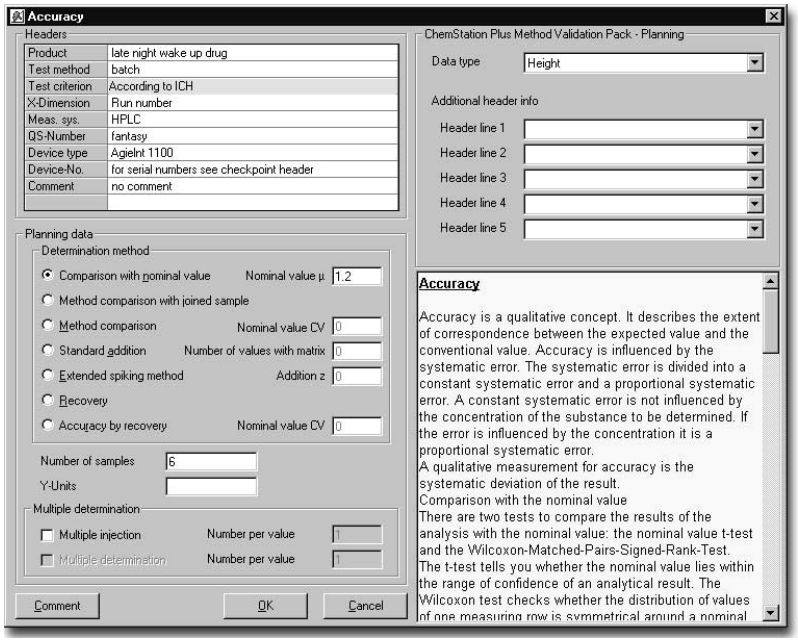

Figure 26
Checkpoint planning window (example for accuracy) with sections for checkpoint header data, test planning data, number of results y-units and multiple determination.

Level 2: Data input

After checkpoint configuration and planning is completed, users can now start data entry. This is the first result related step.

Method Validation Pack offers three types of data input:

1. Automated data upload from the ChemStore database. Users select to load study data from the ChemStore method validation study and all data are automatically imported as configured in the Method Validation Pack Planning and described in the previous section
2. Data import for all result data that is not created and managed in the ChemStore database e.g. data from non-Agilent instruments during robustness testing. The system comes with an import filter allowing to automate data import. For details see the separate section data import
3. Manual data entry - for all data that are not created on a computer system, e.g. pH values, the system allows manual data entry

Data import
Data import uses an import assistant, which offers you data transfer from external result files typically in spreadsheet formats. It imports file formats in CSV, TXT ASCII format and any other format that is manually entered. The import assistant displays a definition dialog enabling Method Validation Pack to automatically load this summary data to its data input grids. The following definitions can be made:

- name and description of the import mask,
- source type (file extension) and path,
- field separator (delimiter),
- row options,
- data positions (with optional transposition of the data) allowing to exclude header and text data,and
- column information (X-Y data, information for multiple injections and determinations).

The import settings can be saved and applied at any later time to import data. The system can handle multiple data import masks allowing to quickly import results from various data sources.

Level 1: Reporting

Method Validation Pack software offers multiple reports. Users can have

- planning reports–print all data from the planning dialog,
- graphics report for each checkpoint–prints only results in graphic representation,
- complete reports on checkpoint level, component level, and
- complete validation reports with all validation settings and all component and checkpoint results.

The validation report includes the following parts:

- Page header and page footer (Footer includes printed user name, date, page # of # and a signature placeholder for manual report sign-off.)
- Report title page
- Default comment page
- Table of contents with page numbers
- Checkpoint sections for each checkpoint consisting of header data, planning comment, measurement results, graphics and statistical results, execution comment and revision information from the document management system.

Report customization
Method Validation Pack uses a Microsoft-Word-based reporting engine. It allows to open the entire method validation report as a MS Word document. This allows for easy data export of the complete validation report and easy modification and customization of the report document. In addition to the customization in MS Word, the following elements are configured within the Method Validation Pack application:

- report language: German or English,
- report fonts and sizes,
- graphics section: line style, background color for data, color of axis and display of limits, axis annotations, and
- text sections: title page, validation comment page, report header and default planning and execution comment. All text sections can also include graphics such as company logos.

This section lists all checkpoints with their planning options and a short explanation of their meaning.

Precision

Precision describes the extent of conformity between results obtained during repeated use of a set analytical method under recurrent and comparable conditions. Monitoring the precision records random errors. Precision can be planned as precision in the true sense, or as repeatability from linearity. In both cases, the nominal values of the variation coefficient can be entered. Precision can be performed with multiple injections. Figure 27 shows the planning dialog for checkpoint "precision"

Planning data
- Determination method:
  - Precision
  - System precision from linearity
- Other data
  - Number of values (change default)
  - Y-units
  - Multiple injection possible

Output settings
- Repeatability limit
- T-value
- Confidence interval
- Error of result
- Trend test according to Neumann
- Outlier test according to Dixon/Grubbs

Robustness/Ruggedness

Robustness is defined as the independence of an analytical result from changes in other parameters, which could influence the result. Ruggedness of an analytical method is given if the deviation of laboratory mean values is not significantly different from the deviation of all measured values. Ruggedness should show the reliability of an analysis with respect to the influence of external parameters. Ruggedness of a method is distinguished by the fact that change of parameters within a reasonable range has no significant influence on the result. The F-test and the t-test can be applied during a statistical test. As a measure for ruggedness, the comparative standard deviation is calculated and listed. Figure 28 shows the planning dialog of checkpoint “ruggedness/robustness”.

Planning data
- Determination method:
  - Comparison of results
  - Comparison with reference
- Other data:
  - Number of series (from 2-50)
  - Y-units
  - Multiple injection possible

Output settings for calculations
- Neumann trend test
- Dixon or Grubbs test for outliers
- Variance homogeneity
- Repeatability limit
- Reproducibility limit
- Error of result
- Range of confidence (repeatability conditions)
- Range of confidence (reproducibility conditions)

The following results are always calculated for robustness testing:
- standard statistics such as mean value, RSD, repeatbility and reproducibility along with confidence intervals for repeatability and reproducibility, and

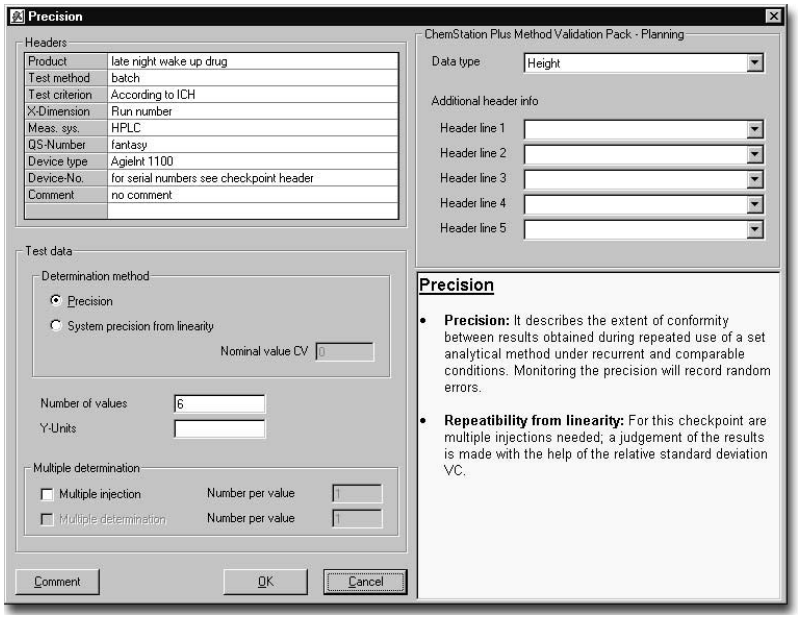

Figure 27
Planning dialog for checkpoint “Precision”

- variance homogenity according to Bartlett.

Lab capability

Knowledge of lab capability is necessary for accurate estimates of process capability (see DIN 55350 parts 33 and 11). It checks for the ratio of result dispersion versus specifications. Lab capability occupies a special position among Validation concepts because it does not exclusively refer to the analytical method. Figure 29 shows the planning dialog of checkpoint “linearity”

Planning data
- Number of samples
- Y-units
- Lower specification
- Upper specification
- Calculation of Xb where Xb is the reference value such as an analytical result value defined as ideal
- Multiple injection possible

Output settings for calculations
No output settings can be configured by the user. For lab capability, the indices Cm and Pm are defined analogous to Cp. Cmk and Pmk are defined analogous to Cpk. The result calculates all indices along with the specification limits and a judgement if lab capability is low, medium or high.

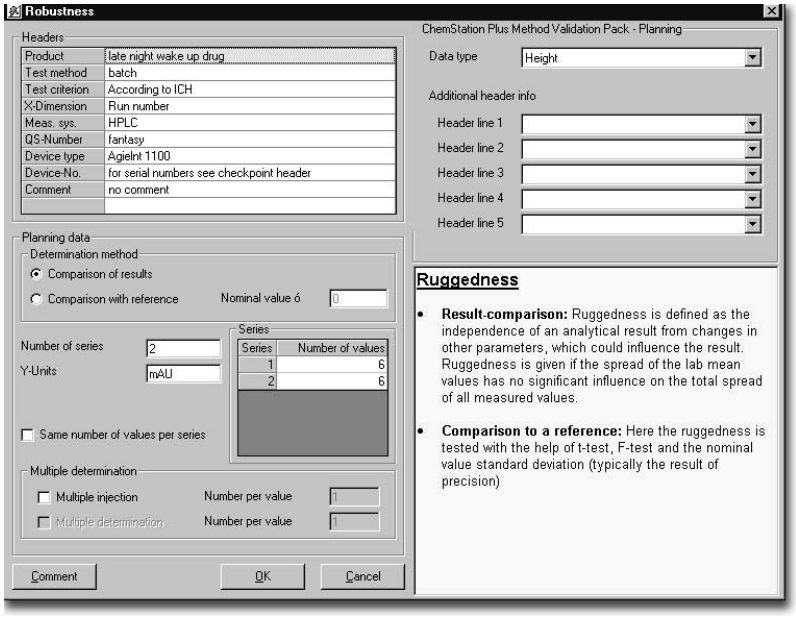

Figure 28
Planning dialog of checkpoint “Robustness/Ruggedness”

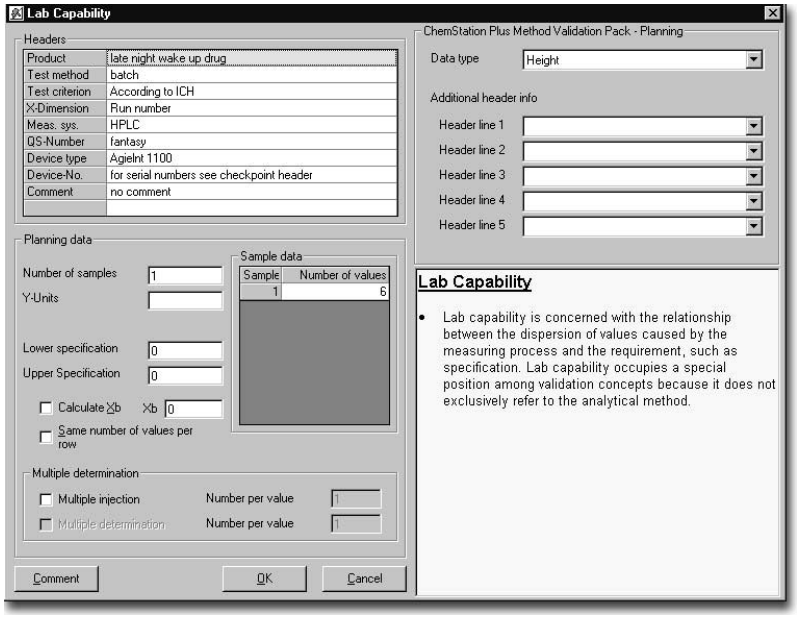

Figure 29
Planning dialog of checkpoint “Lab Capability”

Linearity

Linearity calculates a linear regression using the least square error for the model y = a + bx. Linearity can be carried out by multiple injections and multiple determinations. Figure 30 shows the planning dialog of checkpoint “linearity”.

Planning data

- Determination method:
  - Regression weighting: unweighted, weighted 1/x, weighted $1/x^2$ or
  - Proportionality (test for validity of one point calibrations)
- Other data:
  - Number of levels
  - Y-units
  - Multiple injection possible
  - Multiple determination possible

Output settings for calculations

- Residual standard deviation
- Method standard deviation

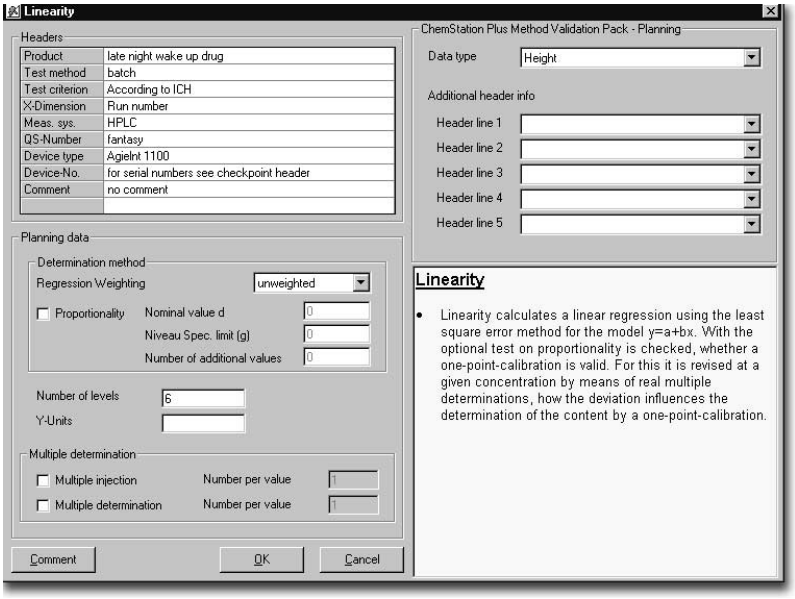

Figure 30
Planning dialog of checkpoint “Linearity”

Calibration function

The calibration function is the correlation between the expected value of the test characteristic, e.g. the extinction (see DIN 55350 part 13), and the content, e.g. a mass concentration. You can choose the maximum degree of curve fit for the calibration curve. 1st order is standard and 3rd order is the maximum (cubic curve). Figure 31 shows the planning dialog of checkpoint “calibration function”

Planning data

- Number of levels
- Unit of values
- Curve fit display 1-3
- Multiple injection possible
- Multiple determinations possible

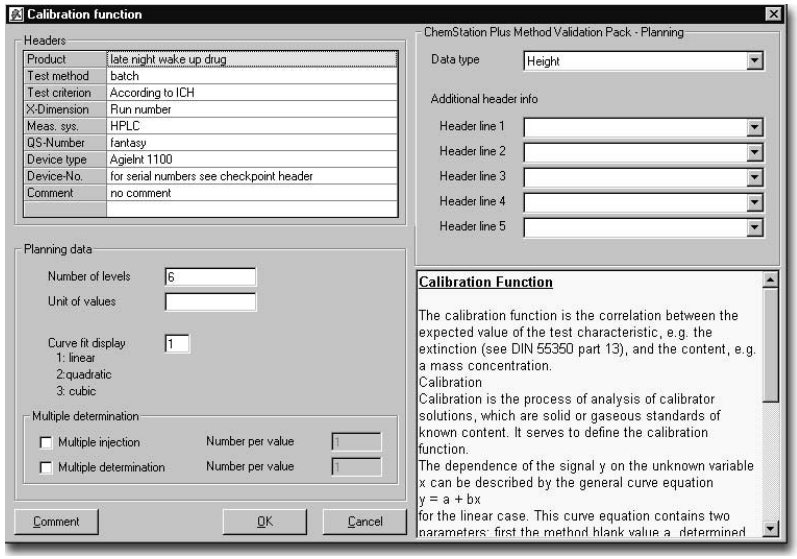

Figure 31
Planning dialog of checkpoint “Calibration Function”

Output settings for calculations

- Vector y=ax+b - curve equation in the case of linearity
- Square sum of the residuals (only calibration function)
- Residual standard deviation
- Mean value and standard deviation of y
- Multiple correlation coefficient
- Results of F- and t-tests
- Method standard deviation

Limit of detection and quantification

The detection limit is the smallest amount of substance that can be detected qualitatively during one analysis with a defined statistical certainty. The quantification limit is the smallest amount of a substance that can be detected quantitatively during one analysis with a statistical certainty to be determined. The quantification limit is higher than the detection limit. You need the relative error of results to calculate the determination limit. Both the detection limit and the quantification limit can be calculated by the standard deviation of blank values (blank value method) or the residual standard deviation of regression data (calibration curve method). Only one of the two methods may be suitable for practical purposes. Both methods, however, are almost equal with respect to the detection limit. The calibration curve method is suited to determine the quantification limit. Figure 32 shows the planning dialog of checkpoint “limit of detection/ quantification”

Planning data

- Determination method:
  - Blank value method according ICH und signal to noise ratio)
  - Calibration line method according to ICH (no calculations executed, only display of chromatogram!)
  - Signal/noise ratio
- Other data
  - Number of samples
  - Y-units
  - Multiple injection possible

Output settings for calculations

- Standard deviation
- Procedure standard deviation
- Critical value yk
- Residual standard deviation (additional for calibration curve method)

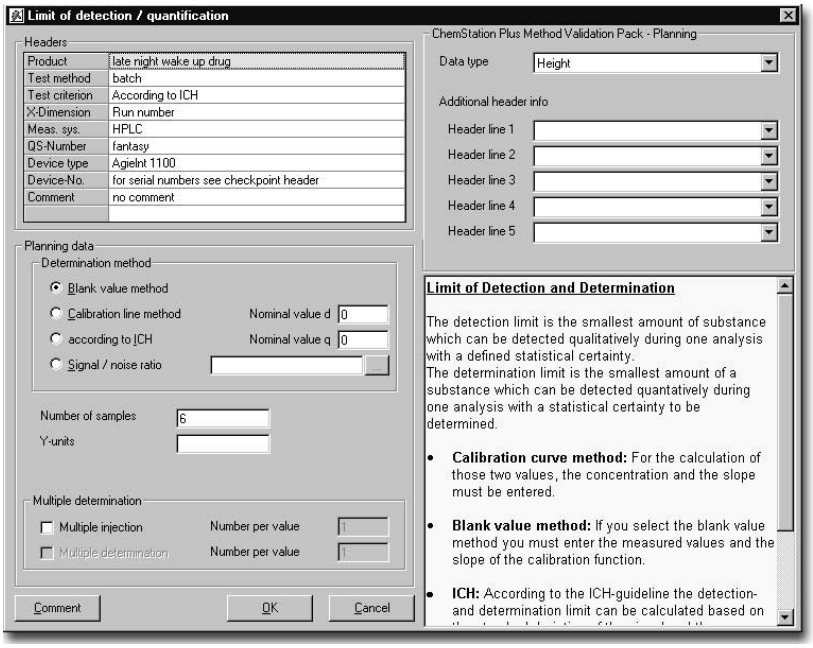

Figure 32
Planning dialog of checkpoint “Limit of Detection/qQantification”

Accuracy

Accuracy describes the extent of correspondence between the expected value and the conventional value. Accuracy is influenced by the systematic error. The systematic error is divided into a constant systematic error and a proportional systematic error. A constant systematic error is not influenced by the concentration of the substance to be determined. If the error is influenced by the concentration, it is a proportional systematic error. A qualitative measurement for accuracy is the systematic deviation of the result. Figure 33 shows the planning dialog of checkpoint "accuracy".

Planning data

- Determination method:
  - Comparison with nominal value
  - Method comparison with joined sample
  - Method comparison with independent sample
  - Standard addition
  - Extended spiking method
  - Recovery
  - Accuracy by recovery
- Other data:
  - Number of samples
  - Y-units
  - Multiple injection possible

Output settings for calculations

- General:
  Result t-Test
- Joined samples:
  - Difference of value pairs
  - Mean value and standard deviation of differences
- Nominal value comparison:
  - Result of Wilcoxon test (additional for nominal value comparison)
- Extended spiking method:
  - Test quantity for a and b
  - Threshold quantity t division
- Standard additional method:
  - Result F-test
  - Result t-test
- Recovery
  - Standard deviation for a, b
  - Residual standard deviation
  - Method standard deviation
  - Test quantities ta and tb
  - t-distribution

Selectivity

Selectivity means that an analytical method can distinguish the substance to be determined from other substances in the sample. Selectivity in chromatography describes the separation capability of the chromatographic system for the components 1 and 2. Figure 34 shows the planning dialog of the checkpoint "selectivity".

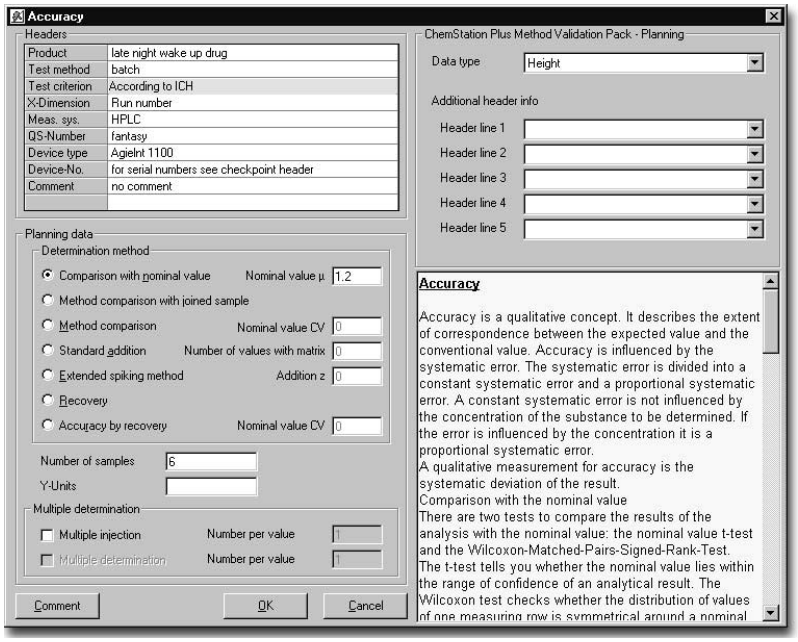

Figure 33
Planning dialog for checkpoint "Accuracy"

Planning data
- Number of values
- Y-units
- Nominal value resolution R
- Add chromatogram bitmap
- Multiple injections possible

Output settings
All data are displayed

Ring experiment

Ring experiments are used to prove that a method can be transported to an entirely different location (other site, company etc.) and that it delivers good results. A ring experiment can be seen as a more general robustness. Figure 35 shows the planning dialog of the checkpoint “Ring experiment”.

Planning data
- Number of rows (one row for one lab)
- Y-units
- Checkmark for same number of values per lab
- Multiple injections possible

Output settings
- Neumann trend test
- Dixon or Grubbs test for outliers
- Variance homogeneity
- Repeatability limit
- Reproducibility limit
- Error of result
- Range of confidence (repeatability conditions)
- Range of confidence (reproducibility conditions)

All output settings are preconfigured during installation to useful defaults. As long as you do not have the need to enable special settings, there is no need to change anything.

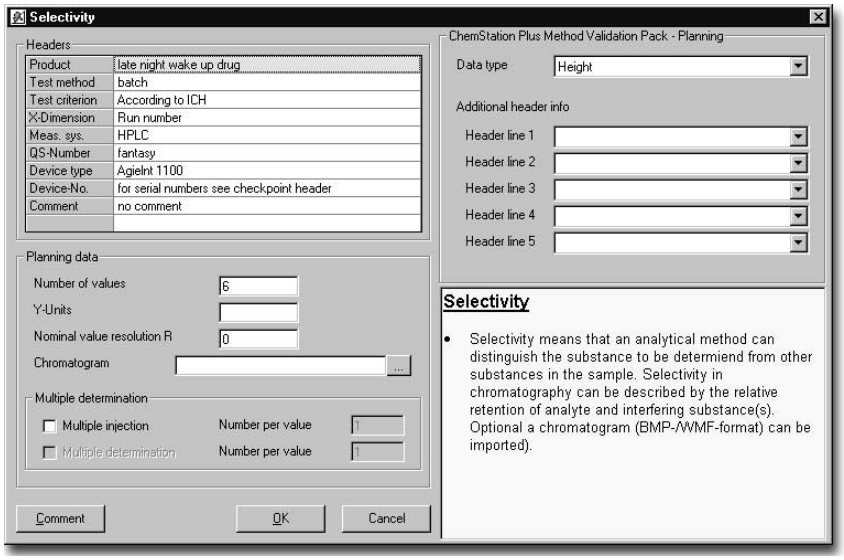

Figure 34
Planning dialog of checkpoint “Selectivity”

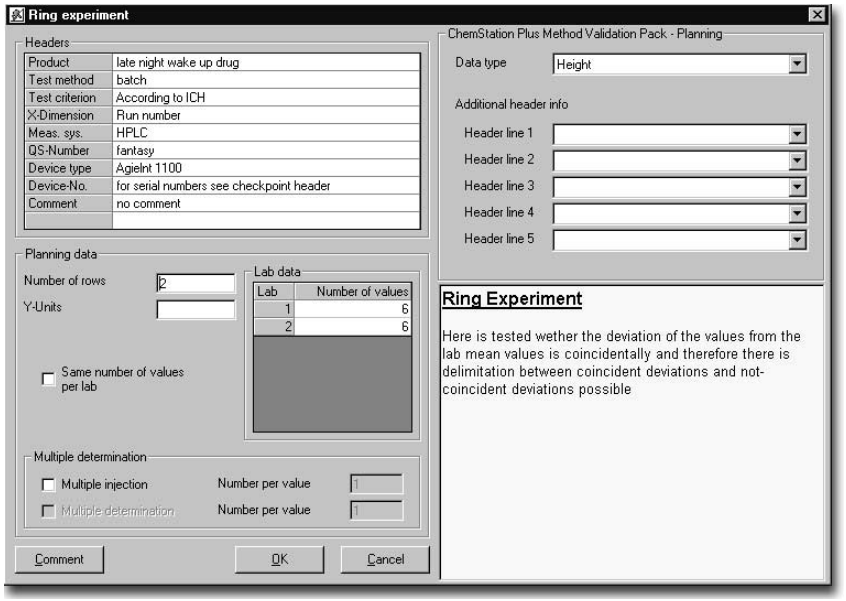

Figure 35
Planning dialog of checkpoint “Ring Experiment”.

As described in previous sections Method Validation Pack interacts with ChemStation for data acquisition and ChemStore for result and data management.

Interaction with ChemStation for data acquisition

If Method Validation Pack is installed in a ChemStation Plus data system ChemStation will offer additional functionality to run and execute method validation sequences. It will receive an additional Method Validation menu item in the ChemStore menu (figure 36), as well as two new buttons in the graphical user interface. The first button switches ChemStation into method validation mode and back to the standard mode. The second button opens the sequence import dialog.

If method validation mode is enabled, the user has access to the method validation sequence import menu. The import window displays a list of pending method validation sequences (MVS files) including status information and user assignment of the MVS files. Users now select the MVS files they want to download from the list of pending files. An MVS file has an assignment to one specific user or it has no user assignment and is thereby an all-user job for all users with a valid logon. As soon as a user has loaded a pending validation sequence for execution in the ChemStation, it is blocked for other users. Partial MVS sequences can be set to *Finalize* which skips the remaining acquisition runs and deletes the file from the list of pending MVS files. Finalizing a MVS sequence will also lock the validation and prevent it from further modification.

MVS sequences are created with a specific command (*Create Study and MVS for ChemStation Plus*) in the Method Validation Pack software. They are automatically built according to the validation configuration in the Method Validation Pack software - no user interaction is required. The MVS template is stored as a text document with the validation in the Document Management System (DMS) of the Method Validation Pack software. Each injection translates into one line in the sequence table; repetitive injections of the same sample receive only one sequence line but write the number of injections in the related sequence column. The MVS files automatically include information on the sample type, number of injections, sample name, and they fill in the method validation name for the analytical method. They also carry additional information in protected custom fields. This information displays the checkpoint name, the component name and a unique run-ID for easy identification in the sample information text dialog. These fields can only be configured and edited through Method Validation Pack software.

To run MVS sequences the opera-

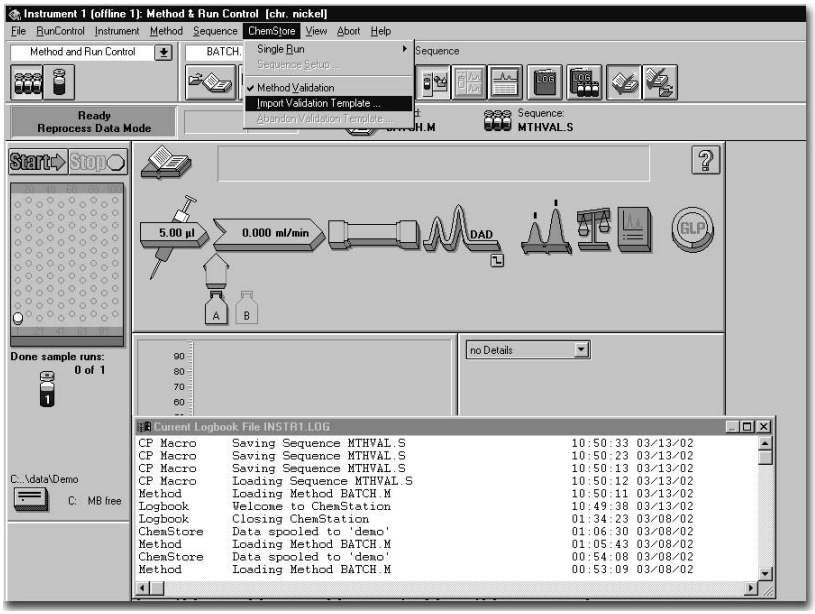

Figure 36
Additional Method Validation menu item in the Data Acquisition ChemStation software module

tor only fills in the vial position for the samples and starts the sequence. For further details on ChemStation functionality, please refer to ChemStation specifications, Agilent Technologies publication number 5988-5314EN.

ChemStore manages the analytical results along with the raw and meta data of the samples in a relational database. This also includes all analytical data of the method validation sequences that have been acquired in ChemStation. The method validation data are stored in method validation studies. Method validation studies are similar to standard ChemStore studies except that they can only be created and modified through the Method Validation Pack software. All method validation study data are visible in ChemStore, but they can not be changed or modified except for reanalysis. As part of the data transfer from Method Validation Pack to ChemStation, the Method Validation Pack software creates a method validation study in ChemStore. The study name is the validation name. Method Validation studies have three custom fields automatically configured with the studies. These fields are

- MV_checkpoint - storing the Method Validation Pack check point information (which test was used with this run)
- MV-Component - the name of the Method Validation Pack component in the validation - comparable to the ChemStation Plus compound.
- MV_runID - storing a unique run identifier that allows full traceability from method validation pack results to ChemStation Plus result management. This is particularly useful for example, if you notify outliers in your method validation. In order to check and/or reanalyze this run, you only have to query for the runID to immediately receive the run with its result that is under investigation.

Interaction with ChemStation for data review

For a first pass review of the data the ChemStation batch review interface can be used. If required the user can do a graphical rework of a chromatogram and generate a new result version that is used for the validation. The result is transferred to the database and the change is documented in the run-related audit trail.

The user decides if the validation is a development validation or a final validation that must run under full 21 CFR Part 11 conditions. In the former case, users with administrative rights can configure the ChemStore study in Method Validation Pack similar to the study configuration in ChemStore. They can select to

- Save raw data with results
- Delete raw data on the local hard disk after transfer to the database
- Save method and sequence along with results
- Save chromatogram and spectra pictures with the result

In a 21 CFR Part 11 validation, all checkmarks are set to true for the data management options as mentioned before.

Based on the hierarchical structure of the Method Validation Pack software, the system has five user levels. They are:

1) Reporting: Logging into the system with a name and a pass word of level 1 (reporting) gives you access to report output only. At this level, data changes are impossible.
2) Data input: Logging into the system with a name and a pass word of level 2 (data input) gives you access to all level 1 tasks and validation data input and graphics/report output.
3) Planning: Logging into the system with a name and a pass word of level 3 (planning) gives you access to all level 1 and level 2 tasks plus checkpoint planning.
4) Configuration: level 4 (configuration) gives you access to con figuration rights and all level 1-3 tasks. You may change the configuration values of each validation.
5) Administration: Logging into the system with a name and a password of administrator level 5 gives you access to all functions of Method Validation Pack including program configuration (global settings).

The user levels are part of ChemStation Plus user administration as shown in figure 37. They are configured in the ChemStore database. All users have two identification pieces, user ID and password. One user ID is valid for all ChemStation Plus modules, so users only have to remember one password for all ChemStation Plus components.

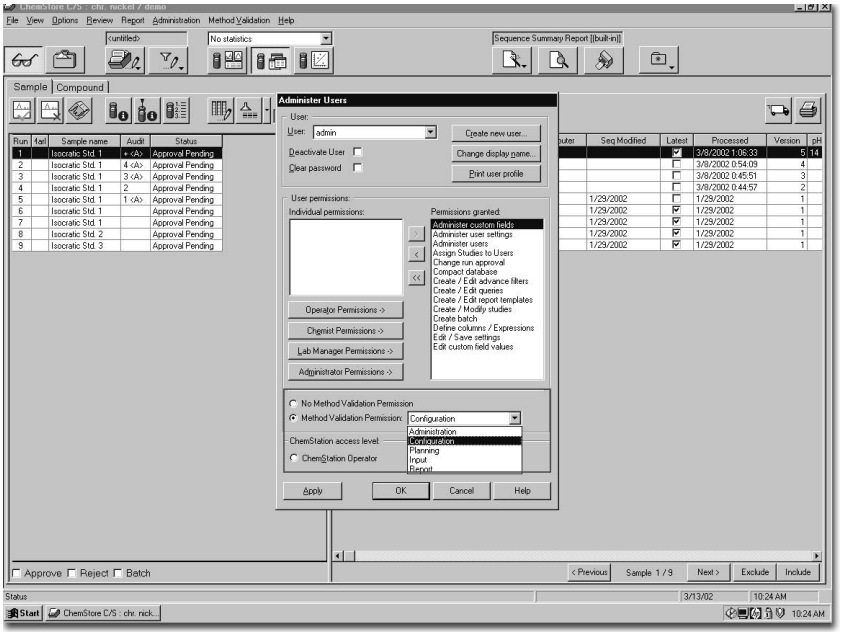

Figure 37
Central user administration for ChemStation Plus including Method Validation Pack user administration and user levels

User authorization

As mentioned under “User management”, only users with a valid ChemStation Plus user ID and their actual password can logon to the Method Validation Pack software. The user management includes a password policy for regular password renewal and user lockout after unsuccessful password entries. For details, please refer to ChemStation Plus Security Pack specifications.

Document management system

Method Validation Pack comes with a full document management system DMS storing all data in a relational Oracle database. For standalone systems, all data are stored in a VDB file, a database file that adheres to a common file format as used by MS Access. DMS stores important information, which is validation raw data, such as configuration and planning, along with the analytical results and the meta data.
The document management system DMS stores all data under the validation name. It creates a validation document for each validation. The validation document has three subsections as shown in figure 38.

- VDB section for validation data base—all data from planning, configuration, setup and analytical results.
- MVS section for method validation sequences—all ChemStation method validation sequences that have been created from a validation data base.
- Report section—all reports are stored as doc files that have been printed for the validation database.

Each section offers a full revisioning of the data. Whenever a new entry in the DMS is made, a new revision is created. The revision is uniquely identified through continuous version numbers, the timestamp of creation along with the user name, the database name and the PC host name. Each revision of each file can be recreated and reopened for later review. All DMS entries are displayed in a hierarchical list. Entries can be selected to view all properties. Additional information that is stored with each revision includes:

- name of entry,
- original path,
- label,
- purpose of entry (manual revision, automatic revision),
- version,
- document type,
- size,
- checksum,
- status (normal, checked-out and finalized),
- login of user, user domain and user computer,
- real name of user (display name),
- reason for check-in,
- check-in date, and
- date of parent entry (i.e. base node entry).

A click in the checkbox of this revision offers review of any document revision. Clicking a version child node once displays its properties. Double-clicking a valida-

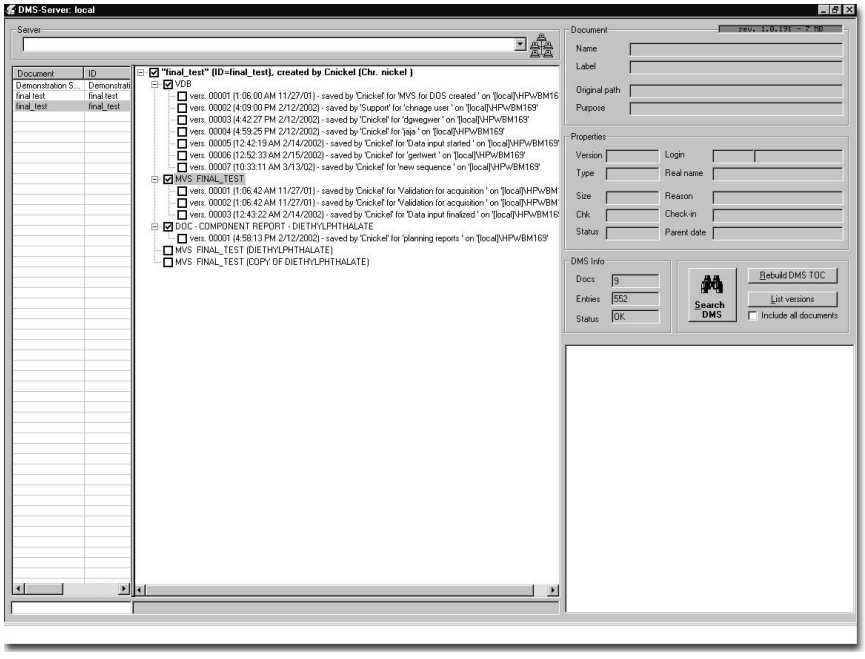

Figure 38
Method Validation Pack document management system DMS

tion (VDB-file), or clicking on its selection field, will restore the selected version. Documents and MVS files are displayed in a preview window, allowing to zoom, print, export or copy the selected document. The actions depend on the type of entry: documents are displayed in a preview window, validations are stored in the file system.

DMS with standalone systems
Standalone systems will typically require managing multiple databases. The system will prompt the user to create a new database file after the size limit of 800 MB is exceeded. A validation that has passed its size limit can still be selected for review. If the system has more than one database, the user must connect first to one database from the list of available databases.

DMS for client/server systems
Client/Server system using an Oracle relational database will store all validations in one database. A list of all available validation databases displays when selecting to open an existing validation, as shown in figure 39. The user selects the validation from the list with a simple click on the actual validation. If users open older revisions of a validation the validation is opened in a locked status as read-only. Only saving it as the latest revision can open it.

Figure 39
Selection dropdown window for database connection

File security for the standalone database

The local validation database must be protected from unauthorized access through Explorer or MS-DOS. Method Validation Pack software uses file security settings to protect the database file. All Method Validation Pack data store under the Method Validation Pack root directory on the PC hard drive. The Document Management System stores in a separate subfolder of the Method Validation Pack program directory. The folder name is DMS. This folder is protected with Windows file security. It offers write-only access to all authenticated users and only an administrative user has full access to the DMS directory.
Understanding and using file security is particularly important in standalone installations where all data is stored in the local database. In a client-server installation, the default storage location should be the Oracle database that is stored on a separate server and that is not accessible to any software operator.

User documentation with Method Validation Pack

Method Validation Pack always displays the current user in the title bar. The system displays the current user name and the database information. The database is either displayed as local login for a standalone database connection or as the Oracle net alias name if the system is connected to the Oracle database, as shown in figure 40.

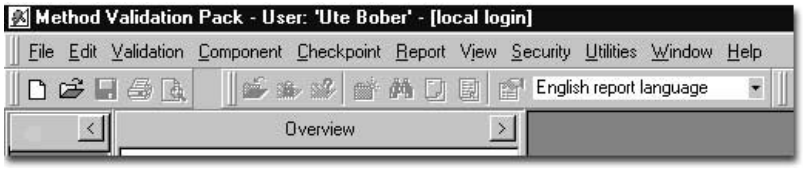

Figure 40
Permanent display of current user name, and database connection with Method Validation Pack software

Audit-trails

Method Validation Pack audit-trail tracks all actions that users execute during program operation. The audit-trail is user-independent, can not be modified and it is completely system generated. Method Validation Pack has three different audit-trail levels, as shown in figure 41:

- program audit-trail,
- default validation audit-trail, and
- validation audit-trail.

The default display size of the audit-trail can be configured in the audit-trail window. The number of entries for display must be between 25 and 30000.

For easier searching through the audit trail, users can group the audit-trail entries. All audit-trail column headers are available as grouping criteria. The grouping functionality uses a simple drag-and-drop functionality to enable or disable grouping. The user only drags the column header into the grouping section and receives a sorting of the complete audit-trail according to the column entries. As an example, the audit-trail should be arranged by user name. The system displays all user name entries as parent nodes. A simple click on the expand icon now displays all audit-trail entries for the selected user as shown in figure 42.

Audit-trail details for validation and default validation audit-trail

The validation and default validation audit-trails display all actions that are related to a validation database.

Both audit-trails offer the following information where each item displays its data in a separate column:

- Date and time of action
- User ID and
- Printed user name
- Level of action (e.g. level 4 for configuration changes)
- Status of the change (saved or unsaved
- Component
- Checkpoint
- Action (the audit-trail lists the menu if the user did only open the menu without changes and it lists any parameter change with the old and the new value)
- Authentication (for all actions that require an electronic signature)

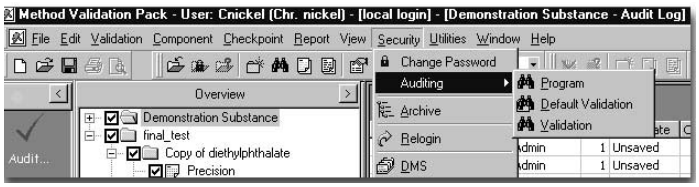

Figure 41
Three levels of audit-trail with Method Validation Pack software

Default validation audit-trail

The default validation audit-trail refers to the general configuration of validations. It covers all changes that are not related to a specific validation database but apply to all new and existing validations upon creation. These settings are new validation properties and new validation output settings. Changes to these settings are displayed in the default validation audit-trail.

Validation audit-trail

The Validation audit-trail tracks all actions on the actual validation.

Program audit-trail

Program audit-trail is designed to track all actions that relate to the general program operation such as save and logon actions. The program audit-trail table items are:

- Date and time
- User ID
- Validation name
- Storage location of the actual validation snapshot copy
- Action (Program start and stop, user logon and logoff, IQ execution, validation opening, use of import mask for data entry, and program options)

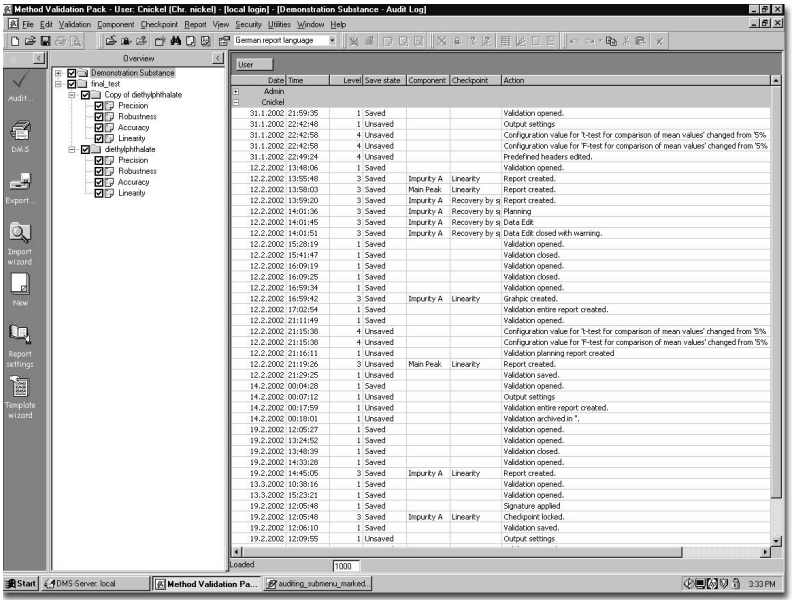

Figure 42
Grouping of audit-trails, in this example grouped by user

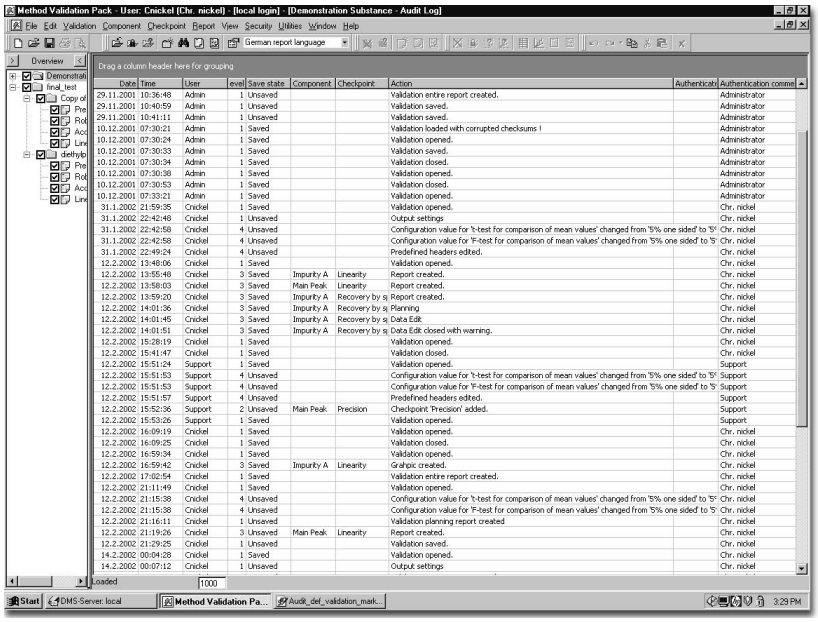

Figure 43
Example for audit-trail entries including all important information on user, time and action for the entry.

Validation locking and electronic signatures

After completion of a checkpoint, an entire component or a full validation, the validation can be locked partially or completely. To avoid locking of incomplete items, the application software will display a warning message and close the lock dialog without changes if the locking item is not complete. Partial validation locking allows locking a single checkpoint or a complete component. After locking the item, no changes are possible to this particular item. It is in a review-only mode allowing only printing reports and reviewing the graphics. Every locking action automatically creates a new revision of the validation in the DMS system. Only users with an access level 3 (planning) or higher have access to the locking functionality. Each locking action requires an electronic signature. The electronic signature uses the password/user ID combination as defined by the FDA (figure 44). The sign-off dialog comes with a time limit of 45 seconds. If the signature was not executed during this period, the dialog will close and the validation status remains unchanged.

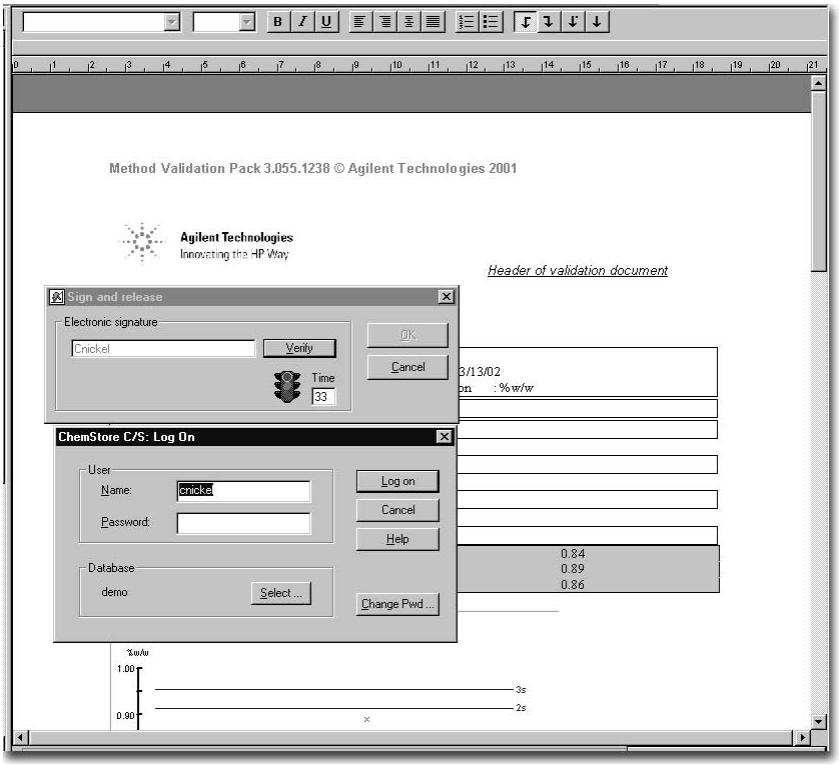

Figure 44
Executing electronic signatures with Method Validation Pack

Prerequisites

Method Validation Pack can operate both PC-based in a standalone installation or in a networked system installation with full client-server functionality. In both scenarios, some prerequisites must be met:

Software

ChemStation Plus standalone – For a fully integrated installation of Method Validation Pack it is required to have the following software installed:

- ChemStore standalone rev. B.02.02 or higher or Security Pack rev. B.02.02 or higher and
- ChemStation rev. A.09.03 or higher for data acquisition

ChemStation Plus

If the system should operate in client-server mode, ChemStore with Oracle Revision 8.1.7 must be installed on the system. In the client-server installation, all ChemStation Plus modules can operate from different PCs. Their installation is completely independent and the system is fully functional as long as all required modules (see above) are installed within this cluster and they can connect with each other.

Non-Agilent software

- MDAC 2.5 (Microsoft Data Access Components 2.5) (installed by ChemStore)
- Adobe Acrobat Reader 4.0 (part of standard bundle)

The Microsoft Data Access Components install a layer to access local databases or central database servers. Method Validation Pack uses Microsoft JET database to save local data (i.e. Microsoft Access format). Microsoft Windows 2000 already contains the 2.5 version of MDAC. This version is fully compatible with Method Validation Pack. Adobe Acrobat Reader 4.0 is required to display the online manual.

Standalone installation

The standalone installation is user installable from the Method Validation Pack (rev. A01.02 or higher) software CD-ROM. All other ChemStation Plus modules as outlined above are also user installable for advanced users. However, Agilent recommends the installation of the ChemStation Plus modules through an Agilent-certified service engineer to prevent from any potential installation problems and for inclusion of software familiarization upon installation.

Client-server installation

The client-server installation must include

- installation of Oracle 8.1.7,
- installation of ChemStore server software,
- creation of the Oracle database
- installation of Method Validation Pack software,
- creation of Method Validation Pack tablespaces in ChemStore Oracle instance (alias “HPCS”) and,
- installation of ChemStore, Method Validation Pack and ChemStation for data acquisition client software on all client PCs.

Agilent offers complete installation, validation and training through its professional services organization. This will be handled as a complete project and the complete service delivery is managed as a project based on the individual customer requirements.

ChemStation Plus Method Validation Pack — Product Options and Configurations

Standalone version

The standalone version of Method Validation Pack requires the additional installation of the ChemStation Plus database module for data management of analytical data. The database can be ordered as G2181BA ChemStore database or as G2183AA Security Pack for full support of 21 CFR Part 11. The installation only requires one of these products.

Description	Product No.
ChemStation Plus Method Validation Pack Requires but does not include ChemStore C/S or Security Pack. Allows for method validation according to DIN/ICH/USP and EP guidelines. Supports 21 CFR Part 11.	**G2184AA**
Software module to add Agilent ChemStore C/S to an existing ChemStation for GC, LC, LC/MSD, CE or A/D.	**G2181BA**
ChemStation Plus Security Pack. Adds the secure ChemStore C/S relational database add-on software module to the ChemStation Plus SW for A/D, GC, CE, LC and CE/LC-MSD. Supports 21 CFR Part 11.	**G2183AA**

Client/server version

Method Validation Pack client/server installation runs on Oracle C/S Rev. 8.1.7. A complete system configuration requires ChemStore C/S server software (G1410A) for each server plus Oracle licenses (G1411A) for each named database user and a ChemStation Plus client license (G2186BA) for each connected client as well as copies of G2184AA for all Method Validation Pack clients. For full support of FDA's 21 CFR Part 11, replace one copy of G2186BA by one G2183AA copy. Agilent provides all Agilent ChemStation Plus software and Oracle 8.1.7 software on Agilent CD-Rom media.

Description	Product No.
ChemStation Plus Method Validation Pack Requires but does not include ChemStore C/S or Security Pack. Allows for method validation according to DIN/ICH/USP and EP guidelines. Supports 21 CFR Part 11. Must have one copy of G2186BA per PC running Method Validation Pack software. For full support of 21 CFR part 11 replace one license of G2186BA with one copy of G2183AA per server *NOTE: The number of Method Validation clients can be smaller than the number of ChemStation plus clients in case method validation will only execute on a subset of all networked ChemStation Plus clients*	**G2184AA** Qty: number of method validation systems in ChemStation Plus C/S networked data systems
ChemStore C/S server application software Includes ChemStore C/S server software, Oracle 8i standard edition software, 5 Oracle application-specific named user licenses	**G1410A** Qty: one per server
Oracle connectivity license. Required for each named user of the ChemStore C/S server database	**G1411A** Qty: (Required for each named user in the ChemStation Plus networked data system) -5
ChemStation Plus ChemStore client license Includes one online ChemStation Plus license for online data acquisition and one ChemStore C/S offline data review license. Includes license and user information only. Requires but does not include ChemStation Plus software client media.	**G2186BA** Qty: Number of clients If G2183AA is added, quantity is reduced by one.
ChemStation Plus Security Pack. Adds the secure ChemStore C/S relational database add-on software module to the ChemStation Plus software for A/D, GC, CE, LC and CE/LC-MSD. Supports 21 CFR Part 11.	**G2183AA** Qty: one per server

Installation, Qualification Services and Training

Installation and familiarization

Agilent Technologies' installation and familiarization service ensure that the Agilent ChemStation Plus is installed correctly and in the right environment.

In addition, Agilent offers a range of on-going support services to help:

- get your system up and running fast,
- resolve problems quickly,
- keep productivity high,
- extend instrument life, and
- comply with regulatory quality requirements.

Qualification services

- Agilent Technologies offers a full range of qualification services to provide the evidence you need to satisfy such agencies as the U.S. Food and Drug Administration (FDA), the U.S Environmental, Protection Agency (EPA), the International Standardization (ISO), and the Organization for Economic Cooperation and Development (OECD).
- Installation qualification(IQ) Operational qualification/ performance verification (OQ/PV)

Training

Agilent's ISO-registered trainings can save you time, help keep your laboratory operating costs low, broaden your capabilities, and ensure that your laboratory complies fully with regulatory and quality requirements.
For your convenience, standardized courses are offered in selected locations worldwide. Onsite courses can be tailored to your specific needs.

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