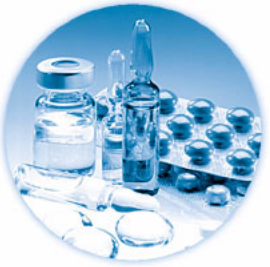

Agilent Cerity Networked Data System for Pharmaceutical QA/QC

Concepts Guide

The Big Picture

Agilent Technologies

Notices

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Software Revision

This guide is valid for A.02.xx revision of the Agilent Cerity Networked Data System for Pharmaceutical QA/QC software, where xx refers to minor revisions of the software equal to or larger than 02 that do not affect the technical accuracy of this guide.

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In This Guide...

The Concepts Guide contains descriptions of the concepts of the Cerity Networked Data System (NDS) for Pharmaceutical QA/QC to help you understand the Cerity NDS for Pharmaceutical QA/QC components, and how they work.

It contains information about the design principles, the system behavior, and the control and information flow of the Cerity Networked Data System (NDS) system. One key focus area is on data security and data integrity as mandated by FDA 21 CFR part 11 (electronic records and electronic signatures) and predicate rules such as GMP, cGMP, GLP etc.

Use these resources for more information.

- For details of the calculations used in Cerity NDS for Pharmaceutical QA/QC:
  the Reference Guide
- For Context-specific task (“How To”) information:
  the help system
- For Details on system installation and site preparation:
  the Installation Guide
- For Details on system administration principles and tasks:
  the online System Administration help.

Thank you for selecting Agilent Technologies.

1 Cerity System Architecture

This chapter contains an explanation of the components of the Cerity NDS for Pharmaceutical QA/QC system, and how they work together.

2 System Security and Data Integrity

This chapter describes the in-built security and integrity tools, and explains how Cerity NDS for Pharmaceutical QA/QC complies with FDA 21 CFR part 11.

3 Basic Concepts of Cerity for Pharmaceutical QA/QC

This chapter explains the Cerity NDS for Pharmaceutical QA/QC graphical user interface, and describes the four Views that you use when you work with Cerity.

4 Data Acquisition

This chapter contains an introduction to the process of acquiring data in Cerity NDS for Pharmaceutical QA/QC.

5 Cerity Instrument Control

The different aspects of instrument control in Cerity NDS for Pharmaceutical QA/QC are described in this chapter.

6 Working with Cerity Methods

The Method is a vital part of the Cerity NDS for Pharmaceutical QA/QC application, and this chapter explains the concepts in detail.

7 Data Analysis Concepts

The concepts of the data analysis process, from integration to report formatting, are explained in Chapter 7.

8 Reporting

Chapter 8 gives a description of the Report Template Editor, which is the basis of the production of Cerity reports.

9 Administration and Maintenance

This chapter explains, among other things, the Cerity Administration and Maintenance utility.

10 Definitions of Terms

Chapter 10 explains the terms that are used in Cerity NDS for Pharmaceutical QA/QC.

Contents

1
Cerity System Architecture

This chapter contains an explanation of the components of the Cerity NDS for Pharmaceutical QA/QC system, and how they work together.

Introduction

The Cerity Networked Data System (NDS) manages all tasks related to the acquisition, processing, and storage of analytical data. The Cerity database management system stores all raw data, meta-data and results data ensuring security, data integrity and system reliability.

Which system do you have?

Your Cerity NDS system is either

- a Professional system with a single workstation (see Figure 1), or
- a client-server system (see Figure 2 on page 16).

Professional system (Agilent G4000AA)

The Cerity NDS Professional system runs on one Windows Workstation.

Although the system is delivered with five named user licenses for Oracle, only one Cerity NDS user can use the system at a time.

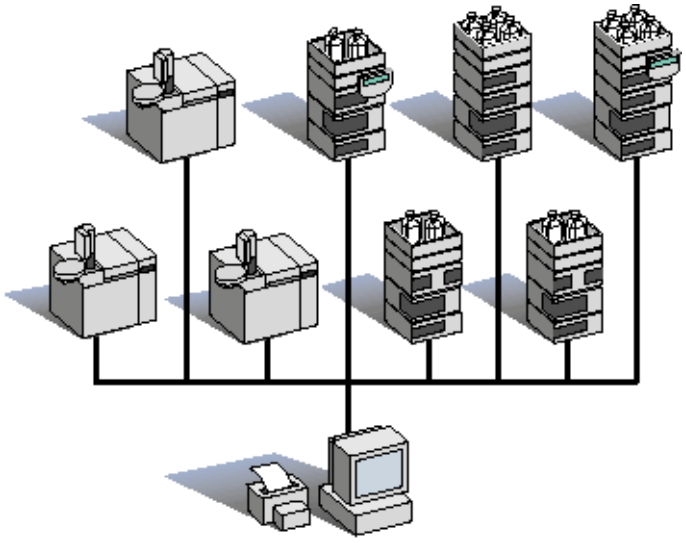


Figure 1 Cerity NDS Professional system

Client-Server system (Agilent G4001AA)

The components for your Cerity NDS Client-Server system are installed and run on designated Microsoft® Windows Workstations. The cluster includes all network devices configured for the Cerity NDS Client-Server system such as instruments, printers, and clients.

You can configure as many licensed users as needed on a Cerity NDS cluster. Cerity NDS users and instrument control are licensed separately. For each named user on the system, one Oracle license is required. Five named user Oracle licenses that are application-specific are included with the client-server system.

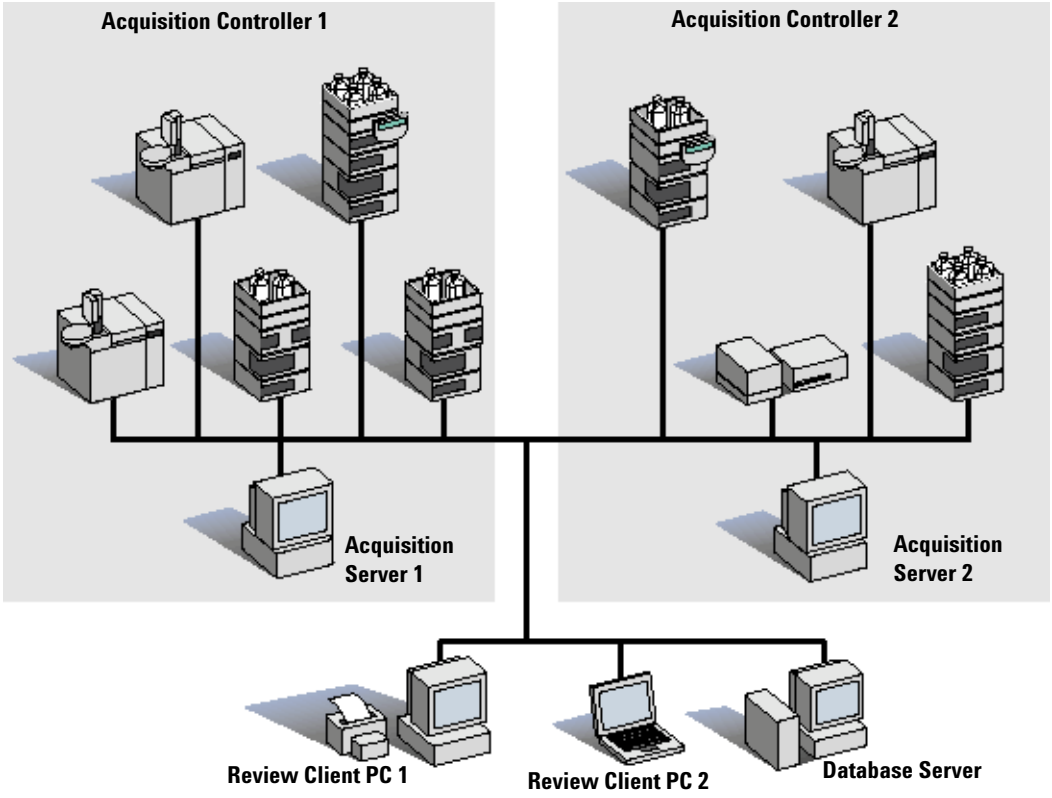


Figure 2 Cerity NDS Client-Server system

Client-Server Architecture

The Cerity NDS client-server system is a multi-tier system with:

- A central database server based on Oracle 9i for permanent data storage, central management and reporting
- Multiple acquisition controllers acting as compute servers and performing the instrument control
- Cerity thick clients enabling multiple users to use the system for data entry and review

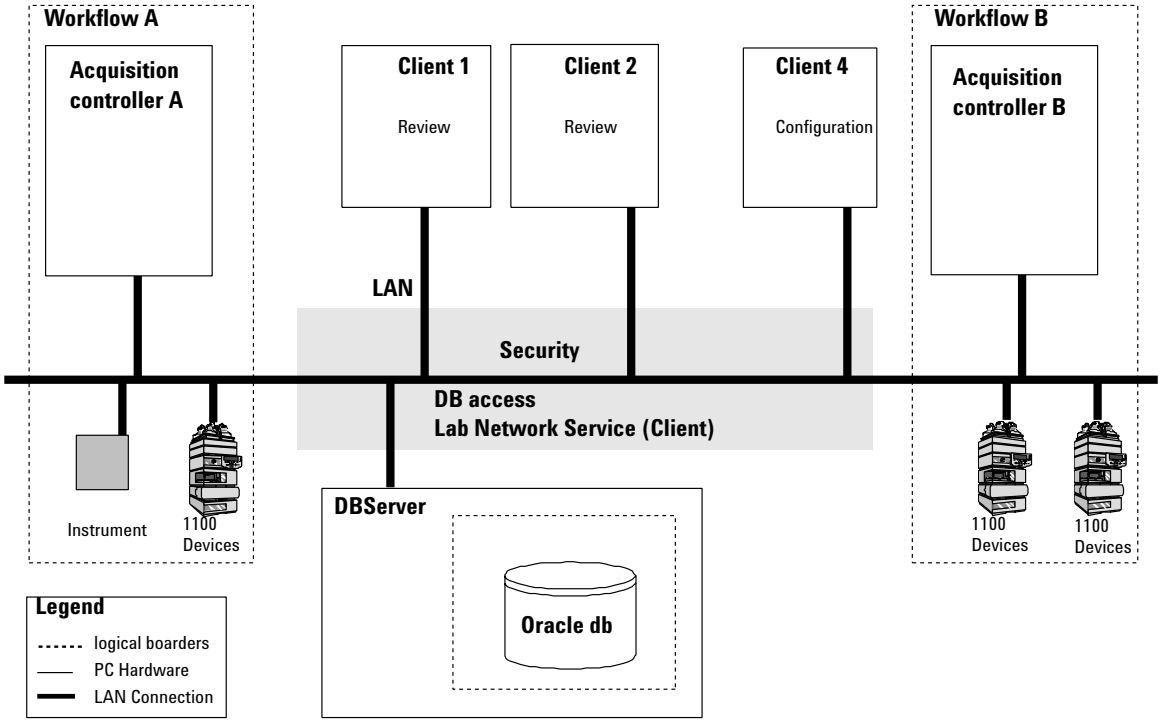


Figure 3 Architectural overview of Cerity NDS Client-Server system

The Cerity NDS uses dedicated services that communicate using the distributed component object model (DCOM) to control and secure the information flow between system components (see Figure 3). An authorized user can review or configure data that the system stores on the central database server from any Cerity NDS client computer. Dedicated acquisition controllers manage instrument control and data acquisition of the instruments connected to the Cerity NDS.

Database server

The Cerity NDS client-server system contains a single database server. The Cerity database server maintains system security, monitors software license usage, and controls the Cerity network services for the laboratory. The Cerity database server stores data in an object-relational Oracle database.

The database server establishes security for report generation, license usage, and network services for the lab. The Cerity database management system stores data that uses the Oracle relational database.

Acquisition controller

Optionally, one or multiple computers can be configured as acquisition controllers. Acquisition controllers execute the processes required for controlling, acquiring, and processing sample data from the instruments connected to the Cerity device drivers. For example, see Figure 4. The automation engine controls the resources available to perform work. Resources can be instruments or places where data is stored.

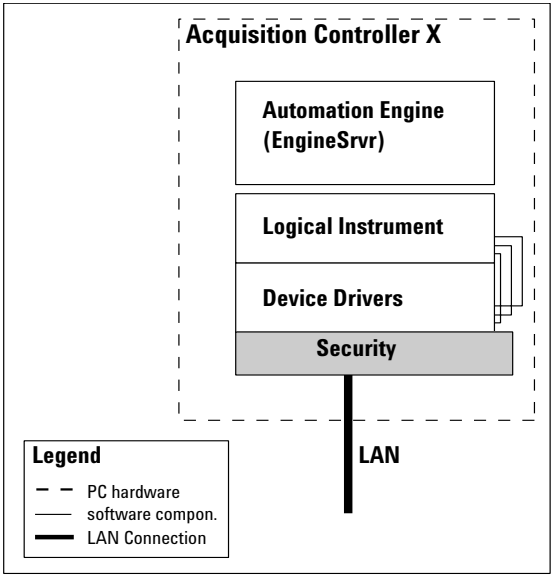


Figure 4 Acquisition Controller

Acquisition controllers may also be used for load balancing of data reprocessing tasks. An acquisition controller without any connected instruments will operate as a reprocessing server in the system.

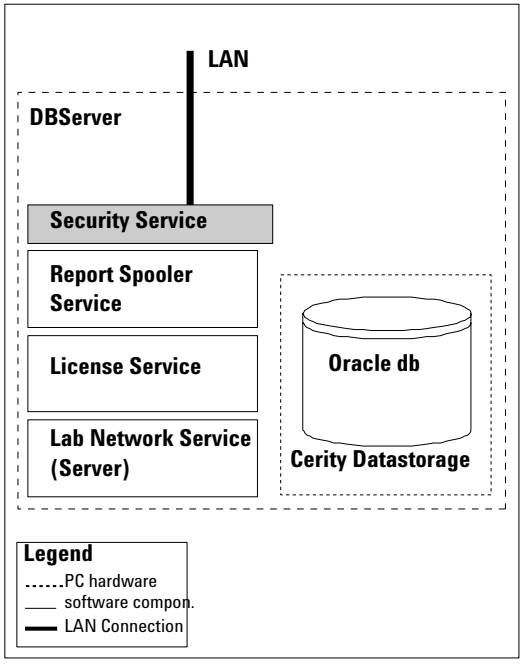


Figure 5 Database Server Security

Review Client

The Cerity client computers can be used for common system tasks such as setting up analytical methods, performing analyses, reviewing results, and administering system security with user roles and electronic sign-off procedures. Figure 3 on page 17 shows Client 4 running the **Cerity Software Administration** application which is based on the Microsoft Management Console (MMC). An authorized Cerity administrator uses Client X to configure user roles and role rights for the users in the laboratory. Authorized users can log into the system from any Cerity client computer (e.g. “Client n”). After the user logs on to the system, they can perform tasks assigned to them in relation to their job role, such as setting up sequences, reviewing results, or approving data.

Terminal Server

Terminal Server Setup

In the terminal server setup, the Cerity Review Client software resides on a central server, rather than on individual clients, and the clients access the software as needed. This reduces the hardware overhead (memory, disk space) on the client terminals.

Each client is allocated a portion of the server's resources (see Figure 6). Thus, the number of clients is limited only by the available resources in the server.

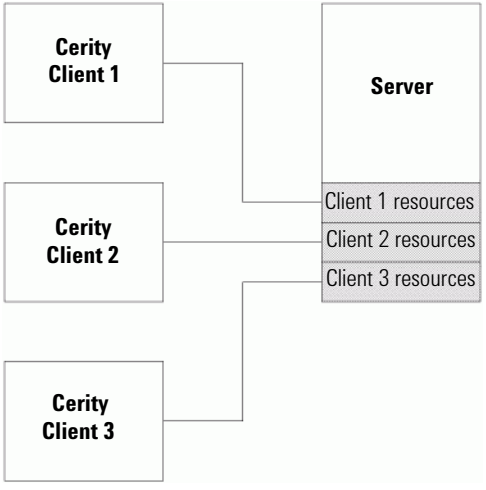


Figure 6 Terminal Server Setup

2
System Security and Data Integrity

This chapter describes the in-built security and integrity tools, and explains how Cerity NDS for Pharmaceutical QA/QC complies with FDA 21 CFR part 11.

Security

The Cerity Networked Data System (NDS) provides the procedures and controls necessary to ensure system security, data integrity, and traceability of electronic records. The design of Cerity NDS helps pharmaceutical QA/QC laboratories meet regulatory requirements for accurate and reliable records in a closed system.

Each time a user logs on to the Cerity NDS and starts a Cerity application, the Cerity NDS both authenticates and provides the client with secure access to the stored data.

Authorized Access

FDA 21 CFR part 11.10d and part 11.300 request that laboratories restrict system access for closed systems to authorized individuals. The Cerity NDS reuses the authentication scheme of the Windows operating system such that the identity of any user authorized to use the Cerity NDS are known to the operating system. The system administrator for the operating system creates a user account for each user on the system. The Cerity administrator uses the user configuration panel in the Cerity Software Administration application to configure each user's access to the Cerity NDS. If a user attempts to log on to Cerity without a user account, the user cannot access the system. See Figure 8 on page 26

Cerity Software Administration Access

The Cerity administrator must first log on to the Windows operating system with Administrator rights and privileges. The Cerity installation sets up the Cerity Administrator's own Windows user account and their own Cerity user account with full access to all components of the Cerity NDS.

The Cerity administrator can access all of the Cerity Software Administration components for configuring each user's limited access to the system. The local Windows system administrator has already assigned a Windows user account to each Cerity user before they start the application. Only the Cerity administrator has full access to the Cerity Software Administration components before the Cerity administrator configures access rights and privileges for all Cerity users on the Cerity NDS.

Cerity Pharmaceutical QA/QC Access

Each time a user logs on to Cerity, the Cerity NDS provides access to the available data sources. A session, or when a user logs on and starts Cerity, establishes the user's security context. The session provides a way to connect to one of the data sources. A user can connect to one data source per session. The user must connect to a database before he or she can start Cerity. Connection to a database requires Logon authentication as a mechanism of validation. There can be multiple databases on a Local Area Network (LAN). Each Cerity NDS contains one database server and each session is characterized by the associated database.

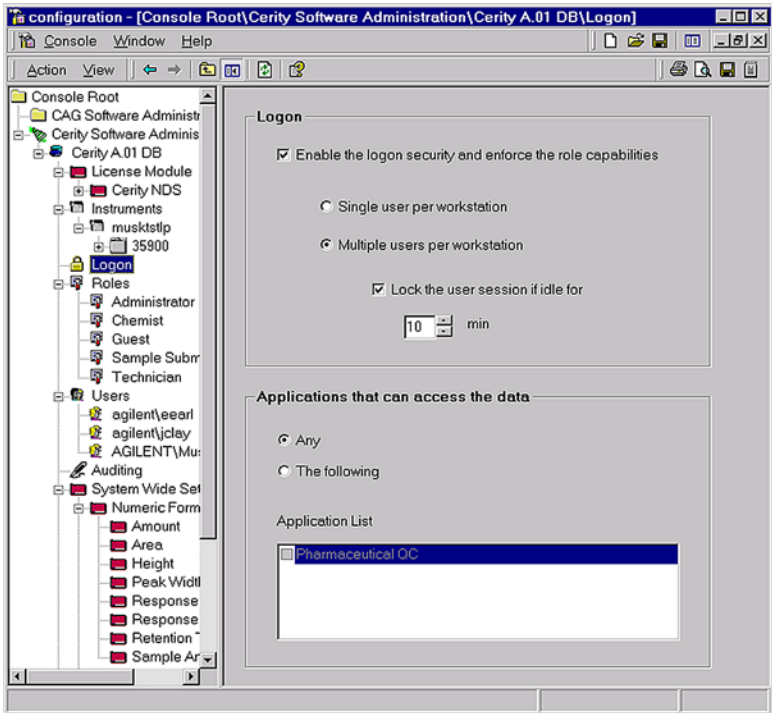


Figure 7 Logon

The Cerity NDS performs as a networked system independent of the operating system and administers access control after a user initially logs on to the operating system. If another user needs to use the Cerity NDS, the user must start another session to access the Cerity system and connect to a database.

Multiple Users Several users in a laboratory may have to share the same equipment and applications. FDA 21 CFR part 11.10g requires authority checks to ensure that only authorized individuals use the system such that for every transaction, the security services determines whether the currently logged on user has authorization to use the system. When multiple users can run Cerity, the Cerity solution allows for a shared logon in the Windows operating system and personal logons for each Cerity session.

To avoid changing the current user logged on to the operating system when shutting down the current Cerity session, the Cerity NDS provides for configuration of additional user logon policies as **Multiple users per workstation**. This setting allows multiple users to log on to the Cerity NDS application, each one with their logon credentials. This configuration is commonly used in environments working in multiple shifts. The Cerity NDS requires the user to enter their logon user credentials (that is, Windows user identification code and password) to log on to the application and connect to a database. The current user's access rights within the Cerity NDS are now in effect for traceability and accountability. If another user attempts to run Cerity on the same computer, the user must start a new session of Cerity and enter their logon identification code and password.

FDA 21 CFR part 11.200 demands stringent controls that prevent impersonation. To protect the session from another user or Cerity user impersonating the user executing the session, the user can lock the Cerity session. To unlock the locked session requires the user's identification code and password. The Cerity NDS provides additional security for multiple users on a workstation by automatic locking of the user session if idle for a selected amount of time. Cerity's implementation of these security measures prevents and safeguards the laboratory from impersonation and accidental, or even intentional, falsification of records.

Cerity Reports Access

Any user can access the **Cerity Report Viewer** to view a report. Only users that have task rights to edit report templates can access the **Cerity Report Template Editor**. The **Cerity Report Template Editor** lets the user edit default report templates that are HTML documents stored on the Cerity file system.

Users who require the right to edit and save report templates must also have write permission to the **CerityReports** share and the following directories:

<CerityReports>\pharmaqc\pharmaqc.dd

<CerityReports>\pharmaqc\templates\ and subfolders

Users allowed write access to the **CerityReports** share are limited to the Cerity administrator and users that the Cerity administrator provides file/directory rights to.

Authority Checks

FDA 21 CFR part 11.10d requires the system administrator to limit system access to authorized users. The Cerity NDS limits system access through an organization of authority checks. Each user authorized to use the system requires a **Current Role** and rights to do a set of tasks for that role.

User roles and rights

The Cerity administrator must assign a **Current Role** for every user that uses the Cerity NDS. The **Current Role** provides authorization or rights to do a set of tasks set up by the Cerity administrator.

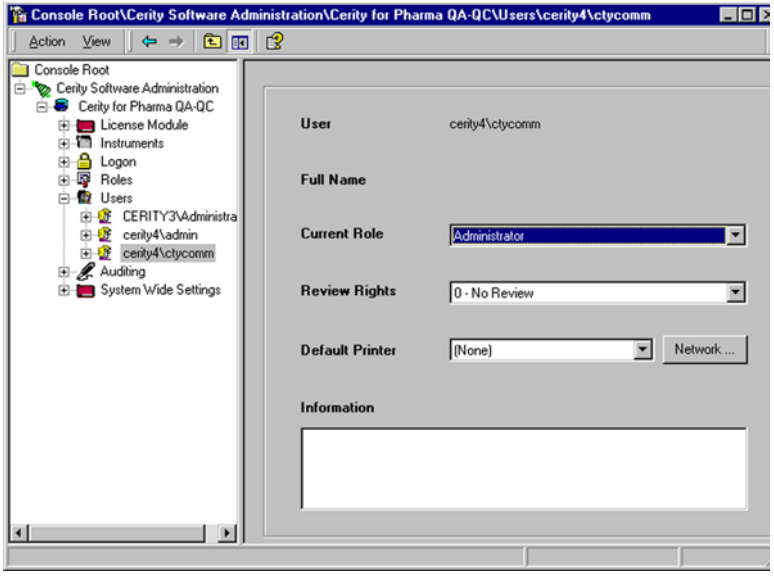


Figure 8 User Configuration

Configuration of roles must match the Standard Operating Procedures (SOPs) of the laboratory. Roles provide a framework for Cerity applications to implement configurable interfaces and functionality. The Cerity system defines an operation or task such as “Method Editing” that the Cerity administrator can associate with a role and assign rights to do that task. When a user starts a Cerity application, the task set associated with the user’s current role determines user access, functionality, and the appearance of the Cerity application. Role task sets serve as *options* that customize the behavior of Cerity applications for each user.

User rights

The Cerity NDS provides a defined set of tasks for each role. These tasks describe various UI options and selections, mapping each to a task name. During the editing of roles, a list of tasks is available to the Cerity system administrator to set or clear rights for each role. Once a user receives a role and task set from the Cerity administrator, interfaces available to the user are modified. For example, if a user does not have the right to do an operation, the corresponding UI option or selection appears dimmed. Modification of task sets is secure, and available only to the Cerity administrator.

NOTE

By default, the **Guest** role has no user rights, and therefore gets an empty application on login. The setup of the **Guest** role is the responsibility of the system administrator.

Integrity

Trustworthy and Reliable Records

System validation and qualification become crucial when an auditor can request regeneration of data to confirm authenticity. FDA 21 CFR part 11.10a requires validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records. The Cerity NDS provides such means to reconstruct the analysis using the exact same method and equipment, even if a particular analysis is no longer performed in the laboratory. The Cerity NDS ensures data integrity:

- methods used are not changed, either deliberately or accidentally,
- raw data is securely stored, together with results and associated meta-data
- results are not changed, either deliberately or accidentally

Agilent Technologies support provides Installation Qualification (IQ) and Operational Qualification/Performance Validation (OQ/PV) for hardware and software to verify protection and validation of activity and information reported in analyses.

Installation and Operation Qualification

Regulatory compliance controls for closed systems look for evidence of factory testing for individual pieces of hardware along with software validation documents that show test plans, test results, and source code. Agilent Technologies provides a **Declaration of System Validation** for all products. The **Declaration of System Validation** documents that the product was developed, tested and successfully validated according to the Software Life Cycles, and Quality Manuals followed by the divisions of Agilent Technologies. Agilent Technologies operations have been certified according to international standards such as ISO 9001 and have maintained their certification status for many years.

Data Management and Referential Integrity

The data management component of the Cerity NDS employs an information object model with a method of retrieval and storage of raw data. The information model is a common or shared data model that all Cerity applications share. The Cerity data model provides a way of maintaining all revisions of methods, calibration data, results data, meta-data, and their relationships. Only users permitted to access configuration information can configure rights to key features such as sequences, samples, methods and instruments. See Figure 3 on page 17.

The Role of Meta-data

The Cerity NDS manages raw data, meta-data, and results. Meta-data is data about data, and is required to describe how the results were derived from the raw data. This includes instrument control parameters, processing parameters, calculations, logbooks and audit trails. All information required for verification of results is always under full revision control and subject to an audit trail. The Cerity object-relational database management system stores and maintains referential integrity between raw data, meta-data, and results data by design.

Archive and Restore

FDA 21 CFR part 11.10b mandates accurate and complete copies of records. The Cerity Archive and Restore application allows the laboratory to store copies of all changes to existing records.

The Archive and Restore application allows the laboratory to maintain a complete history of records and document individual responsibility for the creation, modification or deletion of records (FDA 21 CFR part 11.10e c75). The Archive and Restore application performs the most common database tasks:

- Archive
- Delete
- Restore

The Cerity administrator or users assigned the rights to run the Archive and Restore application must start the application, select a database, and log on to the Cerity NDS to access the Archive and Restore application.

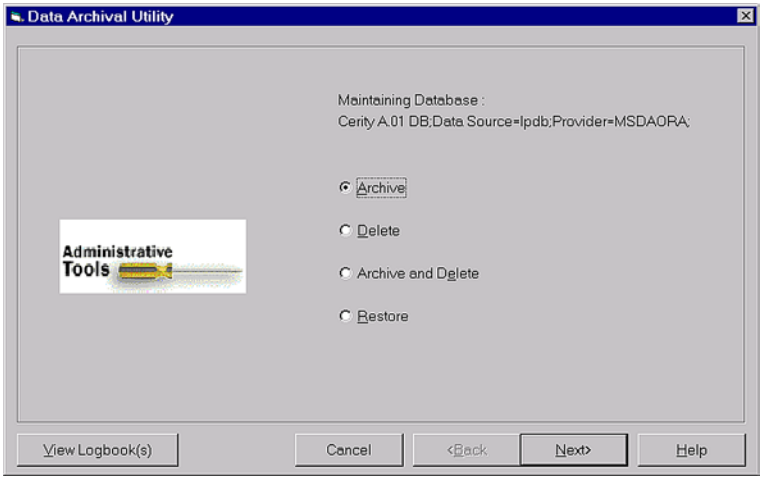


Figure 9 Data Archival Utility

Archive **Archive** allows the user to store the information on file-system-based media. The user can archive samples, methods and instruments. The **Archive** dialog box allows the user to select or query the objects for archiving. During the archive procedure, the selected objects and their previous revisions are archived along with any objects that are associated with the selected objects.

Delete The **Delete** process is query-based and similar to archiving. However before deleting an object from the database, the data objects must already be archived. This procedure meets the FDA CFR part 11.10c, and FDA CFR part 11.10f procedures and controls for closed systems.

NOTE Deletion of records requires role task rights and is part of the audit trail.

Restore

Restore requires retrieving information using the **Archive and Restore** application. The same dialog boxes appear as in the archive procedure. During the restore procedure, the user restores all objects including objects associated with the selected object to maintain traceability and data integrity.

Data can be restored from an off-line archive to the original, or to a different Cerity database with the restore utility. The system ensures the consistency of restored data. If a historical (that is, not the most recent) revision of a record is restored, the system does not allow modifications to the historical revision. Only the most recent revision of a record is available for rework or reprocessing when restored to the original database. This meets FDA 21 CFR part 11.10e requirements such that changes to records shall not obscure previously recorded information.

Retention

Data retention simply means the management of stored data. FDA 21 CFR part 11.10c requires protection of records to enable accurate and ready retrieval throughout the record retention period. Retention of records may last anywhere from ten to thirty years. Sufficient means to archive and restore records is critical.

Archival of records protects data from hardware failures and honest mistakes, as well as from viruses and other malicious activity. Computer systems operating in compliance with GMP, cGMP, GAMP may be associated with raw data in a variety of forms, namely magnetic media (tape, cassette, cartridge, hard/floppy disks), optical disks, computer or instrument printouts and film or fiche copies.

The Cerity storage management system supports data retention by requiring that all data objects use the common interface objects to store and organize raw data. The Cerity storage management system supplies an object model that describes the partitioning and relationships of all data saved in the database. All Cerity applications must comply with this model.

System obsolescence can force a need to migrate electronic data from one system to another. The migration process must validate the raw data to ensure integrity. When migration of raw data is not practical, the Cerity NDS lets the client transfer

the raw data to another medium prior to any destruction of the original electronic records. The Cerity NDS also validates that the electronic records are an exact copy of the original raw data.

Import/Export Specifications

Generating a raw data file compatibility path for more than ten years requires the ability to store raw data in a format that can withstand the obsolescence factor in today's computer generated technology.

The Import/Export component of the Cerity NDS provides an abstract data exchange that can import or export samples, worklists, sequences, and results from a LIMS system.

Import Samples or Sequences The Cerity NDS provides a user interface to import samples or a sequence. The import component requires an XML file and a generic XML DTD (Document Type Definition) to set up a protocol for the data transfer format that defines what can be imported into the Cerity NDS. After the user sets up the data transfer format, the user can complete the **Import Sample XML Data** dialog box to import samples or a sequence (see the online help).

Record Protection

The integrity of data for the Cerity NDS requires strict management by the administrative agent. The configuration and support of traceability of events that change an object in any way, that holds both administrators and users accountable and responsible for actions initiated, is crucial to the integrity of the data and management of the laboratory. The Cerity NDS captures, processes and stores data as part of an automated process in accordance with the principles of GMP guidelines.

For shared data integrity, the Cerity administrative agent manages the following areas for regulatory compliance:

- Object Access Synchronization
- Data corruption
- Device checks

Object Access Synchronization (Locking)

Locking refers to a mechanism for synchronizing access to data objects. Locking meets the FDA 21 CFR part 11.10f requirement to implement system checks to enforce permitted sequencing of steps and events. Locking assures proper serializing when a user accesses an object, such that user interactions with the object occur in an acceptable order.

If two users attempt to access an object, locking controls the order and level of permitted access to the object. The first user that accesses the object gets the lock; the other user's request is blocked. The locking user completes accessing the object and unlocks the object. The blocked user can now request the object. This prevents both users from simultaneous or interleaved access to the member functions of the object, which could cause inconsistent results.

Locking has two responsibilities:

- Coordinate access to shared objects in real time
- Control the modification of an object stored in the database

Locking provides a cooperative synchronization of access to an object and is not a security mechanism. Locks must be short-term. A user should lock an object for no longer than needed for access synchronization and integrity. If a user has access to an object, the user can access the object provided they participate in the object's locking requirements.

Device Checks

FDA 21 CFR part 11.10h states, “Use of device (e.g., terminal) checks to determine, as appropriate, the validity of data input or operational instruction.” Device checks refer primarily to manual data entry to validate the source of data input and qualification of chromatography equipment linked to a Chromatography Data System (CDS). Cerity implements the following device checks:

- Tracks the instrument serial number and firmware revision when supported by the instrument model, and supports the use of column identification tags to trace and record analytical column information for the Agilent 1100 HPLC

- Marks red any fields with missing values for verification of correct format or range of numeric parameters and cell locks that are dependent on proper setup of data input
- Carries out a calibration test of the analog-to-digital (A/D) converter used to acquire data from the signal detector output
- Carries out a qualification test of chromatograph parameters that include pump flow rates, autosampler injection, column heater temperature, and detector wavelength accuracy
- Enables chromatographic performance to be included as part of an automated analysis that implements limit checking and includes system suitability to confirm that the analytical run is acceptable
- Provides a system of roles and rights, set up in Cerity Software Administration, to do tasks that limit user access to tasks performed in the laboratory
- Provides automatic low-level, mid-level, and high-level operation qualification (OQ) and performance validation (PV) tests that Agilent Technologies support runs on the Cerity NDS
- Logs user input automatically, date and time stamped, through Cerity auditing, and can make the user qualify their actions with an electronic signature

Device checks are a way to maintain accurate operation of equipment and prevent entry of improper data to confirm the validity of source data entered into the Cerity NDS. The Cerity Software Administration application ensures that only qualified users perform tasks in the laboratory. OQ/PV tests ensures that safeguards for guarding of shared data integrity work properly and the equipment performs within industry standards. The Cerity NDS continues to safeguard manual data entry with the visual cue of a red text box that both warns and forces the user to enter the data correctly. Cerity also blocks functions that the user is not authorized to use and makes options unavailable based on user choices in the application. Cerity implements limit checks and includes system suitability calculations to facilitate analysis and review of sample data for accuracy. Finally, the Cerity NDS automatically logs every task the user

performs to track user input. The Cerity system stores the hostname of the originating client PC when an electronic record is created or modified so that the user can easily isolate areas where improper data input may have occurred.

Error Handling

The complexity and distributed nature of the Cerity NDS makes error handling and status return a critical responsibility for Cerity applications and utilities for guarding of shared data integrity. The Compliance application that includes IQ for proper installation and OQ/PV for hardware and software tests ensures:

- Proper functioning of fundamental operations that are necessary for a task to function
- Automatic data verification for sequencing runs that check the sequencing engine, calibration calculations, and recalibration
- Interactive verification of software administration modules
- Interactive verification of archive, delete, and restore tasks

Errors that can occur during the operation of the Cerity Network Data System appear in the logbook that applies to the operation or task. All other errors appear as a pop-up window that describes error conditions when the user cannot bring the system back to a new condition. Report these errors to the Agilent Technical Support together with any error code number that appears in the pop-up window.

Locking of Results

Results (single samples or sequences) can be set to a read-only state at the approval stage by a user with the relevant rights. The locked result can be reviewed, but cannot be modified until it is unlocked. Only users with the relevant rights can unlock the result for modification; any attempt to unlock a locked result by a user without the relevant rights results in the display

of an error message. All lock and unlock activities are registered in the audit trail. The revision number of the result is not affected by the lock/unlock activity.

Compliance — IQ/OQ

Regulatory compliance controls for closed systems look for evidence of factory testing for individual pieces of hardware along with software validation documents that show test plans, test results, and source code. Agilent Technologies provides a Declaration of System Validation for all products. The Declaration of System Validation documents that the product was developed, tested and successfully validated according to the Software Life Cycles, and Quality Manuals followed by the divisions of Agilent Technologies. Agilent Technologies operations have been certified according to international standards such as ISO 9001 and have maintained their certification status for many years.

Installation Qualification (IQ)

IQ ensures that new Agilent hardware and software is installed correctly from the moment it is unpacked until the moment it is ready to use - documenting the completeness of shipping, the operating environment, and the components of the system.

Recommended Times

- Installation of new hardware or software
- Repair of a major piece of hardware
- Change to the software so that system security, data integrity, or administrative controls are affected
- Periodically to confirm system configuration

Features

- Verifies and documents a complete shipment
- Includes detailed installation checklists and specifications

- Checks the integrity of installed software and hardware against known standards

Operational Qualification/Performance Verification (OQ/PV)

After an IQ, an OQ/PV is performed to verify and document the ability of Agilent hardware or software to meet specified performance criteria. OQ/PV involves a comprehensive test of the complete system using established conditions and known sample characteristics. The key benefits of this procedure are ensuring the basic accuracy and precision of the instrument or system and uncovering any potential problems before they occur. Agilent recommends that preventive maintenance be performed on your instrument prior to an OQ/PV.

Recommended Times

- Installation of new hardware or software
- Repair of a major piece of hardware
- Change to the software so that system security, data integrity, or administrative controls are affected
- Periodically to verify system performance on the basis of use and risk tolerance (typically every 12 months)

Features

- Uses measuring equipment and standard kits that meets national and international standards
- Verifies and documents a system's ability to satisfy criteria that meet cGMP, GLP, ISO 9000, ISO 19075, and other regulatory standards
- Automatically creates samples and methods

Available Qualifications

The following qualifications are available from Cerity NDS for Pharmaceutical QA/QC.

- Agilent Cerity Software IQ
- Agilent Cerity TSE Thin Client IQ & OQ/PV
- Agilent Cerity Software OQ/PV
- Agilent Cerity Instrument Communication OQ/PV
- Agilent 1100 Series HPLC IQ
- Agilent 1100 Series HPLC OQ/PV
- Agilent 35900E ADC IQ
- Agilent 35900E ADC OQ/PV
- Agilent 6890 GC IQ
- Agilent 6890 GC OQ/PV
- Agilent 6850 GC IQ
- Agilent 6850 GC OQ/PV
- Waters Alliance HPLC IQ
- Waters Alliance HPLC OQ/PV

Features

- Example protocols for pre-qualification approval
- Protocols that include system details at the time of the qualification and clearly describe the preparation for and execution of configuration-specific tests
- Test automation that increases efficiency and minimizes operator error
- Reports for each automated test that include the results and a pass/fail status
- Certificates for each qualification that includes a summary of the test results and the overall qualification status
- Secure storage of protocols, reports, and certificates so that they can be regenerated if required
- Storage of key qualification information that can be recalled for the reoccurring periodic qualifications

Delivery

The qualifications listed above must currently be ordered as services from Agilent Technologies and are delivered by operators who are trained and certified by Agilent.

Failure Resilience

Acquisition Buffering

Cerity acquisition buffering ensures that, if the network fails, resulting in a loss of connectivity to the database, there is no loss of data for sequences that are already running. Acquisition is completed, but data analysis activities are suspended. The acquired data, including meta-data (for example, logbooks) is stored in a buffered area in the acquisition controller, and a special worklist status flag is attached to indicate that the sequence is partial due to a network failure.

When the network connection is restored, the data is spooled to the database and can be retrieved and reprocessed using normal Cerity facilities. This results in an additional revision being produced for these tests.

Clustering

The clustering concept organizes two or more computers to work together to provide higher availability and reliability than can be delivered by a single system. When a failure occurs in a cluster, resources are redirected, and the workload is redistributed. The user experiences only a limited failure while the redirection and redistribution are completed.

Principles of Clustering

The cluster provides high availability by making application software and data available on two or more independent servers (nodes) linked together by a private network. Should one of the servers fail, the workload of the failed server is switched automatically to another server in the cluster by the *failover* process.

Cerity supports **Microsoft Cluster Server (MSCS)** and **Oracle Fail Safe (OFS)**. Cerity system services do not interact directly with the operating system to get and react to cluster events but, through the MSCS, respond to a planned or unplanned cluster failover. Cerity services running on acquisition controllers and clients automatically reconnects to the database server once the failover is completed; they effectively connect to the cluster. Failover delay has been measured at less than one minute but in-flight transactions at the time of the failover are lost. For data processing, these in-flight writes triggers the acquisition buffering mentioned above.

Clustering Configuration

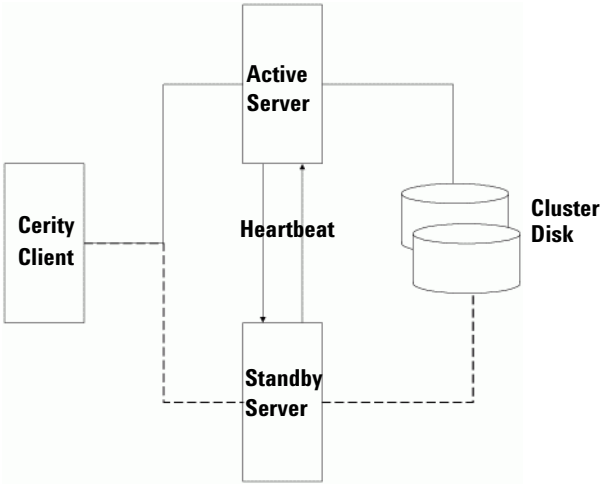


Figure 10 Cerity Clustering

With the **MS Advanced Server**, support for clustering is provided at the operating system level. In the context of Cerity, the active-passive mode (also referred to as Active-Standby) is used.

In a Cerity cluster, each server system is backed up by a server system that is identical in both hardware and software (see Figure 10). Both servers are networked to the Oracle database, which is stored on an external disk array (the *cluster disk*). The two server systems are in constant contact to check availability

(the *heartbeat*). If the main server fails, the *failover* process switches the application to the backup server, which takes over the workload until the main server comes back on line. Availability is interrupted only for the time it takes for the *failover* process to make the switch.

Traceability

Traceability of electronic records in a closed system requires authentication. A computerized audit trail of a laboratory's data system provides necessary evidence of who did what to a record and when. FDA 21 CFR part 11.10e requires an audit trail for "actions that create, modify, or delete an electronic record" and that it be "secure, computer-generated, time-stamped."

An audit trail helps to manage, control and view the history of changes made to the Cerity NDS. For example, audit trails become essential when the client needs to accept or reject results. The Cerity electronic results approval process of Review Rights of users and Acceptance Levels for results are set within the Cerity Software Administration application (FDA 21 CFR part 11.10f). Results for the Cerity NDS operate under a strict review flag set by the Agilent GMP license requirements (FDA 21 CFR part 11.10e c73). The deletion of records is another example of operational system checks enforced by the Cerity NDS. Any record deleted must already be archived and the user's rights to delete records is part of the audit trail set up in the Cerity Software Administration application.

Auditing

Tracking the audit trail to a user provides a clean tracking mechanism to inspect and review decisions made from electronic records. For example, the method logbook tracks all changes applied to a method. Supporting information, such as method logbooks, sequence logbooks, system logbooks, and maintenance logs are necessary to verify the validity of raw data or to reconstruct an analysis stored in the datastore. It is crucial that the audit trail created by the Cerity NDS act independently of the operators. All auditing on the Cerity NDS becomes permanent to avoid tampering of recorded activity (FDA 21 CFR part 11.10e c73). The Cerity NDS provides for the

retention of full audit trails and shows all changes to the data without obscuring the original data (FDA 21 CFR part 11.10e).

Description	Comment	E-Sig	Timestamp	Source	Host
Change the 'Weighed Amount' from '0' to '15' for the 'biphenyl' in the Calibration.	Changing lab procedure	Signed	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Change the 'Compound Calibration Type' from 'RF from Compound' to 'None' for the 'diethylphthalate' in the Calibration.	Changing lab procedure	Signed	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Set the 'Amount Unit' to 'ug' for the 'dimethylphthalate' in the Calibration.	Changing lab procedure	Signed	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Change the 'Amount' from '0' to '10' for the 'dimethylphthalate' in the Calibration.	Changing lab procedure	Signed	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Change the 'Weighed Amount' from '0' to '10' for the 'dimethylphthalate' in the Calibration.	Changing lab procedure	Signed	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Removed Compound New Compound3 , with Expected Time 3.66259869982296 , on Signal VWD1 A	Changing lab procedure	None	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Change the 'Compound Name' from 'New Compound2' to 'biphenyl' for the 'Compound' in the Calibration.	Changing lab procedure	None	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Change the 'Compound Name' from 'New Compound1' to 'diethylphthalate' for the 'Compound' in the Calibration.	Changing lab procedure	None	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Change the 'Compound Name' from 'New Compound' to 'dimethylphthalate' for the 'Compound' in the Calibration.	Changing lab procedure	None	25/09/2001, 20:09:48	AGILENT\MuskService	MUSKTSTPC14
Added Compound New Compound3 with					

Figure 11 Method logbook

Traceability implies tracking activity on the system for audit functionality. The Cerity NDS provides for the following implementations of traceability:

- **System wide activation** - A user's actions require authorization by the system.
- **Electronic Signature** - If a user's actions require additional authorization for auditing, a computer record in electronic form identifies and authenticates an individual equivalent to their handwritten signature such as a user name and password.
- **Object instance activation** - For each object instance in the database, the system manages an independent audit flag. A modification made to a particular object instance requires auditing. For example, if a user creates a new method, the system manages an independent audit flag.
- **Per user (or role) activation** - For each user (or role), the system manages an audit flag. A modification made by a specific user (or any member of the specified group) to any object in the system requires auditing.

When the system prompts the user for an audit reason, the **Save Changes to the Database** dialog box appears:

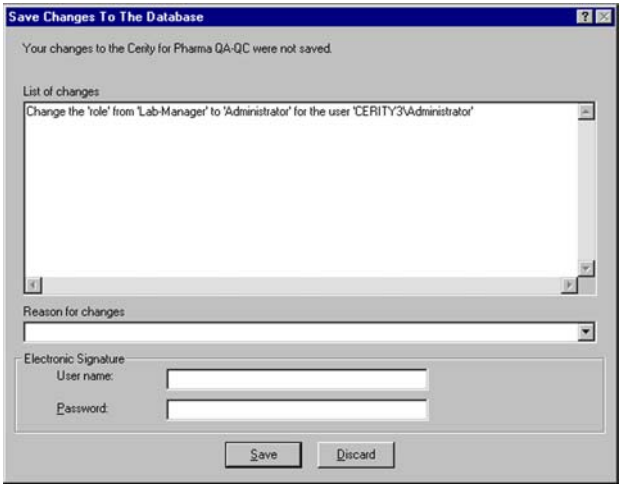


Figure 12 Audit Reason with Electronic Signature

During configuration of the **Auditing** node in the Cerity Software Administration application, the session locks the audit trail system configuration until the administrator completes their changes and releases the object back to the system. All changes are saved automatically to the default database. The datastore stores all recorded changes to objects and other related system activity required for auditing that meet cGMP/GLP requirements including the Electronic Signature of the user (FDA 21 CFR part 11.70 and 11.200). Additional information recorded in the logbooks about system activity and errors is also recorded.

Audit Trail and Logbook Administrative Tasks

To create an audit trail for specific user tasks, the Cerity administrator must:

- Provide a panel with a list of reasons
- Add or delete the list of audit reasons available to the user

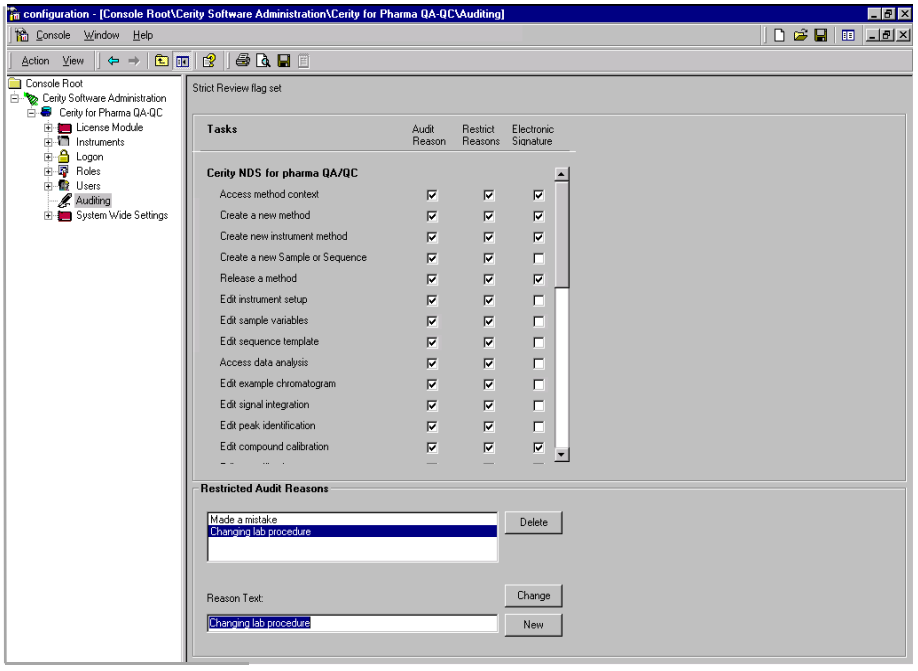


Figure 13 Auditing

The Cerity administrator can choose a task from the Cerity NDS for Pharmaceutical QA/QC list to configure the task for predefined audit reasons, a restricted reason and include an Electronic Signature to perform the task (FDA 21 CFR part 11.10g).

NOTE

The list of role tasks is not identical to the list of tasks that require an audit reason. The Cerity NDS provides configuration for both role tasks and tasks that require audit reasons and electronic signatures.

Audit Features

Viewing the object's audit trail, archiving the audit trail with the object, and adding a new entry to the object's audit trail, are all functions fundamental to an audit trail.

The audit trail captures all activity related to creation, modification or deletion of electronic records in the system (FDA 21 CFR part 11.10e c75) including:

- Instrument activity
- Data acquisition
- Data processing
- Errors
- Warnings
- Pass/Fail results for tests against specifications
- System configuration
- Changes to Access Control Lists (ACL)

The Logon, Auditing, and System Wide Settings nodes in the Cerity Software Administration application provide a shortcut menu to access the Cerity Systems logbook. The user can right-click these nodes from the selection tree and click Display Logbook. The Logbook Viewer appears and displays the Cerity System logbook. The tree view displays the list of all logbooks available in the database (FDA 21 CFR part 11.10e).

The Logon, Auditing, and System Wide Settings nodes share the same logbook. Other logbooks include:

- License logbook
- Instruments logbook
- Roles logbook
- Users logbook
- Method logbook
- Sample logbook
- Sequence logbook
- Archive logbook
- Restore logbook
- Delete logbook
- Compliance test logs for IQ/OQ/PV
- Windows NT Event log

The acquisition servers do not have a logbook because the events write automatically into the instrument logbook.

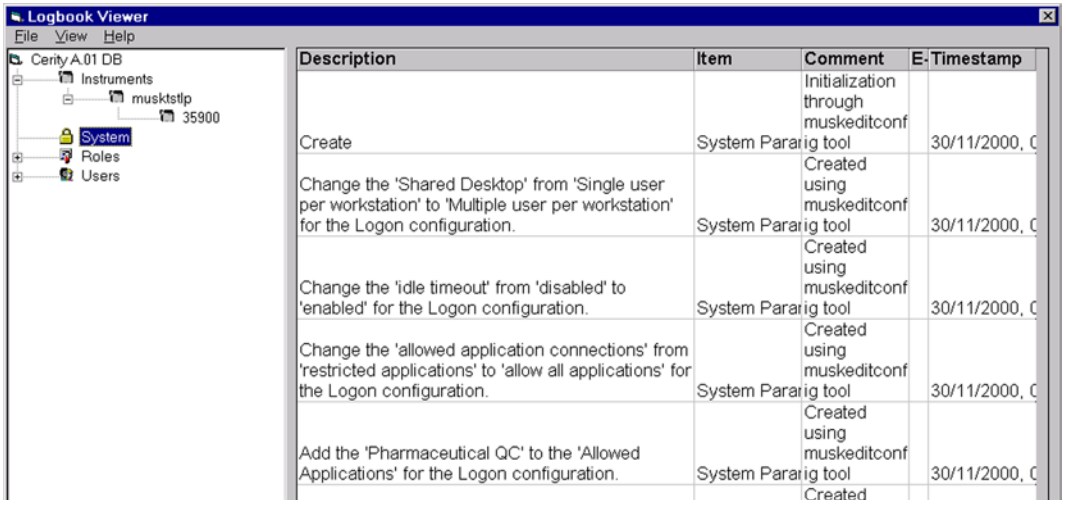


Figure 14 System logbook

Revision Control

The Cerity NDS provides two mechanisms for auditing.

- Audit logs
- Data object revisioning

FDA 21 CFR part 11.10e requests that all changes to existing records need to be documented, regardless of the reason, to maintain a complete and accurate history. The Cerity NDS provides audit logs that record all events and changes to data including date and time, audit reasons, and electronic signature. For example, every time the user changes the current method run on a sample, the Cerity system automatically records detailed information in the appropriate audit trail logs.

Data object revisioning provides automatic *internal retention* of events and changes to data. The Cerity NDS keeps a history of each data object that is changed and then saved in the datastore (FDA 21 CFR part 11.10e c73).

Data object history

The Cerity NDS maintains the history of each data object with a revision number (FDA 21 CFR part 11.10e c75). The revision number lets the Cerity system track the revision cycle of a particular data object. The identification scheme of the data object maintains the integrity of each data object. The internal identification scheme or data object triple is a field combination of:

- Object Global Unique Identifier (GUID)
- Revision number
- Object type

The GUID provides a unique identifier which is associated with a particular data object. The revision number is a long integer that starts from one for the initial revision and is incremented by one for each succeeding revision. The Type refers to what kind of data object it is, such as a Sequence, Sample, Method, or Logical Instrument. Older revisions of a data object are not available for editing and as such cannot be part of the current revision of the data object.

Some data objects, such as a sample or method, have both an internal identification and an external identification. The external identification appears as the method name or sample name.

Object Revision Properties

Any Cerity application can only edit the current revision of a data object. Retrieval of a data object for editing by a Cerity application that is not the current revision returns an error.

Retrieval of earlier revisions is for reference only. Reuse of an earlier revision requires a new object identification. To reuse an earlier revision, you make a copy of the earlier version and then the system provides the object with a new internal object

identification. For example, if you use an existing method, you must give the new method a different name. The new name provides an external identification that corresponds to the internal object identification.

Electronic Signatures

Electronic signatures are controls designed to ensure authenticity, integrity, and confidentiality of electronic records for closed computer systems. They ensure that the signer cannot refute the signed record. FDA 21 CFR part 11.50 requires signed electronic signatures contain the following information:

1. The printed name of the signer
2. The data and time when the signature was executed
3. The meaning associated with the signature

The Cerity NDS automatically records the name of the signer and the data and time in the appropriate logbook. The logbook information establishes the meaning or context of the electronic signature. Signatures that appear in the logbook are stored as part of the electronic record.

FDA 21 CFR part 11.70 requests that electronic signatures must be verifiably bound to their respective records to ensure they cannot be deleted, copied or transferred to falsify a record. All data entry that requires an electronic signature for the Cerity NDS is computer generated, authenticated, time-stamped and stored in a logbook or log file.

FDA 21 CFR part 11.200 requests a user who executes a series of electronic signatures during a single, continuous period of controlled access to the application, the first signing shall be executed using all electronic signature components; subsequent signings shall be executed using at least one electronic signature component by the user. The Cerity NDS requires the user to enter all their electronic signature credentials to log on to the application. Subsequent signings are also executed using all electronic signature credentials. The Cerity NDS uses the

Windows operating system user identification and password policies for Cerity electronic signature credentials. Use of an electronic signature by a Cerity user requires the collaboration of the Cerity administrator to set up their user identification code and password in the Cerity Software Administration application. Only the Cerity administrator can access the Cerity Software Administration application.

FDA 21 CFR part 11.300 requires controls for identification codes and passwords to ensure user security and integrity. Controls must be used to maintain the uniqueness of each combined identification code and password. The FDA needs assurance that the identification code and password issuances are periodically checked, recalled, or revised:

- Laboratories can manage identification code and password policies in the Windows operating system for the Cerity NDS.
- Laboratories can use encryption policies for passwords in the Windows operating system to prevent unauthorized use of passwords.
- The Windows operating system supports defined account lockouts after a specified number of failed attempts to log on to the system.
- Password aging can be set up in the Windows operating system to keep users on the system current, and ensure that unused identification codes and passwords are recalled or revised.

Reporting and Reviewing of Meta-data

Method meta-data, for example, instrument setpoints, data analysis parameters and report templates, are available for printing both to the screen and to a printer. The following report templates are available for viewing and printing method meta-data:

calibration.html	Calibration settings and the compound table
identification.html	Identification settings and the identification table

instrument.html	Instrument setpoints
integration.html	Integration initial events table
limits_mi.html	Single injection and multi-injection limits tables
limits_seq.html	Summary groups limits tables
main_log.html	Method logbook
method_description.html	Method description
quant.html	Quantitation settings for compounds and unidentified peaks
report.html	The print status of the available report templates
seq_method.html	All available settings for the sequence method
seq_vars.html	Values of sequence sample variables
sequence_template.html	Sequence sample table, sequence sample entry table and sample amounts table
smp_vars.html	Values of single sample variables
UVConfirmation.html	UV confirmation settings for each compound
UVConfirmation_spectrum.html	UV confirmation settings, including reference spectrum, for each compound
UVPurity.html	UV Purity settings

For a printout of the complete set of method parameters and setpoints, you use the template seq_method.html.

History Viewer

In order to ensure traceability of method revisions and reprocessing of results, all revisions are tracked, and previous revisions can be accessed in the **Old Revisions** folder for the method or result in the selection tree.

Methods

Old revisions of methods contain all method and data analysis setpoints, which can be accessed from the selection tree in the same way as the current method's setpoints are accessed. The setpoints for the old revisions of the method can be viewed, but the record is locked, and the setpoints cannot be edited.

You can check all method setpoints for the selected old revision in the method printout.

Results

You can access the previous revisions of results for single samples or sequences from the selection tree in the same way as the current result is accessed. The old revisions of the results can be viewed, but the record is locked, and the result cannot be edited.

Old revisions of results can be printed in the same way that the current result is printed.

How the Cerity NDS meets CFR 21 Part 11 requirements

Table 1 Procedures and Controls for System Security and Data Integrity

FDA CFR 21 Part 11 requirement	Cerity meets requirements by
21 CFR part 11.10a - Provides validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.	**a** Qualification services available for hardware and software, page 28 **b** Agilent Technologies Software life cycle, page 28 **c** Division Quality System, page 28 **d** Error handling, page 35
21 CFR part 11.10b - Assures the ability to generate accurate and complete copies of records.	**a** Cerity Archive and Restore application, page 29 **b** Meta-data, page 29
21 CFR part 11.10c - Protection of records to enable their accurate and ready retrieval throughout record retention period.	**a** Strict management of electronic records, page 29 **b** Retention of data, page 31
21 CFR part 11.10d - Limiting system access to authorized individuals	**a** Authorized access, page 22 **b** Authority checks, page 26
21 CFR part 11.10e - Use secure, computer-generated, time stamped audit trails to record operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information.	**a** Cerity audit trails, page 44 **b** Logbooks, page 44 **c** Revision control, page 49 **d** Archive, restore, and delete of electronic records, page 29
21 CFR part 11.10e Comment 73 - The audit trail must be created by the computer system independently of the operators.	**a** Cerity strict review, page 22 **b** Cerity audit trails, page 46 **c** Revision control, page 49
21 CFR part 11.10e Comment 75 - All changes to existing records need to be documented, regardless of the reason, to maintain complete and accurate history, to document individual responsibility, and to enable detection of record falsification.	**a** Archive, delete, and restore of data, page page 28 **b** Cerity audit trails, page 46 **c** Revision control, page 49
21 CFR part 11.10f - Use of operational system checks to enforce permitted sequencing of steps and events.	**a** Level required to acceptance or reject results, page 26 **b** Data must be archived prior to deletion, page 30 **c** Object access synchronization (Locking), page 33

Table 1 Procedures and Controls for System Security and Data Integrity (continued)

FDA CFR 21 Part 11 requirement	Cerity meets requirements by
21 CFR part 11.10g - Authority checks to ensure only authorized individuals use the system, electronically sign a record, alter a record	**a** Authorized access, page 22 **b** Authority checks, page 26 **c** Multiple users on a system, page 24 **d** Cerity audit trails, page 46
21 CFR part 11.10h - The system must implement device checks to determine the validity of the source of data input.	Device checks, page 33
Electronic Signatures	
Controls for Open Systems	
21 CFR part 11.30a	
Signature Manifestations	
21 CFR part 11.50a - Signed electronic records shall contain the following information: • printed name of signer • Local date and time when the signature was executed (c101) • Meaning of the signature. This does not require lengthy explanations (c105)	Cerity electronic signatures, page 51
21 CFR part 11.50b - The items in 11.50a are subject to the same controls as for electronic records and shall be included as part of any human readable form of the electronic record.	Cerity electronic signatures, page 51
21 CFR part 11.70 - Electronic Signatures must be verifiably bound to their respective records to ensure they cannot be deleted, copied or transferred to falsify a record.	**a** Cerity electronic signatures, page 51 **b** Cerity audit trails, page 46
21 CFR part 11.200(1) - Electronic signatures not based on biometrics shall employ at least two distinct identification components such as an identification code and password. 21 CFR part 11.200i - When an individual executes a series of signings during a single, continuous period of controlled system access, the first signing shall be executed using all electronic signature components; subsequent signings shall be executed using at least one electronic signature component that is only executable by, and designed to be used only by the individual.	**a** Cerity electronic signatures, page 51 **b** Cerity session lock, page 22

Table 1 Procedures and Controls for System Security and Data Integrity (continued)

FDA CFR 21 Part 11 requirement	Cerity meets requirements by
21 CFR part 11.200 (2) (3) - Electronic signatures not based upon biometrics shall be administered and executed to ensure that attempted use of an individual's electronic signature by anyone other than its genuine owner requires collaboration of two or more individuals.	Cerity audit trails, page 46
Controls for identification codes/passwords	
21 CFR part 11.300a - Controls must be used to maintain the uniqueness of each combined identification code and password	Cerity electronic signatures, page 51
21 CFR part 11.300b - Ensure that identification code and password issuances are periodically checked, recalled, or revised	**a** Cerity electronic signatures, page 51 **b** Windows NT logon policies, page 51
21 CFR part 11.300d -Use of transaction safeguards to prevent unauthorized use of passwords	Cerity electronic signatures, page 51
Where does the system use electronic signatures? What information does the system store for each use of an electronic signature?	**a** Cerity audit trails, page 46 **b** Cerity logbooks, page 46
Are analyses and their reports reviewed and approved in the system?	Cerity offers up to three levels of results approval. The system can be configured to enforce the sequence of review steps so that the original analyst may perform analyst review, a second person may sign off after a peer review and a third person may sign off after the final review. The accept/reject function is available to authorized users from the Cerity results review workspace, page 26
Can the system support password aging	Windows NT logon policies, page 51
Can the system support disabling or re-enabling of user accounts	The system reuses security and password policies defined by the operating system.
Can the system support account lockouts after a defined number of failed attempts to log on to the system?	Windows NT logon policies, page 51
How does the system record failed logon attempts? How does the system administrator gain access to information about failed logon attempts? How are other security problems identified, recorded, and accessed by the system administrator?	Failed login attempts are recorded in the Event Viewer.

3
Basic Concepts of Cerity for Pharmaceutical QA/QC

This chapter explains the Cerity NDS for Pharmaceutical QA/QC graphical user interface, and describes the four Views that you use when you work with Cerity.

The Cerity Workspace

The Cerity graphical user interface contains the following elements:

- The **menu bar**, in its customary position at the top of the display, contains the menus that allow you to work with Cerity. The menus are context-dependent: they change in accordance with the work you are doing.
- The **toolbars** are also context-dependent, and can be moved to different parts of the screen to suit your own preferences.
- **Context menus**, activated by a click of the right mouse button in many elements of the user interface (for example, tables, chromatograms and spectra), contain just the commands that you need to work with the element.
- The **selection tree**, on the left of the display, allows you to select individual items. It operates in a familiar way, with nodes that can be expanded and contracted. The selection tree can be resized by dragging its right border.
- The **workspace** contains the display elements appropriate to the selected item. Many of the display elements have context menus that are activated by clicking the right mouse button within the element, and most can be resized by dragging the borders.

The Selection Tree

Standard Toolbar - Contains tools for the Current View, and the "New" button.

"New" button- Used to create a method template, sequence or query.

Current View Selection - Used to select one of the four Views.

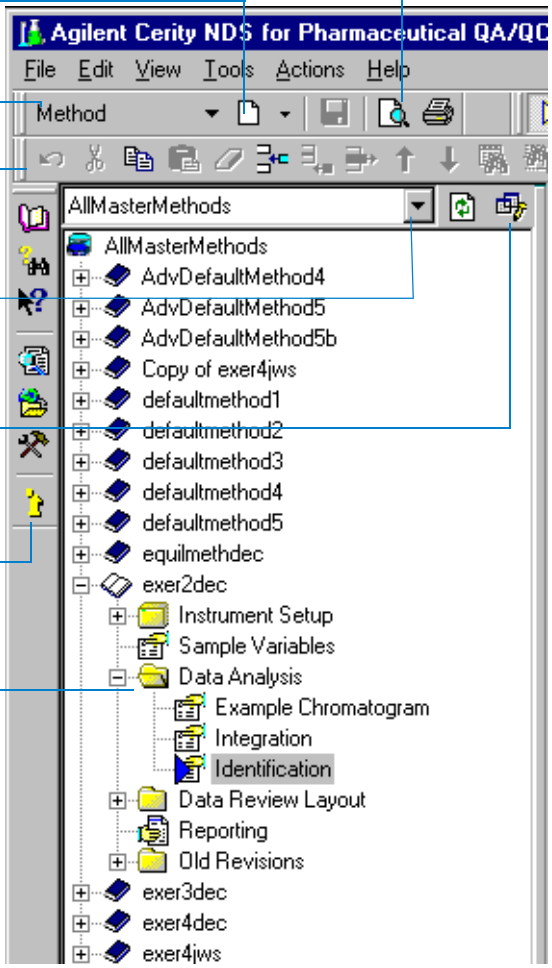
Edit Toolbar - Tools for the Edit Toolbar are always unavailable unless they apply to the workspace.

Query list - Used to select a group of samples, instruments, methods, or results from the database to display in the selection tree.

Query Wizard button - Used to define a new query of samples, instruments, methods, or results to retrieve from the database.

Help Toolbar - Used to find the assistance you need.

Selection Tree - You expand a folder, or select an item in the selection tree to set up or edit data in the workspace.

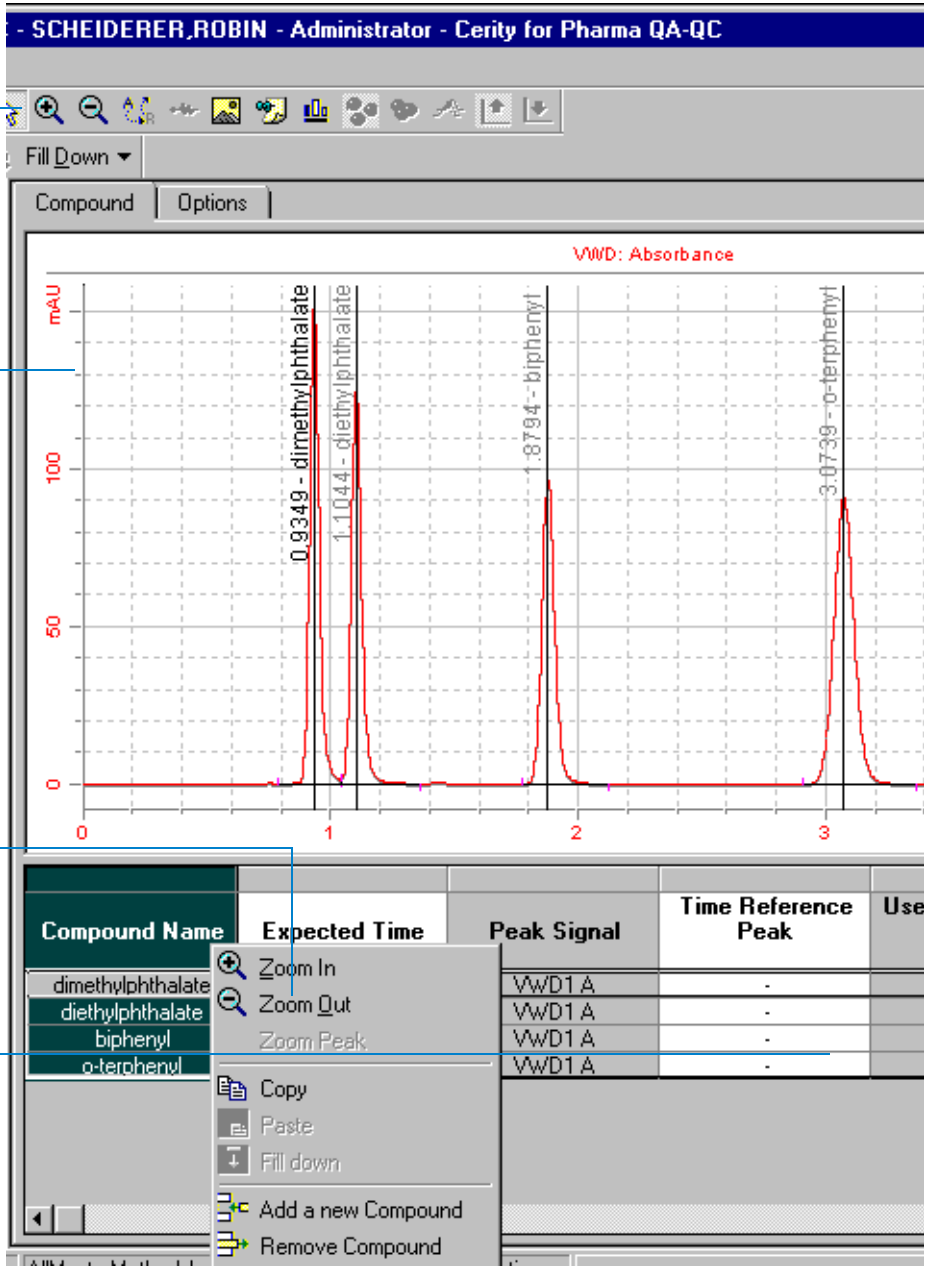


Tools or Action Toolbar - Used to modify a table or carry out a task in the workspace.

Workspace - You use toolbars and commands to display or modify tables, graphics, dialog boxes, or lists

Context Menu - You right-click a cell in the table to display a shortcut menu to modify the table.

Drop-down List - You select a cell in the table to access a list.



Online Assistance

Find assistance for each View in the following areas:

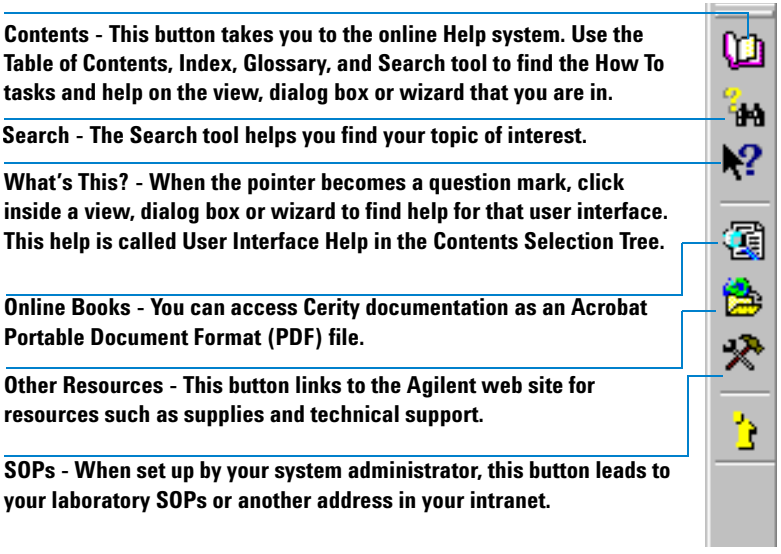
- Context-sensitive help
- Help toolbar
- Help menu
- ToolTips

Context-sensitive help

When you are working in a panel, table, dialog box or other user interface element, pressing the **F1** function key on your keyboard will generally activate the context-sensitive help, and a description of the element and its usage will be displayed. When the focus is not clear, and **F1** does not work (for example in the toolbars), the **What's This?** tool in the Help toolbar (see below) gives you access to the context-sensitive help.

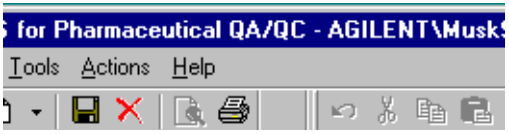
Help Toolbar

See the description of the icons on the Help toolbar below:



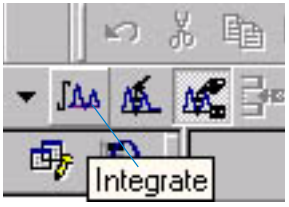
Help Menu

You can access the help from the Help toolbar on the Help menu.



Toolbar ToolTips

Move the mouse pointer over the toolbar button to display the name of the button.



The Four Views

The four views provide the interface between the user and the four primary objects types – entered samples and sequences, instruments, sample and sequence results, and methods – that the Cerity NDS stores in the database. The data consists of raw data and calculated results with all the required meta-data such as parameters, fields, formulas, and configurations.

Sample View

The **Sample** view provides a workspace to enter samples and set up sequences. You access the **Sample** view from the **Sample** option in the Current View list (see Figure 15).

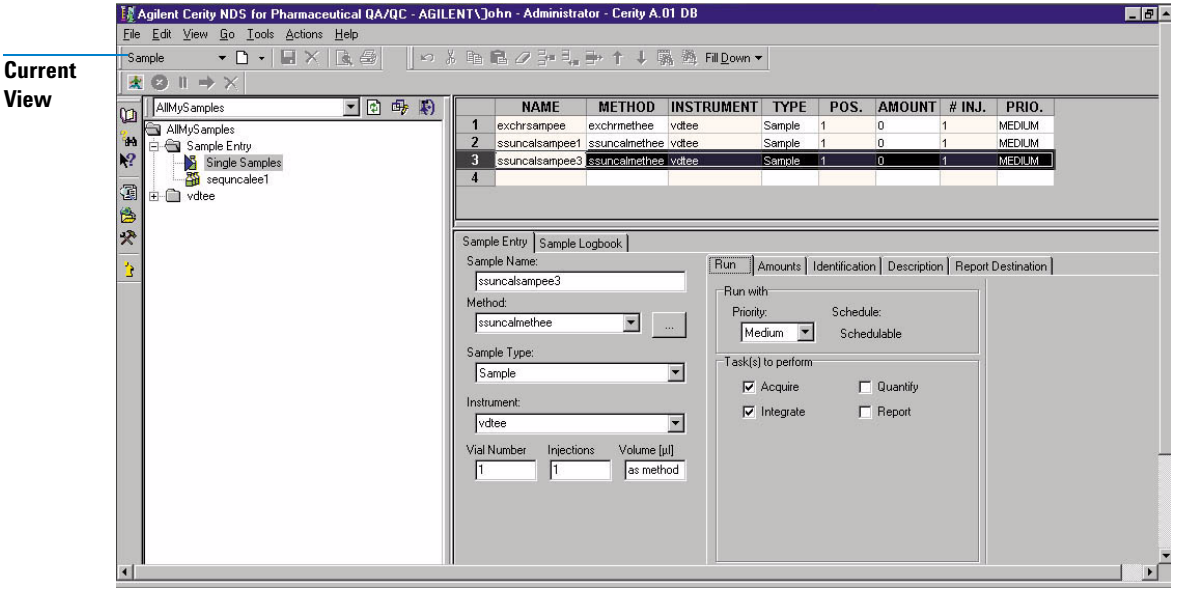


Figure 15 Sample View

Method View

The **Method** view provides a workspace to set up methods and reports. A Cerity method contains all the information necessary to acquire and process a single sample or a set of samples (a *Sequence*). You access the **Method** view from the **Method** option in the Current View list.

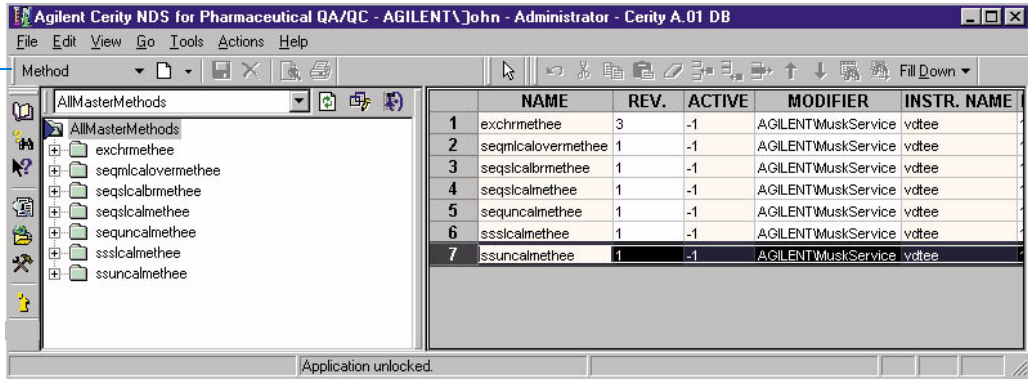


Figure 16 Method View

What you can do with Cerity NDS for Pharmaceutical QA/QC methods

Cerity NDS for Pharmaceutical QA/QC methods let you:

- Assign a method to an instrument for instrument control.
- Use your own multipliers and divisors to calculate a concentration for each sample.
- Use your own custom sample variables for custom calculations and reporting.
- Use a sequence table as a template for all your similar or repeated sequences.
- Use an example chromatogram to help you integrate and identify peaks.
- Use the UV spectra of reference compounds to confirm the identity of peaks.

- Use UV spectra to check the homogeneity of a chromatographic peak.
- Sum entire areas of the chromatogram.
- Enter variable compound amounts for each sample for single-level or multi-level calibrations.
- Quantify samples in sequences using the standard before the samples, the standards before and after the samples or all the standards in the sequence.
- Run samples with a method containing already existing response factors, or run sequences whose sample quantitation is updated with calibration standards in the sequence.
- Quantify uncalibrated compounds and unidentified peaks using the response factors of calibrated compounds.
- Use your own custom variables and formulas to calculate result group statistics and other calculations required in your laboratory.
- See pass/fail notations and warnings when variables and calculations are not within predefined limits.
- See any available field, variable or calculation in the result layout and in the reports.
- Use already existing system suitability variables to test performance

Use predefined report types associated with templates that you change or create to generate the reports you need.

Instrument View

The **Instrument** view provides a workspace to view the status of an instrument. You can run samples and sequences and track their run status from the **Instrument** view. You access the **Instrument** view from the **Instrument** option in the Current View list.

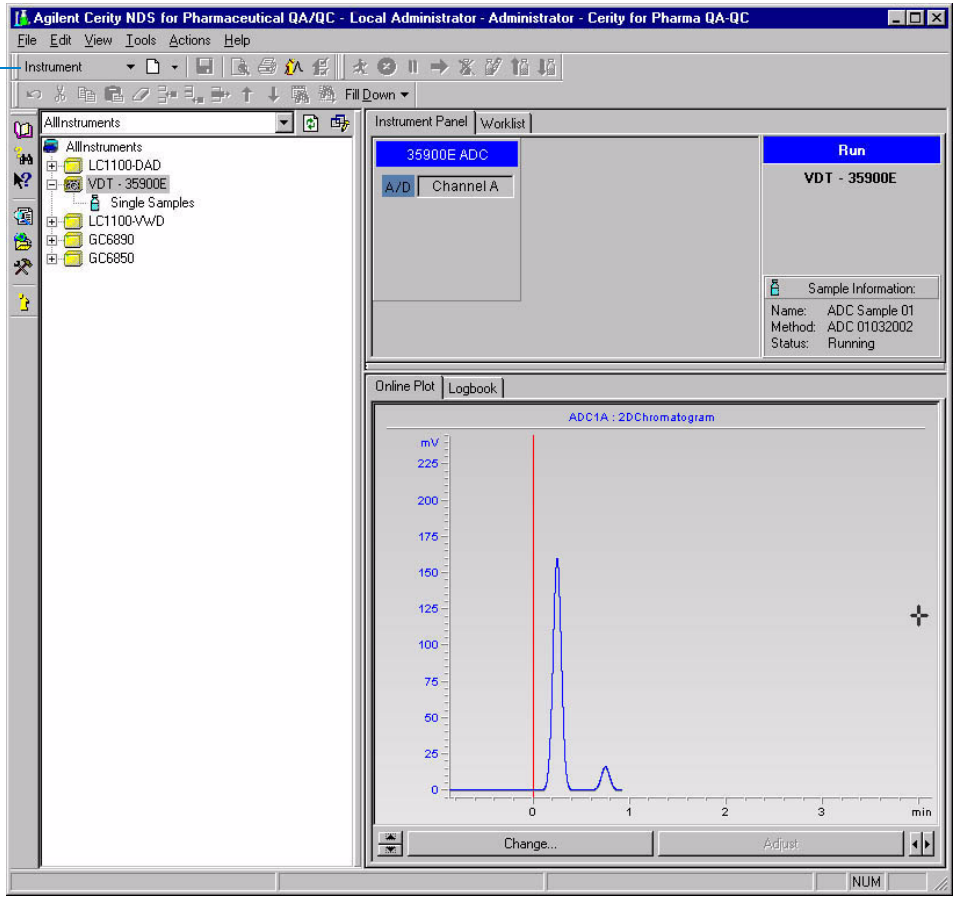


Figure 17 Instrument View

Result View

The **Result** view provides a workspace to review and reprocess samples and sequences. You access the **Result** view from the **Result** option in the Current View list.

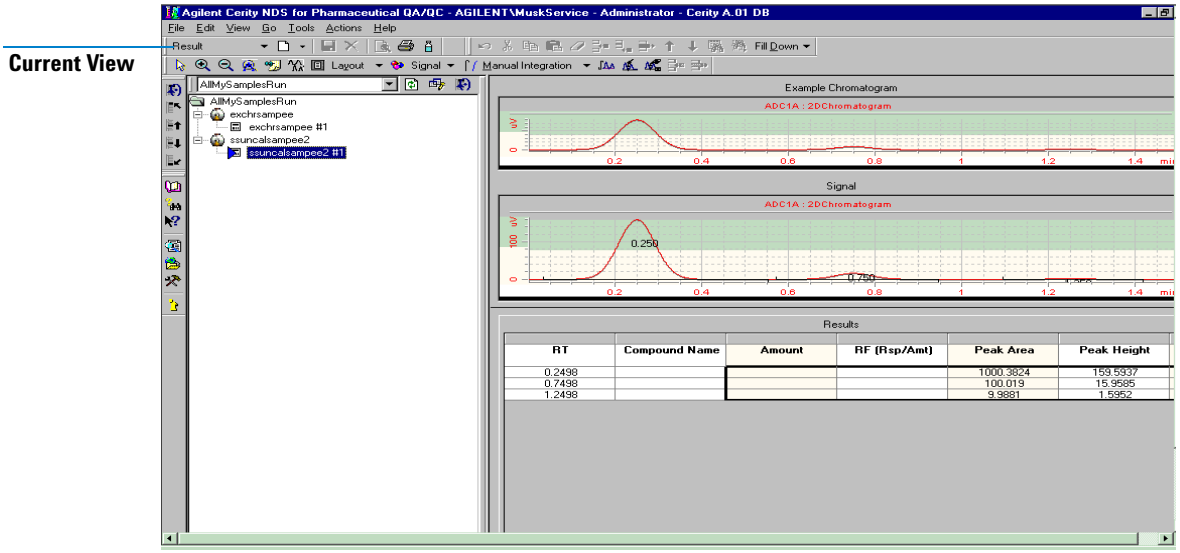


Figure 18 Result View

What you can do with Cerity NDS for Pharmaceutical QA/QC results

You can do the following tasks when you review, reprocess and approve results:

- Review the results for all the different sets of result data
- Reintegrate
- Change sample and sequence information
- Remove calibration points
- Recalculate **UV Purity** values
- Redo calculations with the method originally attached to the result

- Reprocess with the current revision of the method
- Enter values for compound and sample variable additions to the method
- Reprocess with a different method
- Import and reprocess an Agilent ChemStation or an ANDI file
- Accept or reject a result
- Mark that a result needs rework.
- Lock the result so that it cannot be modified until it is unlocked.

Reporting

Cerity NDS for Pharmaceutical QA/QC provides for easy generation of reports. Reports can include:

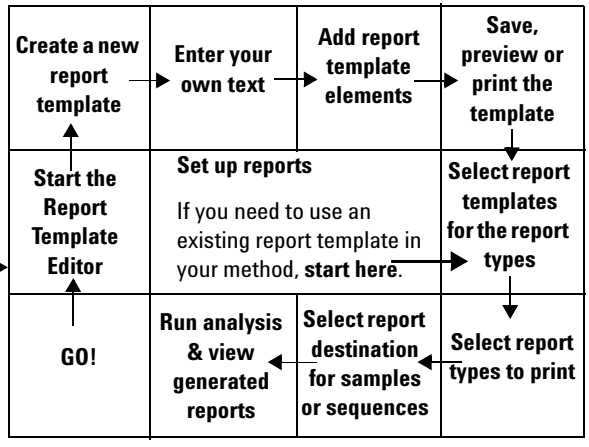
- chromatograms and images
- results and summary tables
- standard and custom calculations
- header and footer information

See the Chapter 8, "Reporting," starting on page 221 for more detail on how Cerity NDS for Pharmaceutical QA/QC generates reports.

Reports are generated after quantitation is complete for a sample. Report generation organizes and presents field and result values for types of reports using pre-defined templates. Report generation does not perform any calculations. You select the report types and templates in the method. You view or print reports in the Cerity **Report Viewer**.

The road map below shows the path for analysts and advanced users to set up, generate, and view reports. Start with **GO!**

If you need to create or edit a report template to use in your method, **start here**.



Database Searches

Query Wizard

The **Query Wizard** helps you search for the information you need. The Cerity NDS provides a **Query Wizard** for each View.

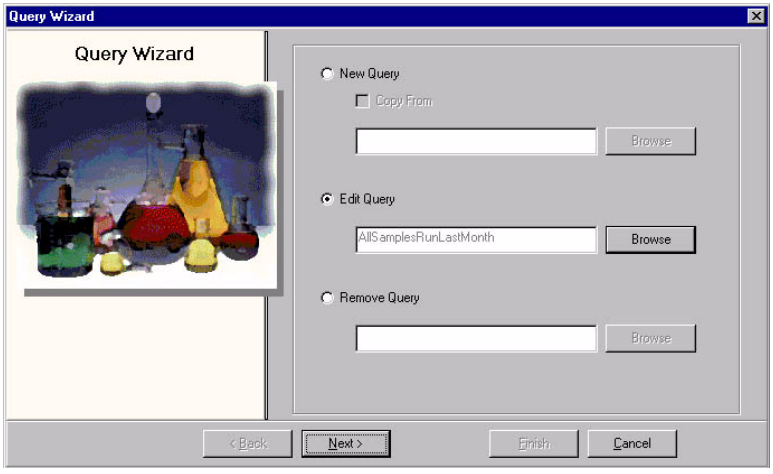


Figure 19 Query Wizard

To review or reprocess results, you must first find the results of interest.

Result queries

To view results from the database you query the system. The Cerity NDS comes with default queries to help you get started.

- Select a query from the **Query List** above the selection tree, and view results already created with the **Query Wizard** (see Figure 20 on page 73).

- If you are an advanced user, you can also define your own customized queries with the **Query Wizard**. You define queries when you set up criteria to search the database for the results that you need to view.

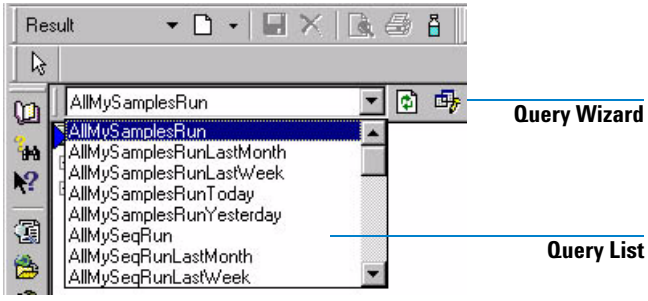


Figure 20 Query List and Query Wizard

Method queries

You also select queries to find the methods that you may have to edit.

Other queries

You can also search for a defined set of unrun samples or sequences or of configured instruments, but you would do this infrequently.

Data Handling

Data storage

The Cerity NDS *database server* stores methods and acquired data. After analysis is complete, the results are saved to the database. You can retrieve data for review using Cerity NDS query tools.

The amount of data storage needed is dependent upon:

- Number of concurrent users
- Number of concurrent instruments
- Amount of accessible data on line in the database
- Number of processed samples
- Number of reprocessing cycles (Revisions and audit trail information generated with each cycle increase the data volume.)

Saves to the Database

A Cerity NDS administrator can configure auditing behavior for specific tasks performed in Cerity NDS for Pharmaceutical QA/QC. Cerity NDS provides a form to set up audit comments and stores a log of audit entries when you make saves to the database.

Audit entries

When you save changes to a method, entered sample or sequence, or a result, or when you move from one method or sample to the next, the **Save Changes to the Database** dialog box appears. This is the form that Cerity NDS provides to enter audit comments.

You may have to review the list of changes and select a reason for the changes. An Electronic Signature that includes user name and password may be required to record the changes.

Cerity NDS lets system administrators configure which tasks in the system require mandatory audit comments and electronic sign-off.

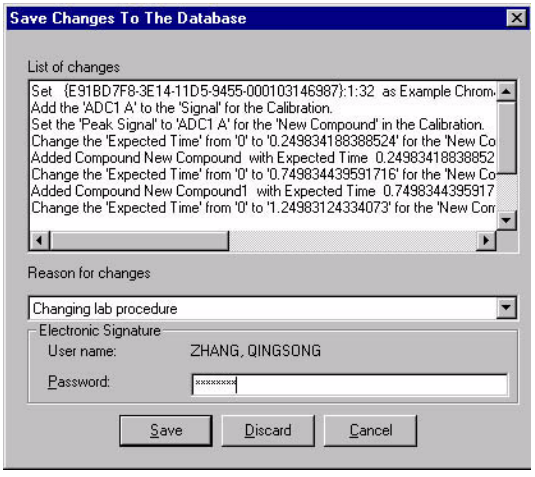


Figure 21 **Save Changes To The Database** dialog box

Audit Logbooks

Cerity NDS always maintains strict revision control and user-independent audit trails on the electronic records that it manages. All audit trails appear in the Logbooks found in the respective Views.

Methods The **Method Logbook** appears in the Description workspace for methods when you select a method in the selection tree of the **Method** View.

Single Samples The audit trail for entered, but not run, samples can be found in the **Sample Logbook**. The **Sample Logbook** appears in the Single Samples workspace for the **Sample** View or **Instrument** View.

After single samples have been run, the Logbook for each sample can be displayed in the **Result** View by clicking the **Sample Details** button on the toolbar.

Sequences

The audit trail for entered, but not run, sequences is displayed in the **Sequence Logbook** for a sequence in the **Sample** View or **Instrument** View.

After a sequence has been run, you can find the **Sequence Logbook** in the **Result** View when you select the sequence in the selection tree.

Sample or Sequence Runs

You can find the audit trail for a sample run or sequence in the Logbook in the instrument workspace in the **Instrument** View.

Figure 22 shows an example of a Logbook; the columns of the Logbooks that are not self-explanatory are explained in Table 2.

Description	Item	Comment	E-Sig	Timestamp	Source	Type	Host
Change the 'To' from '1000' to '180' for the 35900SetPoints, Channel A.	35900SetPoints, Channel A	Updated	None	06/11/2002, 08:22:37	wadlc001\demo	Audit	WADLC001
Change the 'From' from '0' to '-20' for the 35900SetPoints, Channel A.	35900SetPoints, Channel A	Updated	None	06/11/2002, 08:22:37	wadlc001\demo	Audit	WADLC001
Change the 'External State (Remote Bus Mode)' from 'ACTIVE' to 'OFF' for the 35900SetPoints, Channel A.	35900SetPoints, Channel A	Updated	None	06/11/2002, 08:22:37	wadlc001\demo	Audit	WADLC001
Change the 'Stop Time (min)' from '1' to '1.4' for the 35900SetPoints, Channel A.	35900SetPoints, Channel A	Updated	None	06/11/2002, 08:22:37	wadlc001\demo	Audit	WADLC001
Method revised, new revision: 2	---	---	None	06/11/2002, 08:22:18	wadlc001\demo	Information	WADLC001
Created.	Method	Initial configuration	Signed	06/11/2002, 08:22:05	wadlc001\demo	Audit	WADLC001
Method created by operator: Demo User							

Figure 22 Method Logbook showing all columns

Table 2 Explanation of the Logbook contents

Column Name	Example of displayed contents	Purpose
E-Sig	Signed None	Identifies actions for which an electronic signature (E-Sig) is configured and applied in the Cerity NDS Software Administration.
Source	cerity_test\sspencer Automation UserStamp	When **E-sig** is configured, the user name of the signatory is captured. When **E-Sig** is not configured, either the UserStamp associated with the action, or, in the case of automated actions, Automation is captured.
Type	Audit Information	Displays whether the details are intended for Audit or for general information purposes.
Comment	Changing lab procedure Method released	When audit reasons are configured in the Cerity NDS for Pharmaceutical QA/QC Software Administration, displays the Method Logbook showing all columns (see Figure 22).

Export of Results

The common interface object provides a uniform interface on object data regardless of its format. You can export results data to a LIMS system by “closed-loop data entry” or an ANDI data file.

4
Data Acquisition

This chapter contains an introduction to the process of acquiring data in Cerity NDS for Pharmaceutical QA/QC.

Sample and sequence entry

A Cerity NDS for Pharmaceutical QA/QC single sample or sequence contains all method, sample and sequence information needed to acquire and process data. This information is added to all run information and raw and processed data to produce the Cerity NDS for Pharmaceutical QA/QC result for the single sample or sequence.

Single sample entry

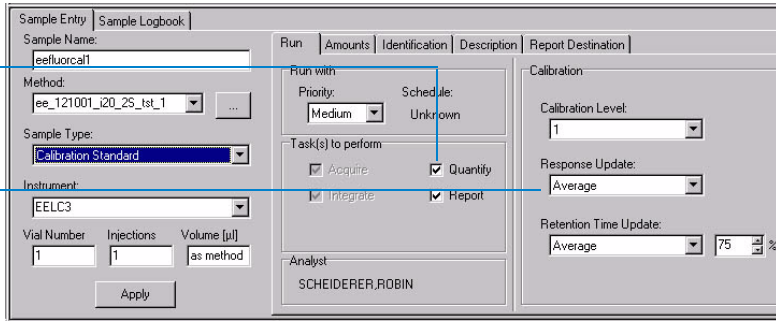
You can enter single samples in any one of three locations:

- **Sample** View – Single Samples workspace under the Sample Entry folder
- **Sample** View – Single Samples workspace under the Instrument folder
- **Instrument** View – Single Samples workspace under the Instrument folder

Whichever location you start from, the **Sample Entry** panel allows you to enter the same sample information. You click the **Apply** button to make sure that the information is entered into the system.

Run tasks to perform - You must mark Quantify in order to identify compounds.

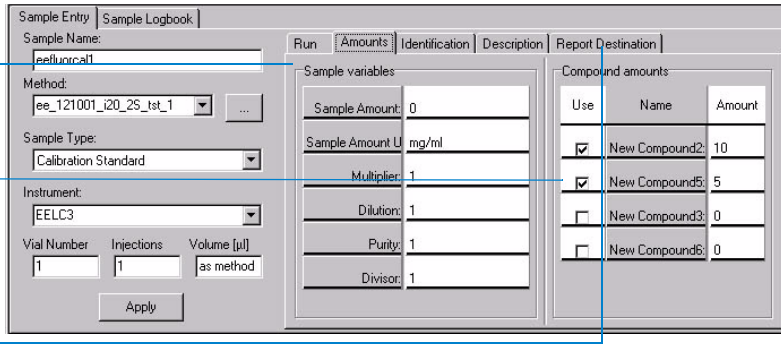
Calibration updates - You can select the level and type of update for your calibration standards.



Sample variables - You enter the sample amount and the values for any multipliers or divisors set up as sample variables in the method.

Compound amounts - If you specified variable compound amounts in the calibrated method, you can also change these amounts.

Report Destination- See "Report types" on page 113, for information to help you set up, generate, and print reports.



Sample entry saves You click the **Apply** button in the Sample Entry Workspace to enter the sample information into the sample table and the **Save** button to save entries and changes to the database.

Sample Logbook As you save your sample to the Cerity NDS database, Cerity NDS for Pharmaceutical QA/QC auditing may require you to enter an audit reason and provide your Electronic Signature before you can run the sample. A description of the changes appears in the **Sample Logbook**.

Sequence Entry

A Cerity sequence is an element of a Cerity method. It consists of a group of samples that are run automatically using the same method. The samples may be classified as **Blank**, **Sample**, **Calibration** or **QC** (Quality Control). Each sample in the sequence is entered as a line in a **Sequence Table**; the lines in the table are run sequentially when the sequence is started.

New sequences You use the **New** button to create new sequences.

After you create a sequence, you can enter sequence information in three places:

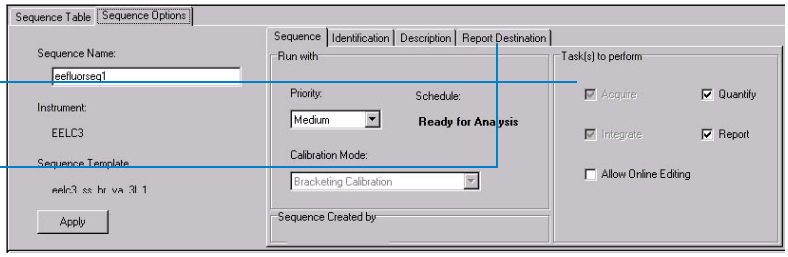
- **Sample** View under Sample Entry

- **Sample** View under the Instrument folder
- **Instrument** View under the Instrument folder.

Sequence options You can enter sample information in the same **Sample Entry** panel as for single samples, but you find the **Tasks to perform** and the **Report Destination** under Sequence Options.

Tasks to perform - These are the same as for single samples, but Allow Online Editing is for sequences only.

Report Destination - You enter the report destination for the entire sequence here, not in Sample Entry.



Sequence entry saves You click the **Apply** button in the Sample Entry Workspace to put the sample information into the sample table and the **Save** button to save entries and changes to the database.

When a single sample or sequence is entered, its revision number is set to 1. The revision number is incremented when the single sample or sequence is changed.

Sequence Logbook As you save your sequence to the Cerity NDS database, Cerity NDS for Pharmaceutical QA/QC auditing requirements may ask you to enter an audit reason and provide your Electronic Signature before you can run a sequence. A description of the changes appears in the **Sequence Logbook**.

Run Preparation

Equilibrating the instrument and column

When an instrument is created, its revision number is set to 1. The revision number is incremented if the configuration of the instrument is changed interactively.

You can equilibrate the instrument and column from the Instrument Panel in the **Instrument** View.

The Instrument Panel provides a picture of the instrument modules you can configure. You point and click on a module to access the menu items for entering instrument parameters. For example, you can start or stop a pump.

You enter your equilibration parameters in the **Set Pump** dialog box. You can start the pump, and monitor the baseline as it appears in the real-time plot.

Actuals

You can see the set and real-time values of the instrument parameters for a selected instrument when you select **Device Actuals** from the **View** menu.

To enter these “actuals” into the **Device Actuals** window, you select the **Setup Actuals Window** menu item in the **View** menu. Then you can add or remove the settings.

Real-time plot

Before running a sample or sequence, you set up the axes and appearance of the real-time plot using the **Change** item of the context menu. If you are using a detector that is capable of collecing spectra (for example, a diode-array detector or a fluorescence detector) you can mark the **Show Spectra** check box to display the spectra as they are acquired.

Run Scheduling and Tracking

Scheduling samples or sequences

You run single samples or sequences from any one of the following View areas:

- In the Sample Entry folder for the **Sample** View
- In the Instrument folder for the **Sample** View
- In the Instrument folder for the **Instrument** View

Wherever you choose to start the run, you select a single sample or group of samples to run from the sample table. You start a sample run or sequence with the **Run** button once you have selected the single sample(s) or sequences that you want to run.

Use these rules to schedule runs:

- When you start a run for a group of single samples or sequences, the first sample or sequence you select starts to run. The remaining samples or sequences are put into the run queue.
- The order in which you start a sample or sequence run sets the run order in the queue.
- You can set the run order of single samples by priority. Priority status starts with **High** priority followed by **Medium** priority followed by **Low** priority.

You do not need to set up a schedule to “schedule” a sample or sequence.

Tracking the progress of a sample or sequence

You can track the progress of a sample or sequence in two locations:

- In the Instrument folder for the **Sample** View, the **Status** column if the table shows the sample that is currently running. The sample that is currently running is denoted by **Running(x:y)**, where x is the sequence line number and y is the injection number.
- In the Instrument folder for the **Instrument** View, the **Instrument Panel** tab shows the current status of the instrument, and shows the name of the current sequence or sample in the **Sequence Information** panel.

Acquisition of Spectra

If you are using a detector that is capable of acquiring spectra, for example, a diode-array detector or a fluorescence detector, you can select to acquire spectra during the creation of the method. You can then use the acquired spectra for

- compound confirmation, where the acquired spectra are compared with an example spectrum,
- peak purity, where the spectra acquired in a chromatographic peak are used to analyze the homogeneity of the peak.

In addition, you can review, manipulate and report the spectra.

Spectral acquisition parameters

The spectral acquisition parameters are available in the Instrument Setup node of the method setup.

Store You can select to store all spectra in the run, a selection of spectra in the run (to reduce the amount of disk storage required), or no spectra. The selection that is available depends on the detector that you are using; see the online help for details.

Range By default, the full wavelength range of the detector is used to acquire spectra. However, you can select to limit the wavelength range to include only the absorbance bands that you are interested in. Reducing the wavelength range also reduces the disk storage requirements.

Step The step size specifies the resolution of spectral acquisition. Highest resolution is provided by a step size of 1 nm; acquiring spectra at a lower resolution (higher step size) reduces the disk storage requirement, but also reduces the accuracy of the spectra.

Threshold An additional method of reducing the disk storage required is to set a threshold value for the detector signal, below which no spectra are acquired.|

5
Cerity Instrument Control

The different aspects of instrument control in Cerity NDS for Pharmaceutical QA/QC are described in this chapter.

Control of Automatically Recognized Instruments

Agilent 1100-Series HPLC modules, and the Agilent 6850 and 6890 GC instruments are recognized automatically by Cerity if they are turned on when the instrument is started. Each instrument, which in the case of the Agilent 1100 HPLC system consists of a number of modules, is attached to, and serviced by, an acquisition controller, which may be embedded in a Cerity Professional (stand-alone) system, or a separate entity in a client-server system. Each instrument is identified in the system by a unique **Instrument Name**, which is allocated when the instrument is initially added to the acquisition controller.

Adding and deleting instruments

Instruments are added and deleted using the facilities provided by the Cerity Software Administration utility. Instruments are added to existing acquisition controllers using the **Add Instrument Wizard**, which is available from the **Action** menu when the acquisition controller's name is selected in the selection tree.

Adding and deleting modules

Agilent 1100 modules, which are called **devices** in the Cerity Software Administration utility, are recognized automatically by Cerity if they are turned on when the instrument is started. Devices that are not automatically recognized are added using the **Add Device** command, which is available from the **Action** menu when the instrument's name is selected in the selection tree.

Devices can be removed only from instruments that are stopped; you stop an instrument using the **Stop and Suspend** command, which is available from the **Action** menu when the instrument's name is selected in the selection tree.

Instrument control interface

You access instrument control from the **Instrument** view. When you select the instrument name from the selection tree, the upper part of the workspace contains a panel for each of the

modules comprising the selected instrument. The color of the title bar indicates the status of the module, as in the following table:

Gray	Not available
Yellow	Not Ready
Green	Pre-run state or Paused
Magenta	Waiting
Blue	Running
Red	Error state

In each module's context menu, which can be accessed by right-clicking on the module's panel, is a series of commands that allow you to control and configure the module.

The method setpoints associated with the module are available when you select the module from the Instrument section of the method setup in the **Method** view.

Control of Third-Party Instruments

Non-Agilent 1100-Series HPLC modules, for example, instruments from other manufacturers, are handled by the Generic Instrument Control (GIC) application. GIC provides Level 3 instrument control through a specially developed device driver. For details, see the GIC handbooks.

Early Maintenance Feedback (EMF)

The EMF icon at the left of the title bar of the module in the instrument panel shows the current status of the module (see Table 3).

Table 3 EMF status indicators

EMF icon	Instrument status
	All EMF limits are OK.
	At least one EMF limit has been exceeded; maintenance is needed.
	The module is in an unknown state, for example, it is offline.

When an EMF limit is exceeded, an entry is made in the sample and instrument logbooks for every injection. The diagnostic printout for the instrument contains the EMF information.

The EMF counters, which form the basis of the EMF display, are reset using an Agilent 1100 hand-held controller. You can reset the EMF counters only when the instrument is stopped. If no limits are set, the EMF status is indicated as OK.

6
Working with Cerity Methods

The Method is a vital part of the Cerity NDS for Pharmaceutical QA/QC application, and this chapter explains the concepts in detail.

Cerity for Pharmaceutical QA/QC Methods

The Cerity NDS for Pharmaceutical QA/QC method contains all the parameters required for instrument control, data acquisition and data analysis and evaluation. In addition, the method contains your own defined sample variables and templates for sequences (sequence template), result review (data review layout) and reports (report template).

Master methods

A *master method* is a method that only assigned users can edit. However, all users can use a master method. Master methods can be used as templates for new master methods or for instrument methods.

When you are ready to let other users modify the master method, you can release the current revision. If your administrator enables auditing for the **Release a method** task, you may need to enter your user name and password to release the method.

After you released the master method, anyone with role rights to edit master methods can edit this revision. If you modify the master method, the new revision is not released until you release it again.

When a master method is released, it can be assigned to a different instrument from the one for which it was created.

Instrument methods

An *instrument method* is a released master method that has been assigned to a different instrument. Any user can edit or use an instrument method. Instrument methods are always created using a template.

After you release a master method, you can assign it to another instrument in the **Method Wizard**. To assign the method, you must create an *instrument method* with the released method as a template. Users can then edit any of the original settings in the **Method** View if they have the rights set up by the Cerity NDS administrator.

If the instrument to which you are assigning the method is configured differently from the original method, you must make sure that you change the instrument parameters in the **Method** View.

You can start to create an instrument method when you select **Instrument Method** from the **New** list on the Standard toolbar.

An *equilibration method* is a method set up with instrument parameters only, in order to equilibrate the column and to stabilize the baseline.

You can set up an equilibration method to equilibrate the instrument and column before an analysis or at the end of a sequence to prepare the column for the next sequence. Make sure that you set the injection volume for the autosampler to zero.

See "Method View" *on page 66* for more information on the **Method** View, and "Cerity for Pharmaceutical QA/QC Method Sections" *on page 97* for more information on Method sections.

Methods for single samples or sequences

Cerity NDS for Pharmaceutical QA/QC lets you create methods for single samples and methods for sequences. Since the sequence table is an element of the method, only one method is used for all the samples in a sequence.

There are several differences between a method for single samples and a method for sequences:

- The method for sequences contains a table where you can set up a sequence that you use frequently.
- The method for sequences organizes samples and standards into groups for custom calculations and reporting, such as QC sample group, calibration standard group, sample group and custom sample groups.
- You can include **Noise Calculations** for sequences but not for single samples.
- You can select the order of calibration and the calibration procedure for sequences.

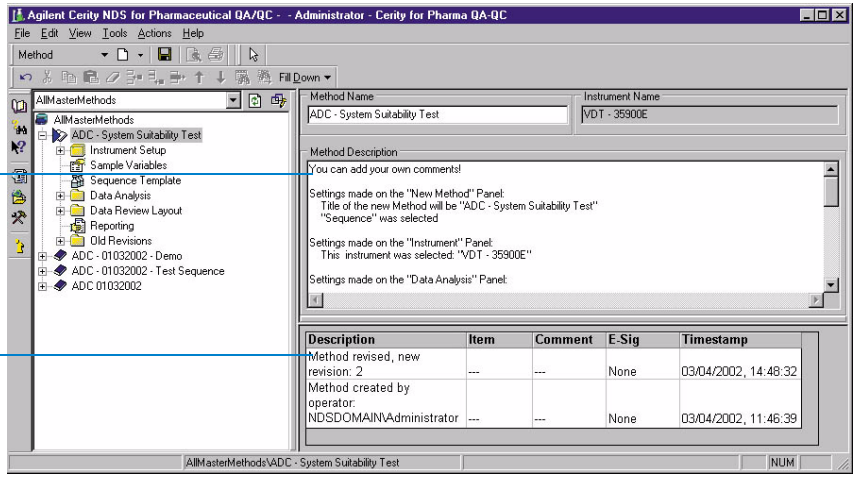
Methods attached to entries and results

When you enter a single sample or create a new sequence, you select the method to use with that sample or sequence. The information and instructions within that method remain attached to the sample or sequence throughout the run and in the results.

This means that if you change a sample entry value or an integration setting and then reprocess, you redo the calculations with the method revision originally attached to the result. If you change the method or want to use a different method to reprocess the results, you must first attach the current revision or the new method to the result.

Method entries and changes

The entries that were made in the Method Wizard when the method was created are shown in the **Method Description** panel. Changes that you make to the method parameters are logged in the **Method Logbook**. Both **Method Description** and **Method Logbook** are displayed when you select the method's node in the **Method** View, as shown in the figure below.



Method Description - Selections in the Method Wizard appear in the Method Description workspace.

Method Logbook - Entries and changes to the method appear in the Method Logbook.

Method revisions

When you create and save a method template with the Method Wizard, you create revision 1 of the method. Each time you change and save the method after revision 1 of the method, a new revision is created. A new revision is also created after you release a master method.

If you select a revision from the Old Revisions folder in a selected method folder, the **Method Description** and **Method Logbook** for the revision appear in the workspace.

Cerity for Pharmaceutical QA/QC Method Sections

You start to create a master method when you select **Method** from the **New** list on the Standard toolbar. The **Method Wizard** leads you through the creation process; on each page of the Method Wizard, you select the basic settings for a different section of your method. You then access the different sections of the method in the **Method** View to specify the method parameters in detail.

Instrument setup

This section lets you enter parameters for the configured instruments. Each module in the instrument has its own node in the selection tree.

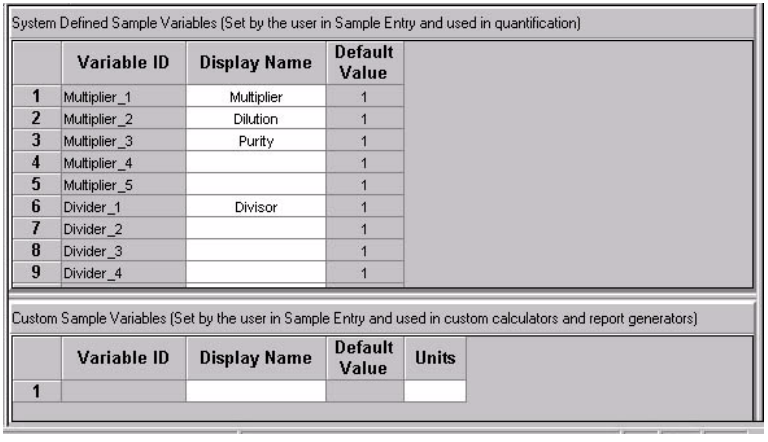
Sample variables

Sample variables are factors and variable definitions that are used for quantitation, custom calculations and reports.

System sample variables

The Pharmaceutical QA/QC application provides Multiplier and Divisor variables for quantitation. Assigning a header name activates the variables.

When you assign a method that uses these variables for a sample or sequence, the variables with their default values appear in the **Amounts** tab of the **Sample Entry** panel. You can modify the value of these variables for each sample before a run.



System Defined Sample Variables (Set by the user in Sample Entry and used in quantification)

	Variable ID	Display Name	Default Value
1	Multiplier_1	Multiplier	1
2	Multiplier_2	Dilution	1
3	Multiplier_3	Purity	1
4	Multiplier_4		1
5	Multiplier_5		1
6	Divider_1	Divisor	1
7	Divider_2		1
8	Divider_3		1
9	Divider_4		1

Custom Sample Variables (Set by the user in Sample Entry and used in custom calculators and report generators)

	Variable ID	Display Name	Default Value	Units
1				

Custom sample variables

You can define your own group of variables as multipliers or dividers used for custom calculations and reports. You can enter header names, default values and comments that appear in the sample report tables.

Sequence Template

A *sequence template* lets you enter the order and number of calibration standards and unknown samples into a sequence table.

The sequence template appears as the sequence table in the **Sample** View after you create a sequence for the method that uses the template. You can schedule the sequence to run without any change to the table based on the template.

If you need to enter calibration standards into the sequence template, you must first complete the calibration setup in Data Analysis.

	Sample Name	Sample Type	Cal. Level	Bracketing	Custom Sample Group	Vial #
1	wfj_171001_i20_1FA_cl_1.1	Calibration	1	Open	1FA_cl_1	1
2	wfj_171001_i20_1FA_cl_2.1	Calibration	2	None	1FA_cl_2	1
3	wfj_171001_i20_1FA_cl_3.1	Calibration	3	None	1FA_cl_3	1
4	wfj_171001_i20_1FA_sa_1.1	Sample			1FA_sa_1	1
5	wfj_171001_i20_1FA_sa_2.1	Sample			1FA_sa_2	1
6	wfj_171001_i20_1FA_sa_3.1	Sample			1FA_sa_3	1
7	wfj_171001_i20_1FA_cl_1.2	Calibration	1	None	1FA_cl_1	1
8	wfj_171001_i20_1FA_cl_2.2	Calibration	2	None	1FA_cl_2	1
9	wfj_171001_i20_1FA_cl_3.2	Calibration	3	None	1FA_cl_3	1
10	wfj_171001_i20_1FA_sa_1.2	Sample			1FA_sa_1	1
11	wfj_171001_i20_1FA_sa_2.2	Sample			1FA_sa_2	1

Example chromatogram

An *example chromatogram* is any chromatogram acquired from a single injection that you choose to use to set up integration and identification.

You can first create an *Example Chromatogram* before you set up data analysis parameters for the method. The Example Chromatogram lets you test your integration parameters and events and identify compounds. You can also use this chromatogram to compare your results for other samples.

See "Produce an example chromatogram" in the Online Help to produce an initial example chromatogram for a method.

Select a chromatogram from the database or run a sample to produce an Example Chromatogram. You need only a skeleton method (instrument parameters only) to produce an example chromatogram. You do not need to select an Example Chromatogram to set up data analysis.

Integration

Initial and timed events You can set initial and timed integration events for either a single signal or for all the signals from a detector.

Tools to integrate a chromatogram You can change the integration settings in this section of the method if you do not like the default integration of the example chromatogram.

- **Integrate** – The **Integrate** button lets you integrate the example chromatogram after you modify the events.

- **Autointegrate** – This function calculates the default settings from the chromatogram.

Compound Identification

Choices to add or remove identification You can use the toolbar or the shortcut menus in both the chromatogram and the compound table to add or remove identification. If you want to identify all the peaks as compounds, the easiest way to do this is to use the **Add Times of Signal** button.

See the section "Integration" on page 118 for more details on integration algorithms and Cerity NDS for Pharmaceutical QA/QC's process to identify compounds.

Peak summing You can set up Peak Summing only if you select the **Peak Summing** option in the **Method Wizard**. You can interactively confine an area in the chromatogram for peak summing.

Confirmation If your method is set up to acquire spectra, you can use the spectra to confirm the identity of the compound by comparison of its apex spectrum with a selected reference spectrum. The reference spectrum can be a single spectrum or

an averaged spectrum, over the full wavelength range or a specified wavelength range, and can include background subtraction.

UV Purity

If your method is set up to acquire spectra, you can use the acquired spectra to check the homogeneity of the chromatographic peak. Each acquired spectrum in the peak is compared with the apex spectrum; the differences are calculated as a purity value, which can be used to display a warning or rejection notice. You can set up the purity calculation using the full wavelength range or a specified wavelength range, using all acquired spectra or a selection only, and including background subtraction. You can also set a noise threshold for the purity calculation, and specify the levels at which the warning and rejection notices are given.

Spectra Handling

The spectra handling setup specifies the parameters for the display of spectra in the data review. You can set up to review the spectra over the full acquired wavelength range or a reduced wavelength range, using all acquired spectra or a selection only, and including background subtraction.

Calibration

The Pharmaceutical QA/QC application provides many choices for setting up calibration. Two that stand out and help distinguish Cerity NDS for Pharmaceutical QA/QC calibration from other programs are:

- You can enter amounts of calibration standards for each sample.
- You can set up calibration to have response factors saved to the method and use calibration standards to confirm calibration infrequently. You can also set up calibration so that you must recalibrate frequently with the calibration standards entered throughout a sequence. See "Calibration" *on page 104* for more information.

Quantitation

A *compound group* is a group of calibrated or uncalibrated compounds for which you can set up custom calculations and limits.

The identified compounds that you removed from the calibration table appear in the **Quantitation** workspace as uncalibrated compounds. For both uncalibrated compounds and unidentified peaks, you can specify a response factor based on a calibrated compound's response factor. You can also set up *compound groups* for calibrated and uncalibrated compounds.

Custom Calculations

The Pharmaceutical QA/QC application lets you include additional calculations and conditional statements that operate on the data provided by quantitation. These custom calculations can be used in further calculations and can be displayed in the **Result** view and printed in reports. They are stored in the database along with the results that are generated automatically by the software. See "Data review layout" *on page 110* for more details.

Limits

You can set limits for the following types of results:

- Single injections
- Multi-injection summaries
- Sample-type groups – for sequences only

The variables and calculations available are those that were available or that you set up for the different result types in the **Custom Calculations** workspace. Within each result type you can set up limits for different groups of samples and apply these limits to all compounds or the compound groups that you set up in quantitation.

All limit check results for the same unique item are combined into one result.

NOTE For example, you can you set up limits for phthalates that appear in your single injection results for the calibration standard. Here, you set up a compound group in quantitation called phthalates and assign both the calibrated and uncalibrated phthalates to the group.

Data Review Layout

The results table and summary items that appear in **Result** View depend on your selections in the Data Review Layout. See "Data review layout" *on page 110* for more information.

Reporting

Set up reporting in the method. You can then change some of your method settings for each single sample or for a sequence. Reports are automatically generated as the sample or sequence is run and can be regenerated during reprocessing. See "Reporting" *on page 221* for more details.

Calibration

Selections for Cerity NDS for Pharmaceutical QA/QC calibration

Calibration determines response factors through the use of calibration standards to calculate absolute component concentrations within the samples.
A *calibration standard* is a sample containing a known amount of the compound to quantify.

A *response factor* is the value of either the response divided by the amount for each peak or the amount divided by response. Or it is calculated from a curve fit.

A *single-level calibration* uses only a single concentration of standard for the calibration curve. The calibration curve displays a straight line with two points, the single standard concentration vs. response point and the zero point.

A *multi-level calibration* uses multiple concentrations of the calibration standard solution, and you can select the curve type that best fits the data.

You make most of your choices for Cerity NDS for Pharmaceutical QA/QC calibration in the **Method Wizard**. After you finish the **Method Wizard** and save your calibration selections, you cannot change them. If you wish to use different calibration sections, you must create a new method with these new selections.

Compound calibration table

You can set up a new calibration table, keep a calibration table from a method that you copy, or set up a manual calibration.

Modes of calibration

For both single samples and sequences, you can set up calibration in the Method Wizard with the following options:

- A Fixed or Variable Amount for Single-level Calibration
- A Fixed or Variable Amount for Multi-level Calibration
- Manual Calibration

If you selected **Variable Amounts** in the **Method Wizard**, you can enter a new amount when you enter a sample or sequence in the **Sample** View. If you selected **Fixed Amounts** in the **Method Wizard**, you must enter the amounts for each compound under **Calibration** in the **Method** View. You can not enter a new amount when you enter a sample in the **Sample** View.

Recalibration and order of quantitation

For sequences you can select the type of recalibration and the order of sample quantitation with the calibration standards:

- **Single update calibration**
  A set of samples is quantified based on the calibration standard or the average of the calibration standards preceding the set of samples.
- **Overall calibration**
  Calibration standards are run and averaged before the samples are quantified (also called “grand average” bracketing).
- **Bracketing**
  A set of samples is quantified based on the average of the calibration standards before and after the set of samples.

Single update calibration

In single update calibration, the calibration table is updated after each calibration standard. The updated calibration table is used to quantify succeeding samples until the next calibration standard. The sequence of events is shown in Figure 23.

The calibration table can be initialized with retention times and response factors by using the **Replace** option for a calibration. This mode is typically used at the beginning of a sequence of HPLC analyses.

To generate a running average of the retention times and/or response factors of the calibration standards, the **Average** option is used for calibration. This mode is typically used after the calibration data has been replaced.

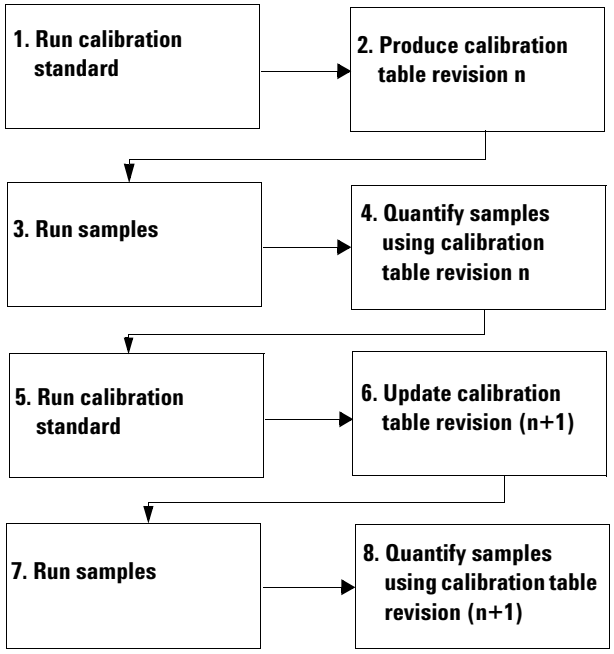


Figure 23 Schematic for single update recalibration

Bracketing

In bracketing calibration, the calibration table is updated using two sets of calibration standards, before and after the samples. Samples are not quantified until the second set of calibration standards has been run. The sequence of events is shown in Figure 24.

The response factors are (replaced) at the beginning of the bracket, and averaged with the calibration values obtained at the closing of the bracket. Retention times are treated in the same way as for single update calibrations.

For the evaluation of system suitability injections, the system allows an initial single update calibration to be inserted at the beginning of the sequence, before the bracketed calibrations.

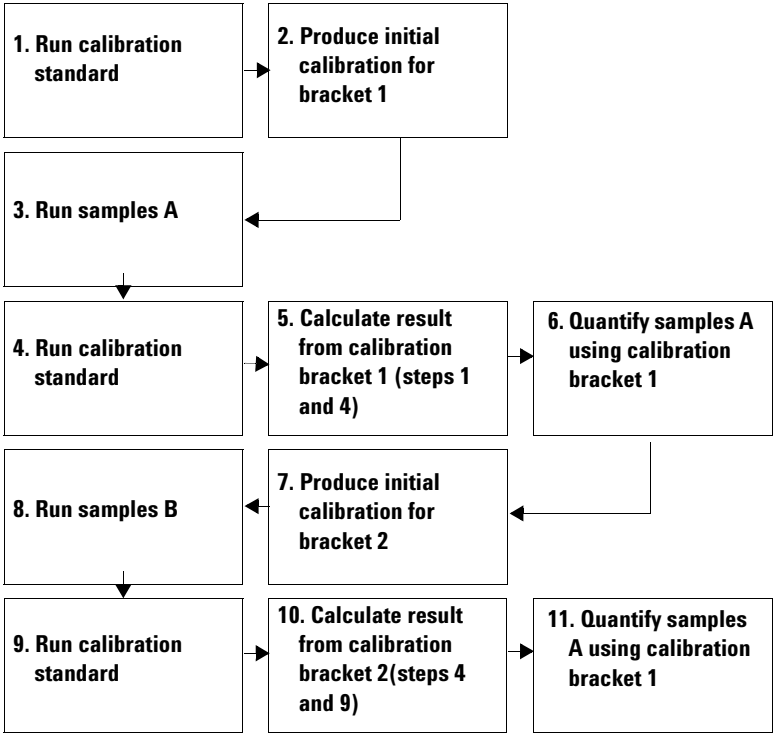


Figure 24 Schematic for bracketing recalibration

Overall Bracketing

In overall bracketing calibration, the calibration table is initialized at the start of the sequence. The results from the first set of standards in the sequence replace the existing calibration results. All calibration standards in the sequence are then used to produce a calibration table at the end of the sequence. This is used to quantify all samples. The sequence of events is shown in Figure 25.

The response factors are replaced at the beginning of the sequence with the values from the first calibration standard, and averaged with the calibration values obtained during the sequence. Retention times are treated in the same way as for single update calibrations.

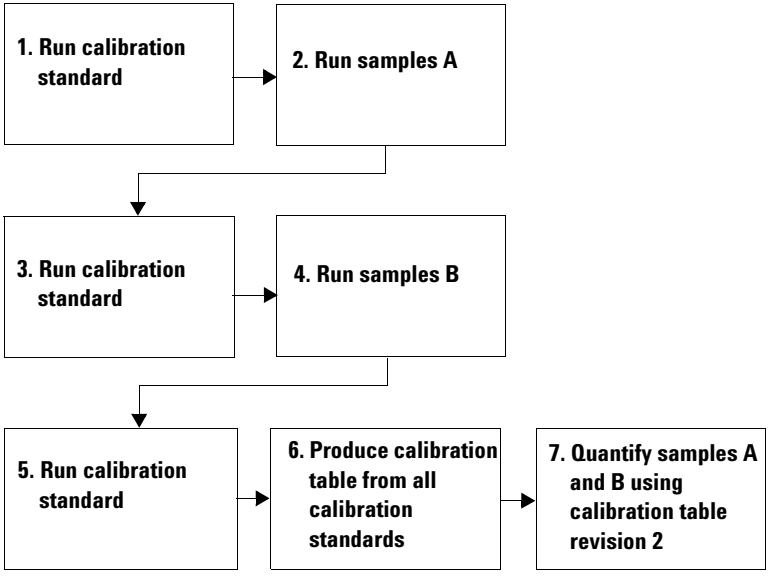


Figure 25 Schematic for overall bracketing recalibration

Calibration procedures

For sequences you can select between two calibration procedures:

- Instrument-specific calibration
- Sequence-specific calibration

Instrument-specific calibration This type of calibration procedure calibrates the instrument for a specific analysis. Use this procedure when the calibration is stable over a long time period. When you run the calibration standards with the method, the response factors and calibration curves are saved to the method. All samples that use this method are then quantified with the response factors in the method. You can choose to update the calibration with new calibration standards. Use this procedure primarily with GC analyses. You run single samples with this type of procedure.

Sequence-specific calibration This calibration procedure calibrates the instrument for the current sequence only. You use this procedure when the calibration is stable for a short time only. Response factors are not saved to the method. They are updated each time you run a sequence with calibration standards for a method. Use this procedure primarily with LC analyses.

Data review layout

Layout types

Cerity NDS for Pharmaceutical QA/QC displays results in the **Result** View for the following sets of results:

- Single Injection, Multi-injection Summary, and Calibration

For sequences, the application displays results for the following sample-type groups:

- QC Sample Group
- Sample Group
- Calibration Standard Group
- Custom Sample Group
- Qualifier Group

Display selections

In the **Data Review Layout** section of the method, you can choose to display in the **Result** View the results and summary tables, the information titles and the status lines for each set of results, with the following differences.

- For the single injection result display only, you can choose to display the signal.
- For the calibration result display only, you can choose to display the calibration table and curve and the residual plot.

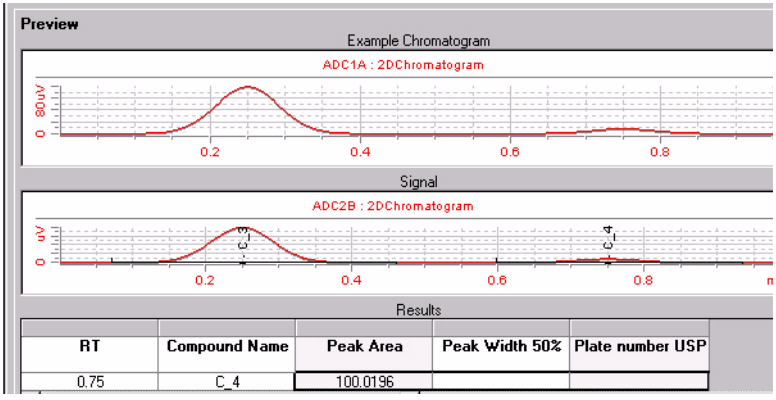
Result selections for the results table

For every table that you choose to display, you can choose the fields and variables that will appear as column headers or items in the tables.

The fields and variables that appear for each set of results are those that the system provides or that you set us as custom variables or custom calculation variables. Only the variables that you set up for each sample-type group in custom calculations appear for that sample-type group here.

Preview of selections

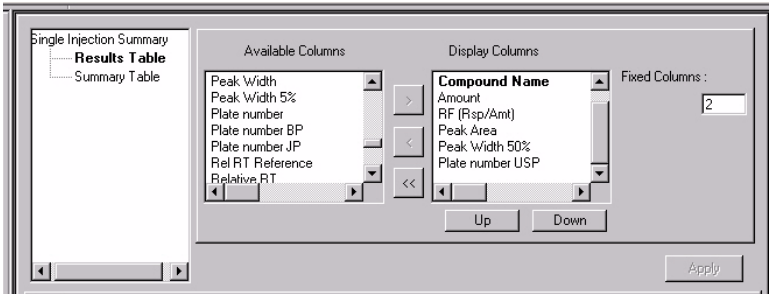
When you make or change a selection, the change appears in the Preview section of the **Data Review Layout** workspace. The change does not appear until you click the **Apply** button.



System suitability

You can produce system suitability values in the **Result** View if you take two actions with Cerity NDS for Pharmaceutical QA/QC:

- Mark the system suitability checkbox in the **Method Wizard.**
- Select the system suitability calculations whose values you want the system to calculate in the **Data Review Layout** element for single injections.



The system suitability results then appear in the **Results Table** for single injections.

Report types

A *report type* is the kind of report generated for a result type.

When you first set up a method, you select the report types that you want to print when a sample or sequence is run with the method. The report types available for the method appear in the **Reporting** workspace. You cannot add new report types to the report type list.

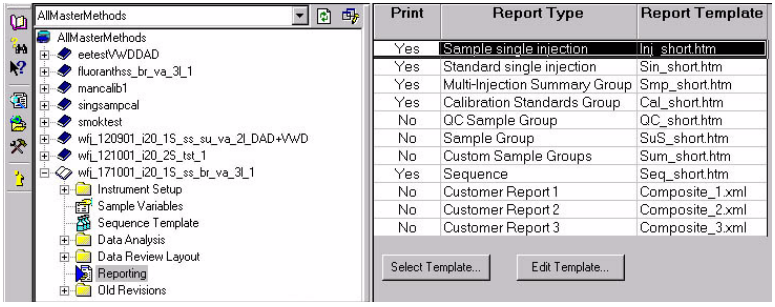


Figure 26 Reporting workspace of the Method View

Report types for single samples

Methods set up for single samples provide report types for three result types:

- Sample single injection
- Standard single injection
- Multi-injection summary

Report types for sequences

Methods set up for sequences include eleven report types:

- Sample single injection
- Standard single injection
- Multi-injection summary

- Calibration standard group
- QC sample group
- Sample group
- Custom sample groups
- Sequence
- Customer Reports 1,2 or 3

Report destination

You can change the report types to print, already made in the **Method** View, when you enter a single sample or set up a sequence. You do this in the **Report Destination** tab of the **Sample Entry** panel in the **Sample** View.

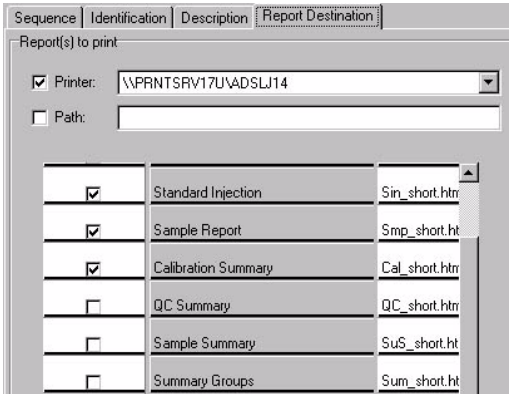


Figure 27 Report destination tab of the Sequence Options panel

NOTE You must add the name of the sample or sequence to the path to let you quickly find the reports for the sample or sequence.

The Cerity NDS administrator sets up the path and printer to save and print your reports. You can change the printer to print the generated reports and/or change the path to save your reports in the **Report Destination** tab in sample entry.

Cerity Report Viewer

The Cerity NDS administrator sets up the path to the directory that stores your reports. The Cerity **Report Viewer** opens the directory that stores your reports for samples and sequences. You can only print the report from the Cerity **Report Viewer**.

You can print method reports from the **File** menu in the **Method** View. The database populates the fields within the method template and places the report in the Cerity **Report Viewer**. You can print the report from the **Report Viewer.**

7
Data Analysis Concepts

The concepts of the data analysis process, from integration to report formatting, are explained in Chapter 7.

Integration

Overview

To integrate a chromatogram, the integrator:

1. defines the initial baseline,
2. continuously tracks and updates the baseline,
3. identifies the start time for a peak and marks this point with a vertical tick mark,
4. finds the apex of each peak and prints the retention/migration time,
5. identifies the end time for the peak, and marks this point with a vertical tick mark,
6. constructs a baseline, and
7. calculates the area, height, and peak width for each peak.

This process is controlled by *integration events*. The most important events are **initial slope sensitivity**, **peak width**, **area reject** and **height reject**. The software allows you to set initial values for these and other events. The initial values take effect at the beginning of the chromatogram. In addition, the auto integration function provides a set of initial events that you can optimize further.

In most cases, the initial events will give good integration results for the entire chromatogram, but there may be times when you want more control over the progress of an integration.

The software allows you to control how an integration is performed by enabling you to program new integration events at appropriate times in the chromatogram.

For more information, see "Integration Events" on page 149.

Principle of Operation

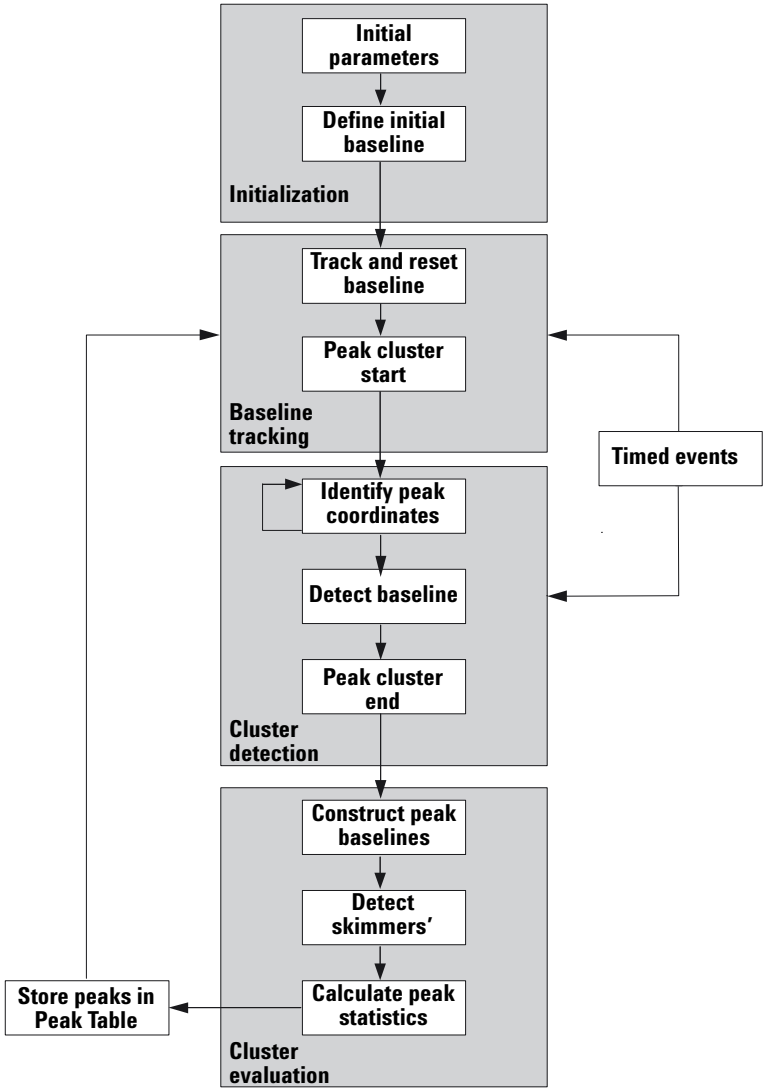


Figure 28 Integrator Flow Diagram

Defining the Initial Baseline

Because baseline conditions vary according to the application and detector hardware, the integrator uses parameters from both the method and the data file to optimize the baseline.

Before the integrator can integrate peaks, it must establish a *baseline point*. At the beginning of the analysis, the integrator establishes an initial baseline level by taking the first data point as a tentative baseline point. It then attempts to redefine this initial baseline point based on the average of the input signal. If the integrator does not obtain a redefined initial baseline point, it retains the first data point as a potential initial baseline point.

Tracking the Baseline

The integrator samples the digital data at a rate determined by the initial peak width or by the calculated peak width, as the run progresses. It considers each data point as a potential baseline point.

The integrator determines a *baseline envelope* from the slope of the baseline, using a baseline-tracking algorithm in which the slope is determined by the first derivative and the curvature by the second derivative. The baseline envelope can be visualized as a cone, with its tip at the current data point. The upper and lower acceptance levels of the cone are:

+ upslope + curvature + baseline bias must be lower than the threshold level

- upslope - curvature + baseline bias must be more positive (i.e. less negative) than the threshold level

As new data points are accepted, the cone moves forward until a break-out occurs.

To be accepted as a baseline point, a data point must satisfy the following conditions:

- it must lie within the defined baseline envelope.

- the curvature of the baseline at the data point (determine by the derivative filters), must be below a critical value, as determined by the current slope sensitivity setting.

The initial baseline point, established at the start of the analysis is then continuously reset, at a rate determined by the peak width, to the *moving average* of the data points that lie *within the baseline envelope* over a period determined by the peak width. The integrator tracks and periodically resets the baseline to compensate for drift, until a peak up-slope is detected.

Allocating the Baseline

The integrator allocates the chromatographic baseline during the analysis at a frequency determined by the peak width value. When the integrator has sampled a certain number of data points, it resets the baseline from the initial baseline point to the current baseline point. The integrator resumes tracking the baseline over the next set of data points and resets the baseline again. This process continues until the integrator identifies the start of a peak

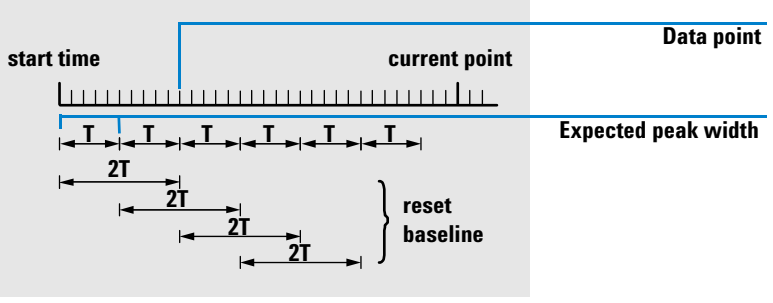


Figure 29 Baseline

At the start of the run, this baseline setting is used as the beginning baseline. If this is not set, the first data point is used. This baseline point is then periodically reset according to the following formula:

Areas are summed over a time T (expected peak width). This time can never be shorter than one data point. This continues as long as baseline condition exists. Slope and curvature are also

taken. If both slope and curvature are less than the threshold, two summed areas are added together, and compared with the previous baseline. If the new value is less than the previous baseline, the new value immediately replaces the old one. If the new value is greater than the previous value, it is stored as a tentative new baseline value and is confirmed if one more value satisfies slope and curvature flatness criteria. This latter limitation is not in effect if negative peaks are allowed. During baseline, a check must also be made to examine fast rising solvents. They may be too fast for upslope detection. (By the time upslope is confirmed, solvent criterion may no longer be valid.) At first time through the first data point is baseline. It is replaced by the 2 T average if signal is on base. Baseline is then reset every T (see Figure 29 on page 121).

Identifying the Cardinal Points of a Peak

The integrator determines that a peak may be starting when potential baseline points lie outside the baseline envelope, and the baseline curvature exceeds a certain value, as determined by the integrator's slope sensitivity parameter. If this condition continues, the integrator recognizes that it is on the up-slope of a peak, and the peak is processed.

Start

1. Slope and curvature within limit: continue tracking the baseline.
2. Slope and curvature above limit: possibility of a peak.
3. Slope remains above limit: peak recognized, cardinal point defined.
4. Curvature becomes negative: front inflection point.

Apex

5. Slope passes through zero and becomes negative: apex of peak, cardinal point defined.
6. Curvature becomes positive: rear inflection point.

End

7 Slope and curvature within limit: approaching end of the peak.

8 Slope and curvature remain within limit: end of peak, cardinal point defined.

9 The integrator returns to the baseline tracking mode.

Peak Recognition

The integrator uses several *tools* to recognize and characterize a peak:

- peak width,
- peak recognition filters,
- bunching,
- peak recognition algorithm,
- peak apex algorithm, and
- non-Gaussian calculations (for example tailing, merged peaks).

Peak Width

During integration, the peak width is calculated from the peak area and height:

$$Width = Area/Height$$

or, if the inflection points are available, from the width between the inflection points.

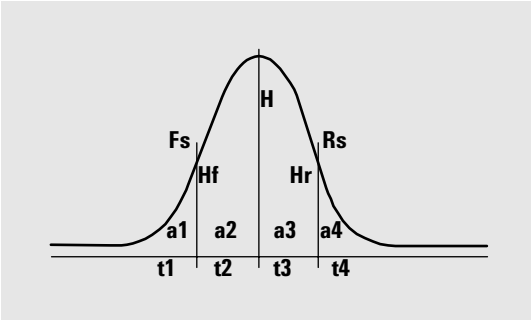


Figure 30 Peak width calculation

In Figure 30, the total area, A, is the sum of the areas a1, a2, a3 and a4. Fs is the front slope at the inflection point, Rs is the rear slope at the inflection point. If either inflection point is not found, the peak width is defined as:

$$Width = \text{Adjusted area} / \text{Adjusted height}$$

The peak width setting controls the ability of the integrator to distinguish peaks from baseline noise. To obtain good performance, the peak width must be set close to the width of the actual chromatographic peaks.

There are three ways the peak width is changed:

- before the run, you can specify the initial peak width,
- during the run, the integrator automatically updates the peak width as necessary to maintain a good match with the peak recognition filters,
- during the run, you can reset or modify the peak width using a time-programmed event.

For peak width definitions used by System Suitability calculations, see the Quality Control chapter of the Technical Reference Guide.

Peak Recognition Filters

The integrator has three peak recognition filters that it can use to recognize peaks by detecting changes in the slope and curvature within a set of contiguous data points. These filters contain the first derivative (to measure slope) and the second derivative (to measure curvature) of the data points being examined by the integrator. The recognition filters are:

Filter 1 Slope (curvature) of two (three) contiguous data points

Filter 2 Slope of four contiguous data points and curvature of three non-contiguous data points

Filter 3 Slope of eight contiguous data points and curvature of three non-contiguous data points

The actual filter used is determined by the peak width setting. For example, at the start of an analysis, Filter 1 may be used. If the peak width increases during the analysis, the filter is changed first to Filter 2 and then to Filter 3. To obtain good performance from the recognition filters, the peak width must be set close to the width of the actual chromatographic peaks. During the run, the integrator updates the peak width as necessary to optimize the integration.

The integrator calculates the updated peak width in different ways, depending on the instrument configuration:

For LC configurations, the default peak width calculation uses a composite calculation

$$(0.3 \times \text{Right inflection point} - \text{Left inflection point}) + 0.7 \times Area/Height$$

For GC configurations, the default peak width calculation uses area/height. This calculation does not overestimate the width when peaks are merged above the half-height point.

In certain types of analysis, for example isothermal GC and isocratic LC analyses, peaks become significantly broader as the analysis progresses. To compensate for this, the integrator automatically updates the peak width as the peaks broaden during the analysis. It does this automatically unless the updating has been disabled or the peak width has been set to a specific value with a timed event.

The peak width update is weighted in the following way:

$$0.75 \times (\text{existing peak width}) + 0.25 \times (\text{width of current peak})$$

If a timed integration event disables or sets the peak width to a specific value, the automatic peak width adjustment is disabled.

Bunching

Bunching is the means by which the integrator keeps broadening peaks within the effective range of the peak recognition filters to maintain good selectivity.

The integrator cannot continue indefinitely to increase the peak width for broadening peaks. Eventually, the peaks would become so broad that they could not be seen by the peak recognition filters. To overcome this limitation, the integrator bunches the data points together, effectively narrowing the peak while maintaining the same area.

When data is bunched, the data points are bunched as two raised to the bunching power, i.e. unbunched = 1x, bunched once = 2x, bunched twice = 4x etc.

Bunching is based on the data rate and the peak width. The integrator uses these parameters to set the bunching factor to give the appropriate number of data points (see Table 4).

Bunching is performed in the powers of two based on the expected or experienced peak width. The bunching algorithm is summarized in Table 4:

Table 4 Bunching Criteria

Expected Peak Width	Filter(s) Used	Bunching Done
0 - 10 data points	First	None
8 - 16 data points	Second	None
12 - 24 data points	Third	None
16 - 32 data points	Second	Once
24 - 48 data points	Third	Once

Table 4 Bunching Criteria

Expected Peak Width	Filter(s) Used	Bunching Done
32 - 96 data points	Third, second	Twice
64 - 192 data points	Third, second	Three times

The Peak Recognition Algorithm

The integrator identifies the start of the peak with a baseline point determined by the peak recognition algorithm. The peak recognition algorithm first compares the outputs of the peak recognition filters with the value of the initial slope sensitivity, to increase or decrease the up-slope accumulator. The integrator declares the point at which the value of the up-slope accumulator is >= 15 the point that indicate that a peak has begun.

The peak recognition algorithm is shown in Figure 31.

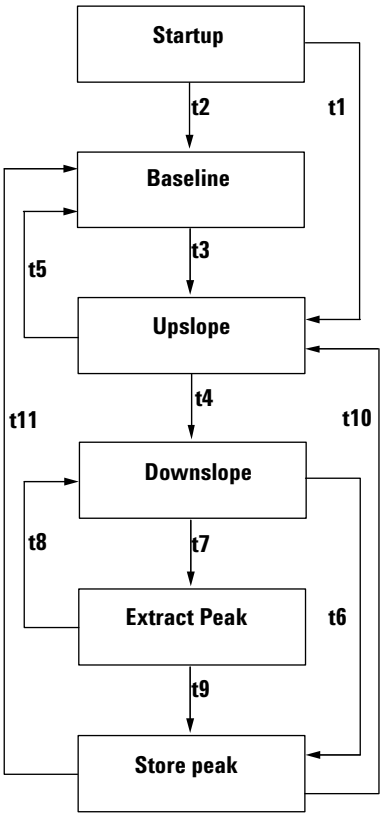


Figure 31 Peak recognition

The criteria are as follows:

t1 Upslope counter is greater than or equal to 1

t2 Upslope counter equals zero

t3 Upslope counter is greater than or equal to 2

t4
- **a** Peak top found and half peak width found or
- **b** Peak top found and downslope counter is greater than or equal to 2

t5
- **a** Peak abort or
- **b** Baseline reset now

t6
- **a** Peak valley found and upslope counter is greater than or equal to 2 or
- **b** Downslope sigma is greater than twice peak end sigma or
- **c** Baseline reset now or
- **d** Baseline reset next valley and peak valley found

t7 Downslope criterion is no longer met

t8 Downslope criterion is met again

t9
- **a** Peak valley found and upslope counter is greater than or equal to 2 or
- **b** Downslope counter equals zero or
- **c** Downslope sigma is greater than peak end sigma or
- **d** Baseline reset now or
- **e** Baseline reset next valley

t10 Upslope counter is greater than or equal to 2

t11 Upslope counter is less than or equal to 1

Peak Start In Table 5, the expected peak width determines which filter's slope and curvature values are compared with the Slope Sensitivity. For example, when the expected peak width is small, Filter 1 numbers are added to the up-slope accumulator. If the expected peak width increases, then the numbers for Filter 2 and, eventually, Filter 3 are used.

When the value of the up-slope accumulator is >= 15, the algorithm recognizes that a peak may be starting.

Table 5 Incremental Values to Upslope Accumulator

Derivative Filter 1 - 3 Outputs against Slope Sensitivity	Filter 1	Filter 2	Filter 3
Slope > Slope Sensitivity	+8	+5	+3
Curvature > Slope Sensitivity	+0	+2	+1
Slope < (-) Slope Sensitivity	-8	-5	-3

Table 5 Incremental Values to Upslope Accumulator (continued)

Derivative Filter 1 - 3 Outputs against Slope Sensitivity	Filter 1	Filter 2	Filter 3
Slope > |Slope Sensitivity|	-4	-2	-1
Curvature < (-) Slope Sensitivity	-0	-2	-1

Peak End

In Table 6, the expected peak width determines which filter's slope and curvature values are compared with the Slope Sensitivity. For example, when the expected peak width is small, Filter 1 numbers are added to the down-slope accumulator. If the expected peak width increases, then the numbers for Filter 2 and, eventually, Filter 3 are used.

When the value of the down-slope accumulator is >= 15, the algorithm recognizes that a peak may be ending.

Table 6 Incremental Values for Downslope Accumulator

Derivative Filter 1 - 3 Outputs against Slope Sensitivity	Filter 1	Filter 2	Filter 3
Slope > Slope Sensitivity	+8	+5	+3
Curvature > Slope Sensitivity	+0	+2	+1
Slope < (-) Slope Sensitivity	-11	-7	-4
Slope > |Slope Sensitivity|	-28	-18	-11
Curvature < (-) Slope Sensitivity	-0	-2	-1

The Peak Apex Algorithm The peak apex is recognized as the highest point in the chromatogram by constructing a parabolic fit that passes through the highest data points.

Non-Gaussian Calculations

Merged Peaks

Merged peaks occur when a new peak begins before the end of peak is found. Figure 32 illustrates how the integrator deals with merged peaks.

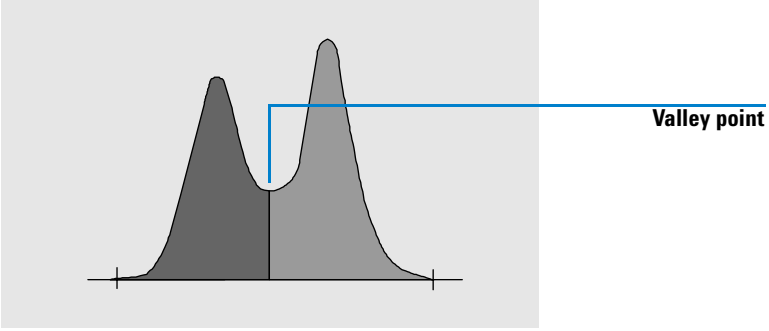


Figure 32 Merged Peaks

The integrator processes merged peaks in the following way:

1. it sums the area of the first peak until the valley point.
2. at the valley point, area summation for the first peak ends and summation for the second peak begins.
3. when the integrator locates the end of the second peak, the area summation stops. This process can be visualized as separating the merged peaks by dropping a perpendicular from the valley point between the two peaks.

Shoulders

Shoulders are unresolved peaks on the leading or trailing edge of a larger peak. When a shoulder is present, there is no true valley in the sense of negative slope followed by positive slope. A peak can have any number of front and/or rear shoulders.

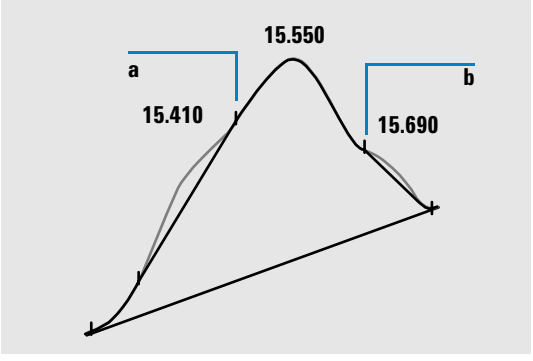


Figure 33 Peak Shoulders

Shoulders are detected from the curvature of the peak as given by the second derivative. When the curvature goes to zero, the integrator identifies a point of inflection, such as points *a* and *b* in Figure 33.

- A potential front shoulder exists when a second inflection point is detected before the peak apex. If a shoulder is confirmed, the start of the shoulder point is set at the maximum positive curvature point before the point of inflection.
- A potential rear shoulder exists when a second inflection point is detected before the peak end or valley. If a shoulder is confirmed, the start of the shoulder point is set at the target point from starting point to curve.

Retention time is determined from the shoulder's point of maximum negative curvature. With a programmed integration event, the integrator can also calculate shoulder areas as normal peaks with drop-lines at the shoulder peak points of inflection.

The area of the shoulder is subtracted from the main peak.

Peak shoulders can be treated as normal peaks by use of an integrator timed event.

Baseline Allocation

After any peak cluster is complete, and the baseline is found, the integrator requests the baseline allocation algorithm to allocate the baseline using a pegs-and-thread technique. It uses trapezoidal area and proportional height corrections to normalize and maintain the lowest possible baseline. Inputs to the baseline allocation algorithm also include parameters from the method and data files that identify the detector and the application, which the integrator uses to optimize its calculations.

Default Baseline Construction

In the simplest case, the integrator constructs the baseline as a series of straight line segments between:

- the start of baseline,
- the tick marks,
- the end of peak

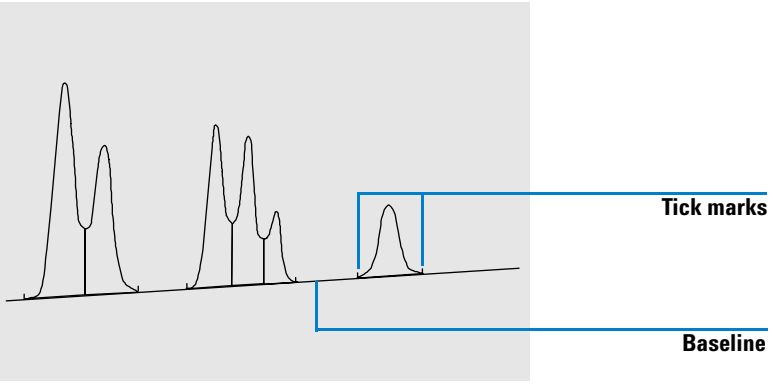


Figure 34 Default Baseline Construction

The Start of the Baseline

If no baseline is found at the start of the run, the start of the baseline is established in one of the following ways:

- from the start of the run to the first baseline point, if the start of run point is lower than the first baseline point,
- from the start of the run to the first valley point, if the start of run point is lower than the first valley,
- from the start of the run to the first valley point, if the first valley penetrates an imaginary line drawn from the start of run to the first baseline,
- from the start of the run to a horizontal baseline extended to the first baseline point.

Tick Marks

Tick marks identify the beginning and end of a peak. Their positions are determined by the peak start and peak end times, saved in the peak table.

The End of the Baseline

The last valid baseline point is used to designate the end of the baseline. In cases where the run does not end on the baseline, the end of the baseline is calculated from the last valid baseline point to the established baseline drift.

If a peak ends in an apparent valley but the following peak is below the area reject value as you have set it, the baseline is projected from the beginning of the peak to the next true baseline point. If a peak starts in a similar way, the same rule applies.

Baseline Penetration

A penetration occurs when the signal drops below the constructed baseline (point **a** in Figure 35). If a baseline penetration occurs, that part of the baseline is generally reconstructed, as shown by points b in Figure 35.

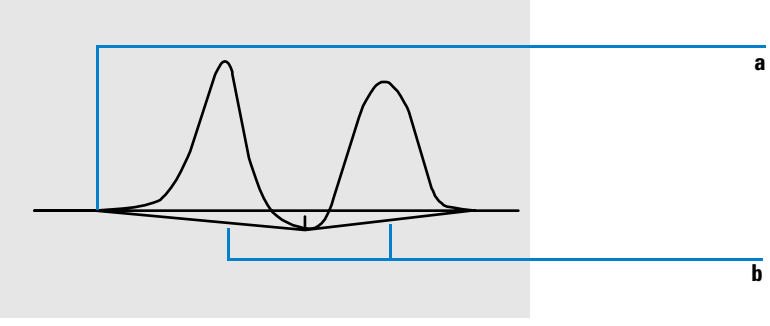


Figure 35 Baseline Penetration

You can use the following tracking options to remove all baseline penetrations:

Classical Baseline Tracking (no penetrations)

When this option is selected, each peak cluster is searched for baseline penetrations. If penetrations are found, the start and/or end points of the peak are shifted until there are no penetrations left (compare the baselines in Figure 36 and Figure 35).

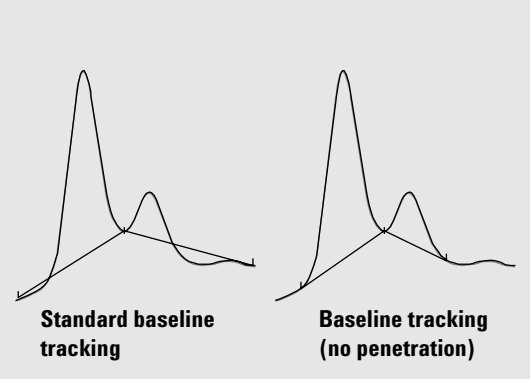


Figure 36 Standard baseline tracking and baseline tracking (no penetration)

NOTE Baseline tracking (no penetration) is not available for solvent peaks, with their child peaks and shoulders.

Advanced Baseline Tracking

In the advanced baseline tracking mode, the integrator tries to optimize the start and end locations of the peaks, re-establishes the baseline for a cluster of peaks, and removes baseline penetrations (see "Baseline Penetration" on page 134). In many cases, advanced baseline tracking mode gives a more stable baseline, which is less dependant on slope sensitivity.

Peak Valley Ratio This user-specified parameter is a constituent of advanced baseline tracking mode. It is used to decide whether two peaks that do not show baseline separation are separated using a drop line or a valley baseline. The integrator calculates the ratio between the baseline-corrected height of the smaller peak and the baseline-corrected height of

the valley. When the peak valley ratio is lower than the user-specified value, a drop-line is used; otherwise, a baseline is drawn from the baseline at the start of the first peak to the valley, and from the valley to the baseline at the end of the second peak (compare Figure 36 with Figure 37).

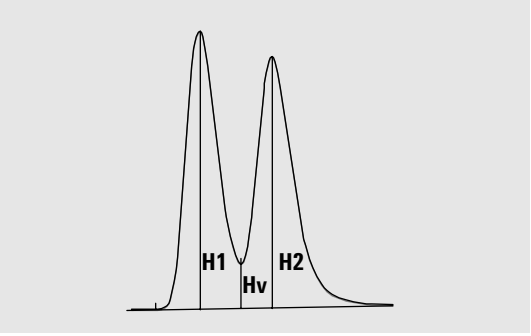


Figure 37 Peak Valley Ratio

The peak valley ratio is calculated using the following equations:

$H1 \geq H2$, Peak valley ratio = H2/Hv

and

$H1 < H2$, Peak valley ratio = H1/Hv

Figure 38 shows how the user-specified value of the peak valley ratio affects the baselines.

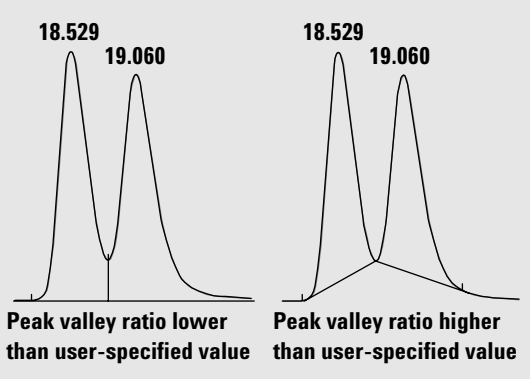


Figure 38 Effect of peak valley ratio on the baselines

Tangent Skimming

Tangent skimming is a form of baseline constructed for peaks found on the upslope or downslope of a peak. When tangent skimming is enabled, four models are available to calculate suitable peak areas:

- exponential curve fitting (new mode),
- exponential curve fitting,
- straight line skim,
- combined exponential and straight line calculations for the best fit (standard skims).

New Mode Exponential Curve Fitting This skim model draws a curve using an exponential equation to approximate the leading or trailing edge of the parent peak. The curve passes under one or more peaks that follow the parent peak (child peaks). The area under the skim curve is subtracted from the child peaks and added to the main peak. More than one child peak can be skimmed using the same exponential model; all peaks after the first child peak are separated by drop lines, beginning at the end of the first child peak, and are dropped only to the skim (see Figure 39). Peaks skimmed in this way are assigned the peak type code **E**.

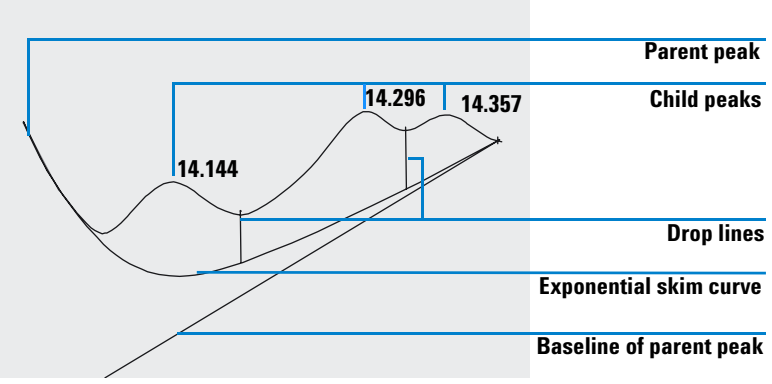


Figure 39 New mode exponential skim

Exponential Curve Fitting (Old Mode) This skim model draws a curve using an exponential equation through the start and end of the child peak (the height of the start of the child peak is corrected for the parent peak slope). The curve passes under each child peak that follows the parent peak; the area under the skim curve is subtracted from the child peaks and added to the parent peak (see Figure 40).

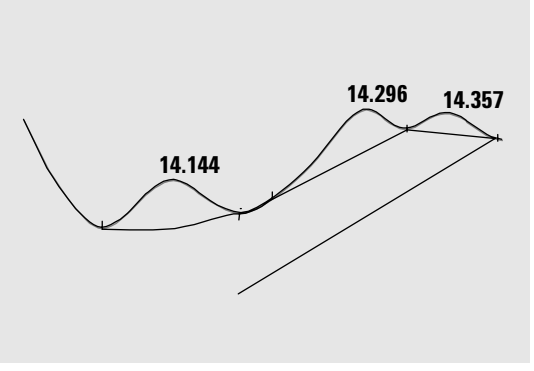


Figure 40 Exponential skim (old mode)

Straight Line Skim This skim model draws a straight line through the start and end of a child peak. The height of the start of the child peak is corrected for the parent peak slope. The area under the straight line is subtracted from the child peak and added to the parent peak (see Figure 41).

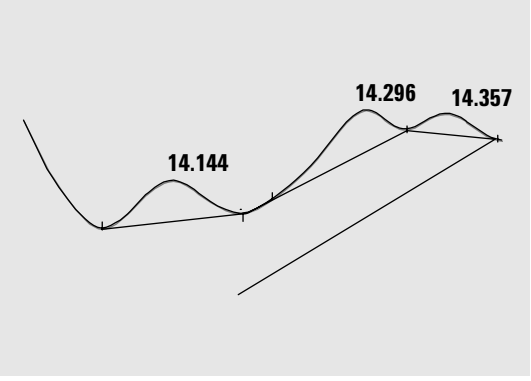


Figure 41 Straight line skim

Standard Skims The appropriate calculation is chosen for a particular application; by default, the chosen method is a combination of exponential and straight line calculations for the best fit.

The switch from an exponential to a linear calculation is performed in a way that eliminates abrupt discontinuities of heights or areas.

- When the signal is well above the baseline, the tail-fitting calculation is exponential.
- When the signal is within the baseline envelope, the tail fitting calculation is a straight line.

The combination calculations are reported as exponential or tangent skim.

Skim Criteria

Two criteria determine whether a skim line is used to calculate the area of a child peak eluting on the trailing edge of a parent peak:

- tail skim height ratio
- valley height ratio

These criteria are not used if a timed event for an exponential is in effect, or if the parent peak is itself a child peak. The separation code between parent peak and child peak must be of type Valley.

Tail Skim Height Ratio This is the ratio of the baseline-corrected height of the parent peak (Hp in Figure 42) to the baseline-corrected height of the child peak (Hc in Figure 42). This ratio must be greater than the specified value for the child peak to be skimmed.

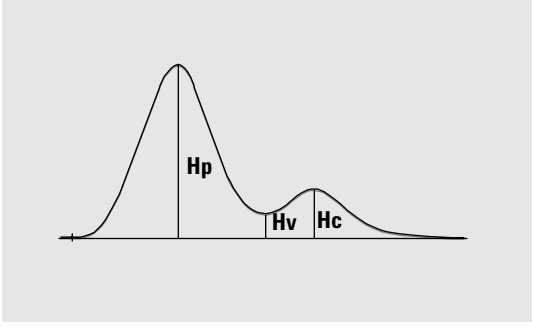


Figure 42 Skim criteria

You can disable exponential skimming throughout the run by setting the value of the tail skim height ratio to a high value or to zero.

Valvalley Height Ratio This is the ratio of the height of the child peak above the baseline (Hc in Figure 42) to the height of the valley above the baseline (Hv in Figure 42). This ratio must be smaller than the specified value for the child peak to be skimmed.

Calculation of Exponential Curve Fitting for Skims

The following equation is used to calculate an exponential skim (refer to Figure 43):

$$Hb = Ho \times \exp(-B \times (Tr - To)) + A \times Tr + C$$

where

Hb = height of the exponential skim at time *Tr*

Ho = height (above baseline) of the start of the exponential skim

B = decay factor of the exponential function

To = time corresponding to the start of the exponential skim

A = slope of the baseline of the parent peak

C = offset of the baseline of the parent peak

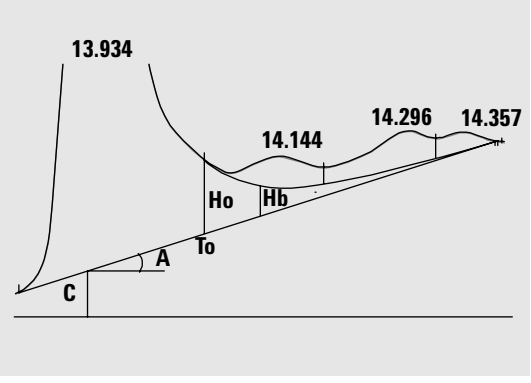


Figure 43 Values used to calculate an exponential skim

The exponential model is fitted through the part of the tail of the parent peak immediately before the first child peak. Figure 44 shows the corrected curve of a child peak after tangent skimming.

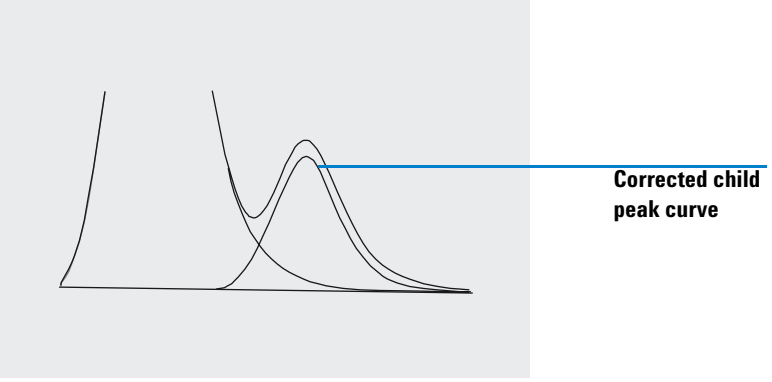


Figure 44 Tail-corrected child peak

Front Peak Skimming

As for child peaks on the tail of a parent peak, special integration is required for some peaks on the front/upslope of a peak, see Figure 45.

Figure 45 Front peak skimming

Front peak skimmimg is treated the same way as tail peak skimming, using the same skim models.

The skim criteria are:

- front skim height ratio
- valley height ratio

The valley height ratio takes the same value for both front peak skimming and tail peak skimming (see “Valley Height Ratio” on page 140); the front skim height ratio is calculated in the same way as the tail skim height ratio (see “Tail Skim Height Ratio” on page 140), but can have a different value.

Unassigned Peaks

With some baseline constructions, there are small areas that are above the baseline and below the signal, but are not part of any recognized peaks. Normally, such areas are neither measured nor reported. If unassigned peaks is turned on, these areas are measured and reported as unassigned peaks. The retention time for such an area is the midpoint between the start and end of the area, as shown in Figure 46.

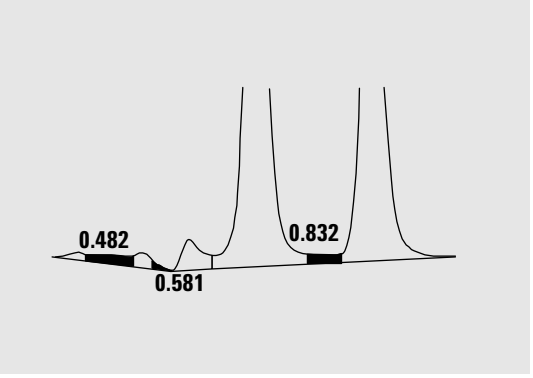


Figure 46 Unassigned Peaks

Peak Separation Codes

In reports, each peak is assigned a two- or three-character code that describes how the signal baseline was drawn.

Characters 1 and 2

The first character describes the baseline at the start of the peak and the second character describes the baseline at the end of the peak.

B The peak started or stopped on the baseline.

V The peak started or stopped with a valley drop-line.

P The peak started or stopped while the baseline was penetrated.

H The peak started or stopped on a forced horizontal baseline.

F The peak started or stopped on a forced point.

M The peak was manually integrated.

U The peak was unassigned.

Additional flags may also be appended (in order of precedence):

Character 3

The third character (which is blank for a normal peak) describes the peak type:

S The peak is a solvent peak.

N The peak is a negative peak.

+ The peak is an area summed peak.

T Tangent-skimmed peak (standard skim).

X Tangent-skimmed peak (old mode exponential skim).

E Tangent-skimmed peak (new mode exponential skim).

m Peak defined by manual baseline.

n Negative peak defined by manual baseline.

t Tangent-skimmed peak defined by manual baseline.

R The peak is a recalculated solvent peak.

f Peak defined by a front shoulder tangent.

b Peak defined by a rear shoulder tangent.

F Peak defined by a front shoulder drop-line.

B Peak defined by a rear shoulder drop-line.

U The peak is unassigned.

D The peak was distorted.

A The integration was aborted.

U An under-range condition occurred.

O An over-range condition occurred.

Step 1. Peak Area Measurement

The final step in peak integration is determining the final area of the peak.

Peak areas are calculated from the contents of the cardinal point file. Cardinal points are the points chosen by the integrator to define and quantify a peak (see "Identifying the Cardinal Points of a Peak" on page 122). These include baseline points, valley points, peak apex, points at peak half height. Cardinal points have a horizontal coordinate of elapsed time, a vertical coordinate of height from the baseline, area, and other parameters that the integrator uses to calculate the peak areas.

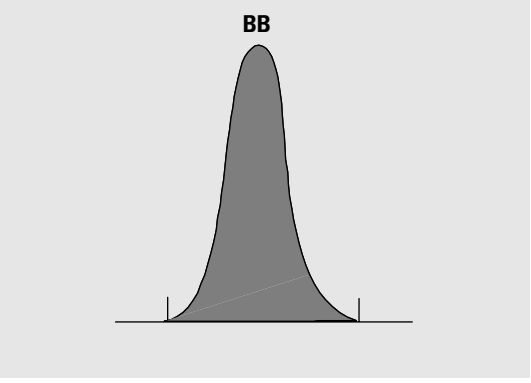


Figure 47 Area measurement for Baseline-to-Baseline Peaks

In the case of a simple, isolated peak, the peak area is determined by the accumulated area above the baseline between peak start and stop (identified by tick marks).

Determination of the area

The area that the integrator calculates during integration is determined as follows:

- for baseline-to-baseline (BB) peaks, the area above the baseline between the tick marks, as in Figure 47 on page 146

- for valley-to-valley (VV) peaks, the area above the baseline, segmented with vertical dropped lines from tick marks, as in Figure 48

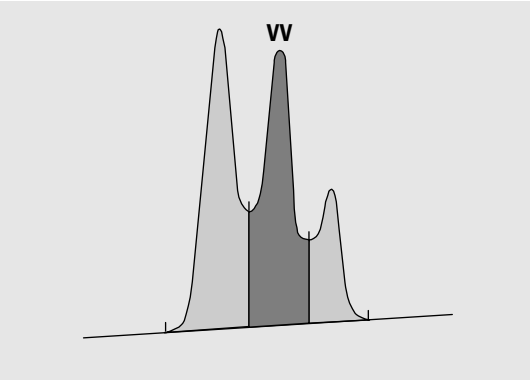


Figure 48 Area Measurement for Valley-to-Valley Peaks

- for tangent (T) peaks, the area above the reset baseline,
- for solvent (S) peaks, the area above the horizontal extension from the last-found baseline point and below the reset baseline given to tangent (T) peaks. A solvent peak may rise too slowly to be recognized, or there may be a group of peaks well into the run which you feel should be treated as a solvent with a set of riders. This usually involves a merged group of peaks where the first one is far larger than the rest. The simple drop-line treatment would exaggerate the later peaks because they are actually sitting on the tail of the first one. By forcing the first peak to be recognized as a solvent, the rest of the group is skimmed off the tail.
- negative peaks that occur below the baseline have a positive area, as shown in Figure 49 on page 148.

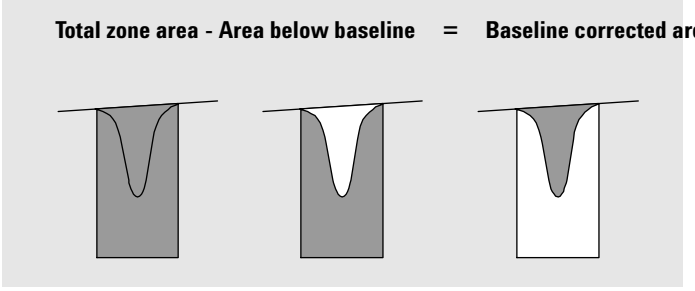


Figure 49 Area Measurement for Negative Peaks

Units and Conversion Factors

Externally, the data contains a set of data points; they can be either sampled data or integrated data. In the case of integrated data, each data point corresponds to an area, which is expressed as $Height \times Time$. In the case of sampled data, each data point corresponds to a height.

Therefore, in the case of integrated data, height is a calculated entity, obtained by dividing area by the time elapsed since the preceding data point. In the case of sampled data, area is calculated by multiplying the data by the time elapsed since the preceding data point.

The integration calculation makes use of both entities. The units carried internally inside the integrator are: $counts \times milliseconds$ for area and $counts$ for height. This is done to provide a common base for integer truncations when needed. The measurements of time, area and height are reported in real physical units, irrespective of how they are measured, calculated and stored in the software.

Integration Events

The integrator provides you with a number of initial and timed integrator events. Many events are on/off or start/stop pairs.

Initial Events

Initial Peak Width

Initial peak width sets the integrator's internal peak width to this value for the start of run. This initial peak width is used to scale the accumulator that detects peak up-slope, down-slope, and tailing. The integrator updates the peak width when necessary during the run to optimize the integration. You specify the peak width in units of time that correspond to the peak width at half-height of the first expected peak (excluding the solvent peak).

Slope Sensitivity

Slope sensitivity is the setting for peak sensitivity. This is a setting that changes on a linear scale.

Height reject

Height reject sets peak rejection by final height. Any peaks that have heights less than the minimum height are not reported.

Area reject

Area reject sets peak rejection by final area. Any peaks that have areas less than the minimum area are not reported.

Shoulder detection

When shoulder detection is on, the integrator detects shoulders using the curvature of the peak as given by the second derivative. When the curvature goes to zero, the integrator identifies this point of inflection as a possible shoulder. If the integrator identifies another point of inflection before the apex of the peak, a shoulder has been detected.

Peak Width

The peak width setting controls the selectivity of the integrator to distinguish peaks from baseline noise. To obtain good performance, the peak width must be set close to the width at half-height of the actual chromatographic peaks. The integrator updates the peak width when necessary during the run to optimize the integration.

Choosing Peak Width

Choose the setting that provides just enough filtering to prevent noise being interpreted as peaks without distorting the information in the signal.

- To choose a suitable initial peak width for a single peak of interest, use the peak's time width as the base as a reference.
- To choose a suitable initial peak width when there are multiple peaks of interest, set the initial peak width to a value equal to or less than the narrowest peak width to obtain optimal peak selectivity.

If the selected initial peak width is too low, noise may be interpreted as peaks. If broad and narrow peaks are mixed, you may decide to use runtime programmed events to adjust the peak width for certain peaks. Sometimes, peaks become significantly broader as the analysis progresses, for example in isothermal GC and isocratic LC analyses. To compensate for this, the integrator automatically updates the peak width as peaks broaden during an analysis unless disabled or set with a timed event.

The Peak Width update is weighted in the following way:

$$0.75 \times (\text{existing peak width}) + 0.25 \times (\text{width of current peak})$$

If a timed integration event disables or sets the peak width to a specific value, the automatic peak width adjustment is disabled.

Height Reject and Peak Width

Both peak width and height reject are very important in the integration process. You can achieve different results by changing these values.

- Increase both the height reject and peak width where relatively dominant components must be detected and quantified in a high-noise environment. An increased peak width improves the filtering of noise and an increased height reject ensures that random noise is ignored.

- Decrease height reject and peak width to detect and quantify trace components, those whose heights approach that of the noise itself. Decreasing peak width decreases signal filtering, while decreasing height reject ensures that small peaks are not rejected because they have insufficient height.

When an analysis contains peaks with varying peak widths, set peak width for the narrower peaks and reduce height reject to ensure that the broad peaks are not ignored because of their reduced height.

Tuning Integration

It is often useful to change the values for the slope sensitivity, peak width, height reject, and area reject to customize integration.

Figure 50 shows how these parameters affect the integration of five peaks in a signal.

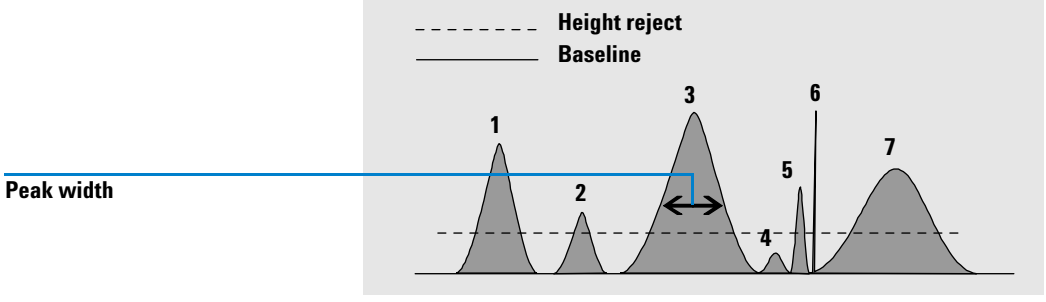


Figure 50 Using Initial Events

A peak is integrated only when all of the four integration parameters are satisfied. Using the peak width for peak 3, the area reject and slope sensitivity shown in Figure 50, only peaks 1, 3, 5 and 7 are integrated.

Peak 1 is integrated as all four integration parameters are satisfied.

Peak 2 is rejected because the area is below the set area reject value.

Peak 3 is integrated as all four integration parameters are satisfied.

Peak 4 is not integrated because the peak height is below the Height Reject.

Peak 5 is rejected because the area is below the set area reject value.

Peak 6 is not integrated; filtering and bunching make the peak invisible.

Peak 7 is integrated.

Table 7 Height and Area Reject Values

Integration Parameter	Peak 1	Peak 2	Peak 3	Peak 4	Peak 5	Peak 7
Height reject	Above	Above	Above	Below	Above	Above
Area reject	Above	Below	Above	Below	Below	Above
Peak integrated	Yes	No	Yes	No	No	Yes

Timed Events

You can use timed events to customize signal baseline construction when default construction is not appropriate. These events can be useful for summing final peak areas and for correcting short- and long-term baseline aberrations. For further information about integration events see “Integration Events” on page 149.

Autointegrate

Overview

The Autointegrate function provides a starting point for setting initial events. This is particularly useful when you are implementing a new method. You start with a default integration events table that contains no timed events; you can then optimize the parameters proposed by the Autointegrate function for general use.

Principles of Operation

The Autointegrate function reads the chromatogram data and calculates the optimal values for the initial integration parameters for each signal in the chromatogram object.

The algorithm examines 1% at the start and end of the chromatogram and determines the noise and slope for this part. Noise is determined as 3 times the standard deviation of the linear regression divided by the square root of the percent number of points used in the regression. These values are used to assign appropriate values to the height reject & threshold for the integration. The algorithm then assigns a temporary value for the peak width, depending on the length of the chromatogram, using 0.5% for LC and 0.3% to 0.2% for GC. The initial area reject is set to zero and a trial integration is performed. The trial is repeated several times if necessary, adjusting the parameters each time until at least 5 peaks are detected or integration is performed with an initial height reject of 0. The trial integration is terminated if the above conditions are not met after 10 trials.

The results of the integration are examined and the peak width is adjusted based on the peak widths of the detected peaks, biasing the calculation towards the initial peaks. The peak symmetry of the detected peaks is used to include only those peaks with symmetry between 0.8 & 1.3 for the peak width calculation. If not enough symmetric peaks are found, this limit is relaxed to minSymmetry/1.5 and maxSymmetry*1.5. The baseline between the peaks is then examined to refine the earlier values of height reject & threshold. The area reject is set to 90% of the minimum area of the most symmetric peak detected during the trial integration.

The chromatogram is re-integrated using these final values for the integration parameters, and the results of the integration are stored.

Autointegrate Parameters

The following parameters are set by the autointegrate function:

- Initial threshold

- Initial height
- Initial peak width
- Initial area reject

Manual Integration

Overview

This type of integration allows you to integrate selected peaks or groups of peaks. Except for the initial area reject value, the software's event integration is ignored within the specified range of manual integration. If one or more of the peaks resulting from manual integration is below the area reject threshold, it is discarded. The manual integration events use absolute time values. They do not adjust for signal drift.

Manual integration enables you to define the peak start and stop points, and then include the recalculated areas in quantification and reporting. Manually-integrated peaks are labeled in reports with the peak separation code M.

Manual Integration offers the following features:

Draw Baseline Draw Baseline specifies where the baselines are to be drawn for a peak or set of peaks. You can also specify whether peaks in the range given should be automatically separated at all valley points.

Negative Peaks Negative Peaks specifies when to treat any areas below the baseline as negative peaks. You can also specify whether peaks in the range given should be automatically separated at all valley points.

Tangent Skim Tangent Skim calculates the areas of peaks tangentially skimmed off a main peak. The area of the tangent skimmed peak is subtracted from the area of the main peak.

Split Peak Split Peak specifies a point where to split a peak with a drop-line.

Delete Peak(s) Deletes one or more peaks from the integration results.

Peak Separation Codes for Manually-Integrated Peaks

- Manually-integrated peaks are labeled in the integration reports by the peak code MM.
- If there is a peak before the manually-integrated peak, and the end of this peak changes because of the manual integration, it is given the code F (forced).
- A solvent peak which has been affected by manual integration, such as tangent skim, are labeled R (re-calculated solvent).

Documenting Manual Integration Events

The results generated after applying the manual integration events are saved, and an audit log of the manual integration operations is created. Manual integration events are specified with absolute values for retention time and height, and are therefore chromatogram-specific. As a consequence, the system does not automatically apply manual integration events to other chromatograms.

Peak Identification

Overview

Peak identification identifies the components in an unknown sample based on their chromatographic characteristics that have been previously determined by the analysis of a well-defined calibration standard. The reference chromatogram, containing all compounds of interest, is selected and displayed in the workspace as the example chromatogram (see Figure 51).

The identification of these components is a necessary step if the analytical method requires quantification. The signal characteristics of each component of interest are stored in the calibration table of the method.

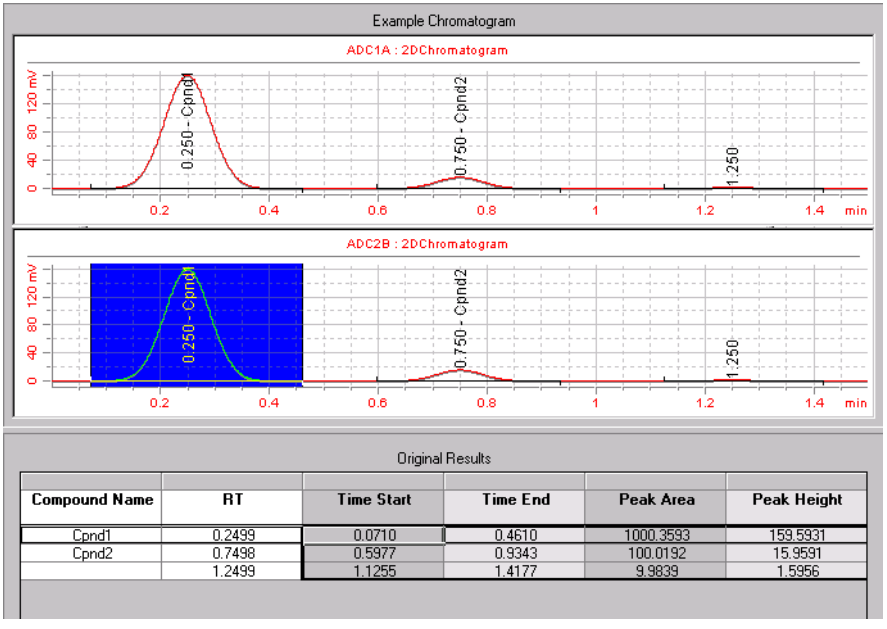


Figure 51 Example Chromatogram

The function of the peak identification process is to compare each peak in the signal with the peaks stored in the identification table.

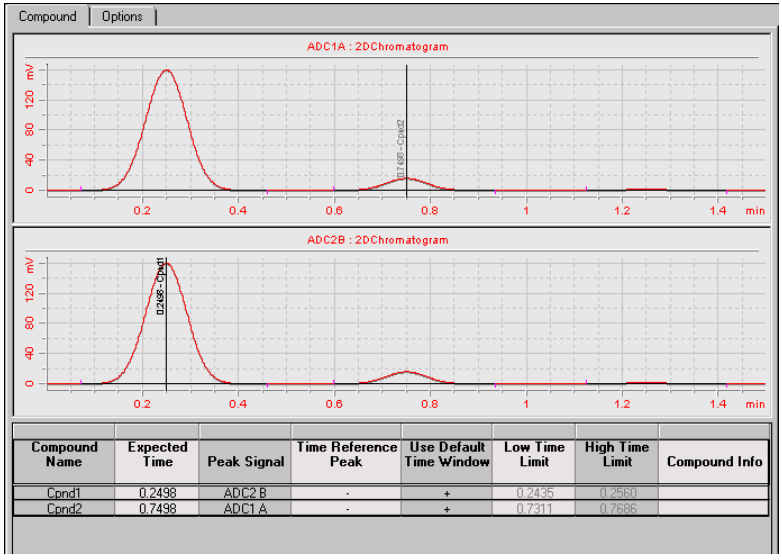


Figure 52 Peak ID Table

The identification table, shown in the peak identification workspace below the chromatogram (see Figure 52) contains the expected retention times of components of interest. A peak that matches the retention time of a peak in the identification table is given the attributes of that component, for example, the name and response factor. Peaks that do not match any of the entries in the identification table are classified as unidentified peaks. The process is controlled by:

- the retention time in the identification table for peaks designated as time reference peaks,
- the retention time windows specified for reference peaks,
- the retention times in the identification table for peaks that are not time reference peaks,
- the retention time window specified for these non-reference peaks.

Principles of Peak Identification

Figure 53 shows the main steps in the process of peak identification.

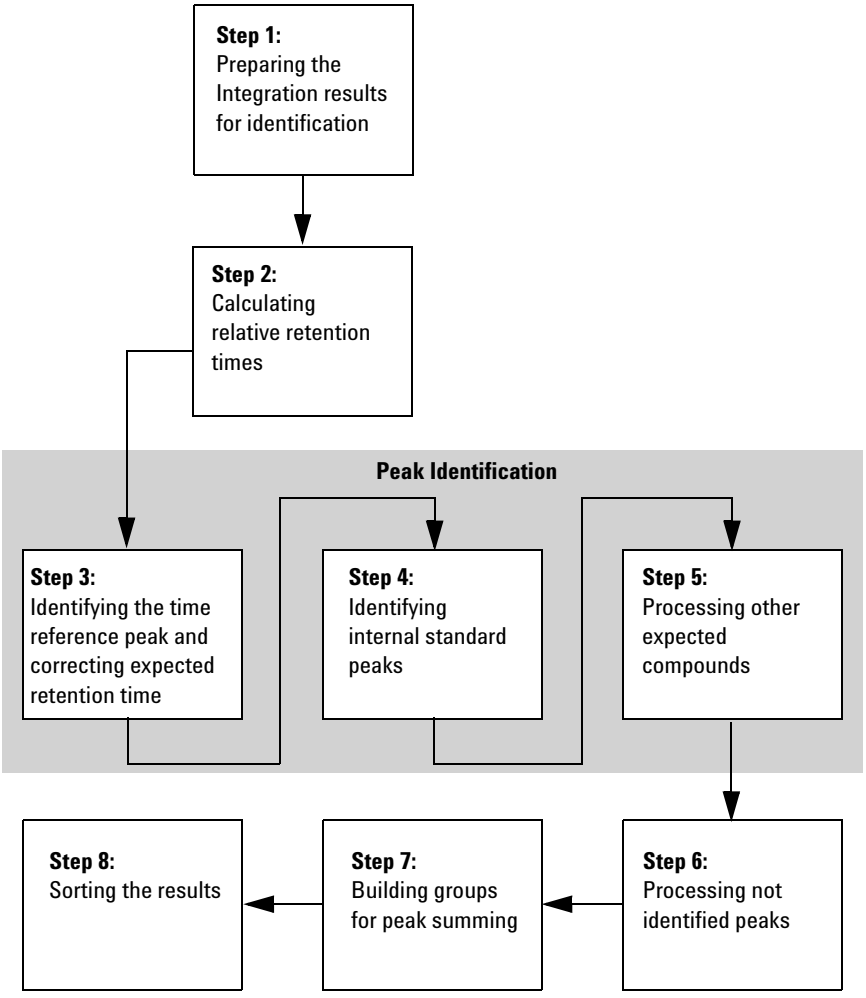


Figure 53 Peak Identification Flow Diagram

Step 1: Preparing the integration results for identification

The first step of the identification process copies and initializes the identification parameters from the calibration information into the identification results.

Step 2: Calculating relative retention times

In the fourth step, the reference peak for the calculation of relative retention times is searched for, and relative retention times for each peak are calculated. If the reference peak cannot be found, the time stored in the identification results is used for the calculation.

Steps 3 – 5: Peak identification

The peak identification process makes three passes through the compounds in the calibration information and integrated peaks.

In the first pass, Step 3, the time reference peaks in the calibration information are identified in the results. The drift of the time reference peaks is used to correct the expected retention times of the other calibrated peaks. This is done separately for each signal.

In the second pass, Step 4, the internal standards are identified in the results.

In the third pass, Step 5, the other expected compounds in the calibration data are processed.

The peak identification process copies the information from the expected peaks that have been found to the measured peaks, and links the peaks with the corresponding expected compounds and the signals. For peaks that are expected but not found, new, empty entries are created.

Step 6: Processing unknown peaks

In Step 6, each unknown peak is attached to an existing identified compound as long as it lies within the time window and the compound has no other peak in the same signal. If there are unknown peaks that cannot be attached to an existing

compound, each set of peaks from different signals that lie within the same time window is grouped together as a new unidentified compound.

Step 7: Building groups for peak summing

In this step the compound table is scanned for peak sum compounds. Each peak of a peak sum compound represents a section of the chromatogram for which a peak sum is built. The peaks within the time window limits of the peak sum peaks are processed, and their responses are summed.

Step 8: Sorting the results

In the final step, the peaks are sorted by measured retention time (or expected retention time if no measured time is available). Compounds are sorted by the order of their main peaks.

Peak Identification Rules

The following rules apply in the peak identification process:

- if a sample peak falls within the expected peak time window of a component peak from the identification table, and the signal identifier (signal name or description) is identical, the peak is given the attributes of that component,
- if more than one sample peak falls within the expected peak time window, then the peak closest to the expected retention time is identified as that component,
- if more than one peak falls within a time reference or internal standard window, then the largest peak in the window is identified as that component,
- if a sample peak does not fall in any peak matching window, it is listed as an unidentified component.

Techniques of Peak Identification

There are different techniques that can be used to match sample peaks with those in the identification table.

Using Absolute Retention Times

The retention time of the sample peak is compared with the expected retention time specified for each component in the identification table.

Using Corrected Retention Times

The expected retention times of component peaks are corrected using the actual retention times of one or more reference peaks, and the matching process is done using these corrected retention times. The reference peak or peaks must be specified in the identification table.

Using Relative Retention Times

A relative retention time for each sample peak is calculated; this is then compared with the relative retention time specified for each component in the identification table.

Identifying Peaks Using Absolute Retention Times

The peak identification process takes each of the expected compounds in the calibration information and searches for the corresponding compounds in the integrated results. Each expected compound has one or more peaks; if the compound has more than one peak, the main peak is identified first, then the secondary peaks are identified.

For positive identification, the measured time must lie within a time window, and the signal identifier of the measured peak must match that of the calibrated peak.

The time window within which the measured peak is searched is a time interval constructed around the expected time of the peak. It is used to allow for drift in the analytical system. The

time interval may be asymmetric with respect to the expected peak time, that is, the expected peak time is not necessarily in the centre of the time window. If time reference peaks have been specified, corrected time windows are used (see "Identifying Peaks Using Corrected Retention Times" on page 163).

Figure 54 shows a retention time window for peak 2 which is between 1.809 and 2.631 minutes, where the expected retention time is 2.22 minutes. There are two possibilities for peak 2: one is at 1.85 minutes, the other at 2.33 minutes.

- If the expected peak is a non-reference peak, the peak closest to the expected retention time of 2.22 minutes is selected.
- If the expected peak is a time reference or internal standard, the largest peak in the window is selected.

In both cases, the peak at 2.33 minutes is selected. If the two peaks in the window are the same size, then the peak closest to the center of the window is selected.

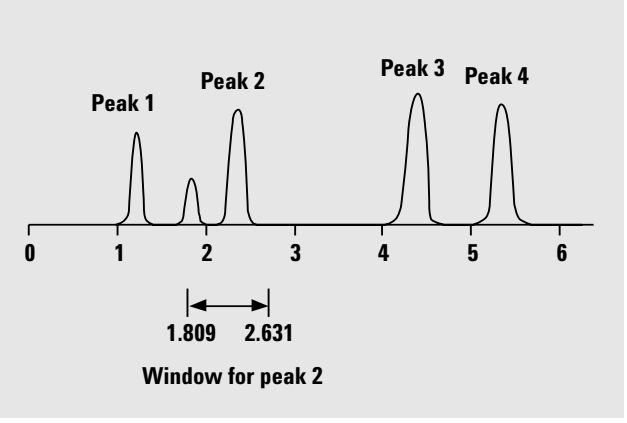


Figure 54 Retention Time Windows

Multiple matches

Most frequently, only one peak matches the time window and the signal identifier of the expected peak. In this case, the calibration peak information is copied to the results and the peak is linked to the corresponding expected compound.

If multiple measured peaks are found in the expected peak time window, the peak closest to the expected time is selected.

If multiple measured peaks are found in a reference time window (either a time reference or an internal standard), the largest peak in the window is selected.

If a measured peak fits into more than one expected peak time window, it is cloned for each window and marked as duplicated.

Peaks other than the best match, and duplicated peaks, are removed, leaving only the best matches.

Missing Peaks

If no measured peaks are found in the expected peak time window, the expected peak information is copied from the calibration data to the results, linked to the expected compound and flagged as “not found”.

Identifying Peaks Using Corrected Retention Times

Identifying peaks by absolute retention times is not always reliable, because individual retention times may vary slightly due to small changes in conditions or technique. As a result, peaks may occur outside the peak matching windows and therefore not be identified.

A technique that can be used to correct for the inevitable fluctuations that occur in absolute retention times is to express component retention times relative to one or more reference peaks.

Reference peaks are identified in the identification table; the relative peak matching technique uses the retention times of the reference peak or peaks to modify the location of the peak matching windows to compensate for shifts in the retention times of sample peaks.

If no reference peak is specified, or at least one reference peak cannot be identified during the run, then the absolute retention times are used for peak identification.

Single Reference Peaks

A retention time window for the reference peak is created around its retention time. The largest peak falling within this window is identified as the reference peak. The expected retention times of all other peaks in the identification table are corrected in proportion to the ratio of the expected retention time to the actual retention time of the reference peak:

$$Corrected\ Expected\ Peak\ Time = Expected\ Peak\ Time \times \frac{Actual\ Reference\ Time}{Expected\ Reference\ Time}$$

Multiple Reference Peaks

Correcting retention times based on a single reference peak makes the assumption that the deviation of actual retention times from the expected retention times changes uniformly and linearly as the run progresses. Often during a long run the retention time changes non-uniformly. In such cases, better results are obtained using multiple reference peaks spaced at intervals across the run. This splits the signal into separate zones; within each zone, the deviation between retention times is assumed to change linearly, but the rate of change is determined separately for each zone.

The correction uses the following formula:

$$\text{Corrected Expected Peak Time} = b + m \times \text{Expected Peak Time}$$

where

b is the offset of the time correction zone

m is the slope of the time correction zone

NOTE The time-correction algorithm may fail if the retention times of multiple reference peaks are too close to each other and are not distributed across the total run time.

Retention Time Correction of Multiple Signals

In multi-signal analyses (see "Peak Identification in Multi-Signal Analyses" on page 166), whether the signals are from the same detector or from different detectors, retention times can be corrected universally for all detectors or specifically for each detector.

Correcting for All Detectors

The correction is made using the same single correction curve for all signals from all detectors. A retention time shift of a reference peak in a signal from one detector results in a correction of the retention time windows in all signals of all detectors.

This technique is useful for analyses using detectors that have the same detection characteristics (for example a diode-array detector and a variable wavelength detector), and are detecting analytes that elute from the same column.

Correcting for Each Detector

A separate time correction curve is used for each signal of a detector. A retention time shift of a reference peak in a signal from one detector results in a correction of the retention time windows of the signals of that detector only.

This technique is important for split-column analyses, or analyses involving detectors with different detection characteristics (for example a diode-array detector and a mass spectrometry detector).

Identifying Peaks Using Relative Retention Times

Many regulatory methods specify that relative retention times be used for the identification of minor components, known impurities or degradation products. Relative retention times are stable parameters, calculated relative to the retention time of a main reference peak:

$$RRT_i = (k'_i + 1)/(k'_{ref} + 1) = (RT_i)/(RT_{ref})$$

where

RRT_i is the relative retention time of the component

k'_i is the capacity factor of the component

k'_{ref} is the capacity factor of the reference

RT_i is the retention time of the component

RT_{ref} is the retention time of the reference

Where relative retention times are used in the peak identification process, the expected retention times in the calibration data are replaced by expected relative retention times. Before the peak identification process starts, the main reference peak to be used for the calculation of relative retention times is identified, and all retention times of the integration results are then converted to relative retention times. The peak identification process then proceeds in the same way as with absolute retention times (see "Identifying Peaks Using Absolute Retention Times" on page 161).

Peak Identification in Multi-Signal Analyses

Peak identification can include any number of calibrated and/or measured signals. Each calibrated compound comprises one or more peaks, which are usually (but not necessarily) in different signals. One of the peaks, usually the largest, in one signal is specified as the target, or main peak. The other peaks, in the other signals, are specified as secondary peaks.

Peak identification differentiates between signals, but not between detectors. That means that signals from different detectors are handled in exactly the same way as different signals from the same detector.

NOTE If the main peak is not identified, for example, because it has drifted out of the retention time window, the secondary peaks are also not identified.

Resolving Identification Conflicts

If, during the peak identification process, multiple measured peaks are found in the expected peak time window, the best match is retained (see "Multiple matches" on page 163) and other matches are discarded.

Similarly, if a measured peak fits into two or more expected peak time windows during the peak identification process, and is cloned for each window, only one of the cloned peaks (e.g. the best match) is used, and the duplicate peaks are discarded.

If one peak falls in the time window for two different compounds, the compound with the better match is identified, and the other compound is marked as unidentified.

This process leaves only the best matches in the results.

Signal Correlation: Assigning Unknown Peaks in Multi-Signal Analyses

At the end of the peak identification process, the results contain an entry for each peak in the calibration information; the peaks are linked with the corresponding expected compounds and signals.

The signal correlation process then attempts to match unknown measured peaks to the known compounds, within a signal correlation window of 0.03 minutes. Signal correlation proceeds as follows:

1. If there are neighboring peaks in other signals that are within the correlation window, the unknown peak is associated with them.
2. If the neighboring peak is a known peak, the unknown peak is linked to the known compound.
3. If the neighboring peak is an unknown peak, the peaks are associated and the signal correlation process is continued until all peaks have been processed.

4 For peak associations that contain only unknown peaks, a new unknown compound is added to the results and the peaks are linked to the unknown compound.

At the end of the signal correlation process, each measured peak is associated with a compound, either known or unknown.

Signal correlation is independent of peak identification. The signals can be correlated even if there are no expected peaks in the calibration information.

Peak Grouping

The peak grouping function calculates a total response for all peaks within a specified time range. The time range can be either contiguous (for example 4 – 6 minutes) or non-contiguous (for example 1 – 3 minutes and 6 – 8 minutes). The peak group is quantified using the response factor of a reference peak.

NOTE It is not possible to use a time reference peak to make retention time corrections to peak groups.

UV Compound Confirmation

The UV compound confirmation calculation is available only for methods that include the acquisition of spectra. The calculation compares the spectrum at the apex of the peak with a selected reference spectrum, and calculates a similarity value.

The UV compound confirmation parameters specify how the peak apex spectrum is used in the calculation, and how the UV compound confirmation is notified.

The UV compound confirmation calculation operates on identified peaks only.

Background Correction

You can select to correct spectra for any contribution from background absorbance using either one or two background spectra. The spectra used for background correction can be selected either automatically or manually. The spectra that are automatically selected are those at the peak start and the peak end. Background spectra selected manually can be from any part of the spectrum.

For details on how the background correction is made, see "Background Correction" on page 172.

Calculations

You can specify a noise threshold for UV compound confirmation. Signals below the threshold value are considered as noise, and are not used in the UV compound confirmation calculations.

Levels

Three levels of notification are available for UV compound confirmation:

- **Accepted** is notified in green when the similarity value is above the specified **Warning** level.
- **Warning** is notified in yellow when the similarity value is below the **Warning** level, but above the **Reject** level.
- **Rejected** is notified in red when the similarity value is below the specified **Reject** level.

If **Warning** and **Reject** are set to the same value, only **Accepted** and **Rejected** are notified.

If the similarity value is below the **Reject** level, the compound is not used in calibration and quantitation calculations. In such a case, the amount is reported as N/A.

UV Purity

The UV purity calculation is available only for methods that include the acquisition of spectra. The calculation compares each extracted spectrum with the spectrum at the apex of the peak, and calculates a similarity value. The UV purity value is the average of the similarity values.

The UV purity parameters specify the spectra that are used in the calculation, how they are used, and how the UV purity is notified.

Wavelength Range

By default, the complete wavelength range of the acquired spectrum is used for the purity calculation. The wavelength range group allows you to specify a reduced range.

Peak Spectra

Number of spectra

You can select to use all the acquired spectra in the UV purity calculation, or specify a reduced number of spectra from each peak that are extracted from the data.

If you select to use a reduced number of spectra, they are extracted at approximately equidistant points about the apex of the peak.

Minimum response range

The **Minimum response range** specifies the minimum difference between maximum and minimum responses that results in the inclusion of a peak in the UV purity calculation. Peaks with less than the **Minimum response range** are not used in calculations.

Background Correction

You can select to correct spectra for any contribution from background absorbance using either one or two background spectra. The spectra used for background correction can be selected either automatically or manually. The spectra that are automatically selected are those at the peak start and the peak end. Background spectra selected manually can be from any part of the spectrum.

For details on how the background correction is made, see "Background Correction" on page 172.

Calculations

You can specify a noise threshold for UV purity calculations. Signals below the threshold value are considered as noise, and are not used in the UV purity calculations.

Levels

Three levels of notification are available for UV purity:

- **Accepted** is notified in green when the UV purity value is above the specified **Warning** level.
- **Warning** is notified in yellow when the UV purity value is below the Warning level, but above the **Reject** level.
- **Rejected** is notified in red when the UV purity value is below the specified **Reject** level.

If **Warning** and **Reject** are set to the same value, only **Accepted** and **Rejected** are notified.

If the purity value is below the **Reject** level, the compound is not used in calibration and quantitation calculations. In such a case, the amount is reported as N/A.

Spectra Handling

Spectra handling is available only for methods that include the acquisition of spectra. The spectra handling parameters specify how the spectra are displayed in the **Spectra** tab of the single sample results view.

Wavelength Range

By default, the complete acquired wavelength range of the spectra is displayed. The wavelength range group allows you to specify a reduced range for display purposes.

Peak Spectra

Number of spectra

You can select to display all the acquired spectra, or specify a reduced number of spectra from each peak that are extracted from the data.

If you select to display a reduced number of spectra, they are extracted at approximately equidistant points about the apex of the peak. For details of how the spectra are extracted, see Chapter 1 of the Technical Reference Guide.

Minimum response range

The **Minimum response range** specifies the minimum difference between maximum and minimum responses that results in the display of a peak. Peaks with less than the **Minimum response range** are not displayed.

Background Correction

You can select to correct spectra for any contribution from background absorbance using either one or two background spectra. The spectra used for background correction can be selected either automatically or manually. The spectra that are automatically selected are those at the peak start and the peak end. Background spectra selected manually can be from any part of the spectrum.

Each compound spectrum in the peak is then corrected by subtracting a weighted average of the two selected background spectra. Each background spectrum is weighted by its relationship in time with the compound spectrum; the apex spectrum of a symmetrical peak has therefore equal contributions from both background spectra subtracted. A spectrum on the upslope of the peak has a greater contribution of the start spectrum subtracted; a spectrum on the downslope has a greater contribution of the end spectrum subtracted. The sum of the weights is always 1.

If only one background spectrum is selected, no weighting is done.

Calibration

Overview

The calibration process can be divided into two separate processes, which take place under different conditions, depending on the analytical situation.

Initial calibration is the starting process for a new analytical method. Response factors (the relationship between the response of the detector and the concentration of the compound) are determined for each compound, using specially-prepared calibration standards, which contain known amounts of the compound. The response factors are used to calculate absolute concentrations of the compounds in the samples. The response and concentration data for the compounds (as well as retention time data for peak identification) are stored in the calibration table.

After the calibration table for the analytical method has been set up, the calibration information (responses and retention times) in the calibration table can be updated based on new injections of the calibration standards. This is the process of recalibration, which can be carried out at any time, optionally including the existing calibration data in the update calculations.

Principles of Calibration

Figure 55 gives the main steps in the process of calibration.

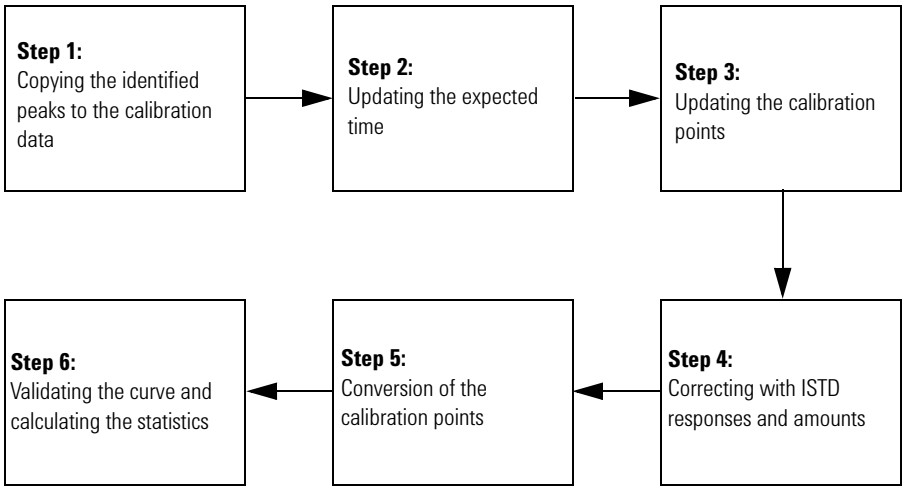


Figure 55 Calibration Flow Diagram

Step 1: Copying the identified peaks to the calibration data

The first step of the calibration process finds the identified peaks and copies them from the peak identification results to the calibration data. All peaks are copied. Invalid peaks (for example, missing internal standards) are flagged.

Step 2: Updating the expected times

In the second step, the time windows of the expected and identified peaks are updated. If specified during method setup, the expected time windows of the expected peaks that have not been found are also updated by interpolation from the measured times of the closest peaks above and below the expected peak time.

Step 3: Updating the calibration points

In step three, the calibrations points of all valid peaks that have been found are updated or recalculated. For fixed-amount calibrations, the calibration point is either averaged or replaced according to the parameters specified in the method. If a calibration point with this value does not already exits, a new

point is added. For variable-amount calibrations, the new calibration points are added to the peak, and the calibration curve is recalculated based on all measured calibration points.

Step 4: Correcting with ISTD responses and amounts

For ISTD methods, step 4 corrects the calibration points with reference to the internal standard responses and amounts. For ESTD methods, no corrections are carried out; relative amounts and relative responses are calculated.

Step 5: Conversion of the calibration curve

The calibration points for all peaks are matched to the specified calibration curve type, taking into account the calibration point weighting factors.

Step 6: Validating the curve and calculating the statistics

In step six, the calibration curve type and the treatment of the origin are validated against the number of calibration points. After validation, the calibration curve coefficients are calculated and evaluated, and the curve statistics are calculated.

Initial Calibration

Calibration Table

The calibration table specifies conversions of peak areas or heights into the units you choose according to the calculation procedure you select. It contains a list of retention times from a calibration run. These retention times are compared with retention times of peaks from a sample run. Where a match occurs, the peak in the sample is assumed to represent the same component as that in the calibration table, see “Peak Identification” on page 156. During an analysis, or while a report is being generated, the amounts entered for each peak are used to calculate the amounts for the calculation procedure

selected for the report. The type and amount of information required for creating a calibration table varies with the type of calculation procedure desired.

The following information is needed to create a calibration table:

- the retention time for each calibration mixture component peak, and
- the amount of each component used in making the calibration mixture, expressed in consistent units.

Calibration Curve

A calibration curve is a graphical presentation of the amount and response data for one compound obtained from one or more calibration standards.

Normally, an aliquot of the calibration standard is injected, a signal is obtained, and the response is determined by calculating the area or height of the peak, similar to Figure 56.

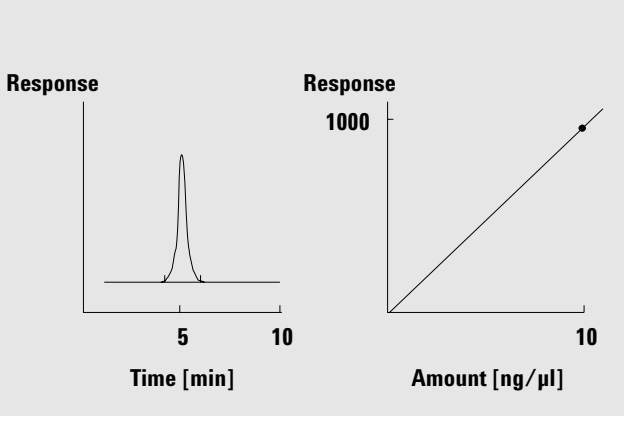


Figure 56 Calibration standard (10 ng/µl) and calibration curve

Samples

A sample contains an unknown amount of the compound to be quantified.

To find out how much of the compound is in the unknown sample, you must:

1. create a calibration curve for the compound,
2. inject an aliquot of your unknown sample and run the analysis in exactly the same way as for the calibration standard,
3. determine from the signal the response, which is the area or height of the peak due to the unknown amount of the compound, and
4. use the calibration curve to calculate the amount of the compound in the unknown sample.

For example, if the area of peak in the unknown sample is 500, you can determine that the amount in the unknown is 5 ng/µl, by using the calibration curve as shown in Figure 57.

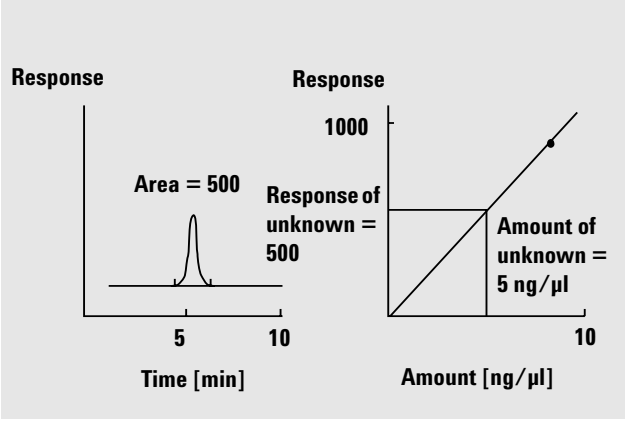


Figure 57 Signal from unknown sample, and calibration curve

Types of Calibration

The software offers two types of calibration: single level and multi-level.

Single Level Calibration

The calibration curve shown in Figure 58 contains one point, that is, one level. For the single-level calibration curve, the response of the detector is assumed to be linear over the working range of concentrations for the samples of interest. The response factor for a given component peak is given by the inverse of the slope of the calibration curve line through the point and the origin. A disadvantage of single-level calibration is that the detector response to the sample concentration is assumed to be linear and pass through the origin on a concentration versus response plot. This is not always true and can lead to inaccurate results.

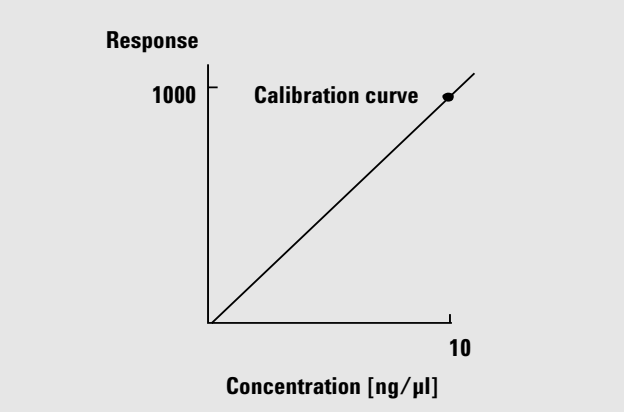


Figure 58 Single-level calibration curve

Multi-level Calibration

To obtain accurate quantitative results, a calibration curve should have at least two levels. These levels should bracket the amounts expected to be found in the unknown samples.

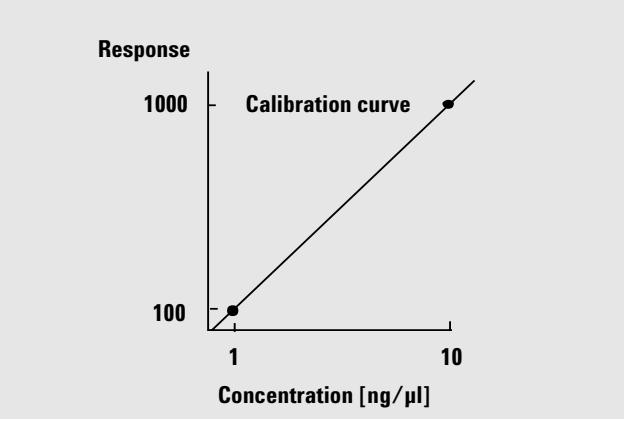


Figure 59 Two-level calibration curve

For example, if you want to quantify a compound, and the unknown samples are expected to range from 1-10ng/µl, then a calibration curve should have at least two levels as shown in Figure 59.

Multi-level calibration can be used either when it is not sufficiently accurate to assume that a component shows a linear response, or to confirm the linearity of the calibration range. Each calibration level corresponds to a calibration standard with a particular concentration of components. Calibration standards should be prepared so that the concentration of each component varies across the range of concentrations expected in the unknown samples. In this way it is possible to allow for a change in detector response with concentration and calculate response factors accordingly.

The multi-level calibration curve shown in Figure 60 has three levels and shows a linear fit through the origin. This method of linear fit through the origin is similar to the single-point calibration. The detector response to concentration is assumed to be linear. The difference between the two calibration types is that with linear fit, the slope of the detector response can be determined by a best fit through a number of points.

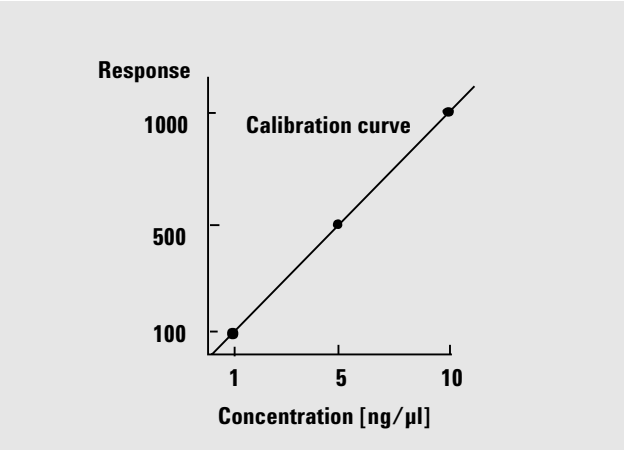


Figure 60 Multi-level calibration curve with three levels

The corresponding calibration table, which is the tabulation of the information used to generate this curve, might look similar to the one shown in Table 8:

Table 8 Calibration Table

Level	Amount (ng/µl)	Response (area counts)
1	1	100
2	5	500
3	10	1000

In this example, the calibration standards that were used to generate the three levels were identified as 1, 2 and 3.

Calibration Ranges.

Each multi-level calibration is valid over the range of concentrations used in the calibration standards. Extrapolation of a calibration curve, especially if it is non-linear, is at best an approximation.

Calibration Curve Fits

Various curve-fit calculations are available for use with multi-level calibration:

- Piecewise Linear
- Linear
- Log
- Power
- Exponent
- Quadratic
- Cubic
- Average Slope

Non-Linear Fits

In some cases, the detector response to changes in sample concentration is not linear. For these types of analysis, a linear regression calibration method is not appropriate and a multi-level non-linear calibration calculation should be used. For the calculation of non-linear calibration curves, a linear least squares fit (LSQ) is applied.

Recalibration

Recalibration is the process used when you want to update a level on a calibration curve. When you recalibrate, you run another sample that contains the same calibration compounds as the original. For methods using fixed-amount calibrations, it is most important to use the same amounts of the calibration compounds. When you run the calibration standard, you obtain updated response factors and retention times. You may also choose to average the response factors over a number of calibration runs so that response factors are weighted equally.

Why Recalibrate?

Most calibrations have a limited lifetime, due to changes in analytical conditions that are not under complete instrument control. Recalibration is necessary to maintain the accuracy of the analysis. For example, assume you have created a calibration table for the compound caffeine, which you use whenever you are required to quantify samples containing caffeine. At some point, you will need to replace the column/capillary. Although the column is replaced with exactly the same type, the new column will not behave in exactly the same way as the previous one did when you first created the calibration table for caffeine. Therefore, to ensure consistency, you recalibrate the levels in the calibration table before using the new column to analyze samples containing unknown amounts of caffeine. By doing this, you are quantifying samples analyzed under the same system conditions.

Manual Recalibration

You can enter peak calibration information manually and normalize the calibration table. Typically, a new calibration method is produced by running a calibration standard mixture, creating a calibration table, and entering the amounts of all calibrated peaks to obtain response factors. This approach is inefficient for some application, such as found in the petrochemical industry, where the same compounds have been analyzed for many years and the response factors for various compounds and detectors are readily available.

You create the calibration table manually by entering peaks and their response factors into the calibration table and recalibrating the method using a standard that contains at least one response reference peak.

Recalibration Options for Fixed-Amount Calibrations

You have a choice of ways to update the responses in the calibration table with the new calibration data.

NOTE Since the fixed-amount calibration always overwrites the calibration table, there is no calibration history for fixed-amount calibrations.

Average The average from all calibration runs is calculated using the following formula

$$Response = \frac{n \times Response + MeasResponse}{n + 1}$$

where

n = number of previous calibrations
MeasResponse = measured response

The new average response replaces the previous value.

Replace The new response values replace the old values, and the counter, n, is reset to 1.

No update Do not use this point as a calibration point.

Recalibration Options for Variable-Amount Calibrations

The choice of recalibration options for variable-amount recalibrations is the same as that for fixed-amount recalibrations, but the mode of operation is different.

Average All previous response values are kept and the new one is added to this list.

Replace All previously stored response values are deleted, and the new response value is used for calibration.

No update Do not use this point as a calibration point.

Ways to Recalibrate

The software offers three ways of recalibrating during a sequence of automated analyses:

- single update, where the calibration table is updated after each calibration standard,
- bracketing, where groups of samples are analyzed using sets of calibration standards run before and after the sample group,
- overall bracketing, where all samples are analyzed using all calibration standards in the sequence.

When recalibrating using a sequence, you specify the calibration strategy, and the software does the recalibration automatically at the appropriate point. For more information, refer to the Method Setup chapter of the Concepts Guide.

Retention Time Update

The calibration calculations set up or update the expected retention times in the calibration information. Different calculations are available to average out the random errors of the calibration runs and to compensate for drift of the analysis conditions:

Averaging the calibration data from more than one calibration run can be used to compensate for the random errors. Drift can be better compensated for by replacing the existing calibration data with the new measured values or by calculating a floating average.

Updating of the peak times is independent of the updating of the calibration points. The calculations are identical for initial calibration and recalibration; recalibration calculations are based on the calibration data since the last time the calibration values were replaced.

Floating Average

The floating average calculates new calibration values using measured values that are weighted. for details of the calculations, refer to the Technical Reference Guide.

Replacing

Replacing substitutes the current expected peak times with the new measured values and resets the peak time update counter to 1.

Update of Unidentified Peaks

The expected peaks that cannot be found in the peak identification results can be updated using the time drift of the adjacent peaks that have been found. The time drift of the peaks that have not been found is interpolated from the expected and measured times of the peaks that have been found at lower and higher times. If there is no peak at lower time, the time is interpolated from zero time to the peak with the lowest time. If there is no peak at higher time, the time is extrapolated from zero time through the peak with highest time. If peaks are missing, a warning is generated.

Sorting of the Calibrated Peaks and Compounds

The peaks are sorted by expected peak time. The compounds are sorted by their primary (main) peak times.

Time Window Limit Calculations

The peaks time window limits are recalculated after the update of the expected peak times. For details of the calculation used, see the Technical Reference Guide

Calibration Point Update

The calibration calculations set up or update the responses and amounts in the calibration information. Updating of the calibration points is independent of the updating of the peak times. Recalibration calculations are based on the calibration data since the last time the calibration values were replaced.

Fixed-Amount Calibrations

For fixed-amount calibrations, where the amounts of calibration standards injected are the same as the entry in the calibration table at each level each time the calibration is run, two calculation methods are available for updating the calibration points:

Averaging the calibration data from more than one calibration run can be used to compensate for the random errors. Drift can be better compensated for by replacing the existing calibration data with the new measured values.

NOTE Since the fixed-amount calibration always overwrites the calibration table, there is no calibration history for fixed-amount calibrations.

Replacing Replacing substitutes the current area or height values with the new measured values and resets the response update counter to 1. The time values are calculated and updated first (see "Retention Time Update" on page 187), and then the responses are updated.

No update Do not use this point as a calibration point.

ISTD Methods

For ISTD calculations, the raw height, area and amount data are replaced by the ratios of the compound and ISTD responses. The calibration curve is calculated from the response ratio and amount ratio of the calibration points.

Variable-Amount Calibrations

When the calibration point response and amount averages are calculated in fixed-amount calibrations, the historical measured values are lost. This means that the calibration curve calculations are difficult to validate. To avoid the problems caused by calibration point averaging, all measurements can be stored as separate points; in this mode, each point may have a different amount and response – this corresponds to the real-life situation, where each calibration standard may have a slightly different concentration.

Average When variable-amount calibration is used, the calibration update always adds new calibration points.

Replacing Replacing substitutes the current area, height and amount values with the new measured values and resets the response update counter to 1. The time values are calculated and updated first (see "Retention Time Update" on page 187), and then the responses are updated.

NOTE In variable-amount calibrations, replacing deletes all calibration history entries of the level that was replaced.

No update Do not use this point as a calibration point.

Quantitation

Overview

After the peaks have been integrated and identified, the next step in the analysis is quantitation. Quantitation uses the response (peak area or height) to determine the concentration of a compound in a sample.

A complete quantitative analysis involves many steps which are briefly summarized as follows:

- Know the compound you are analyzing.
- Establish a method for analyzing samples containing this compound.
- Analyze a sample or samples containing a known concentration or concentrations of the compound to obtain the response due to that concentration.
- You may alternatively analyze a number of these samples with different concentrations of the compounds of interest if your detector has a non-linear response. This process is referred to as *multi-level calibration*.
- Analyze the sample containing an unknown concentration of the compound to obtain the response due to the unknown concentration.
- Compare the response of the unknown concentration to the response of the known concentration to determine how much of the compound is present.

To obtain a valid comparison for the unknown sample response to that of the known sample, the data must be acquired and processed under identical conditions.

Principles of Quantitation

Figure 61 shows the main steps in the process of quantitation.

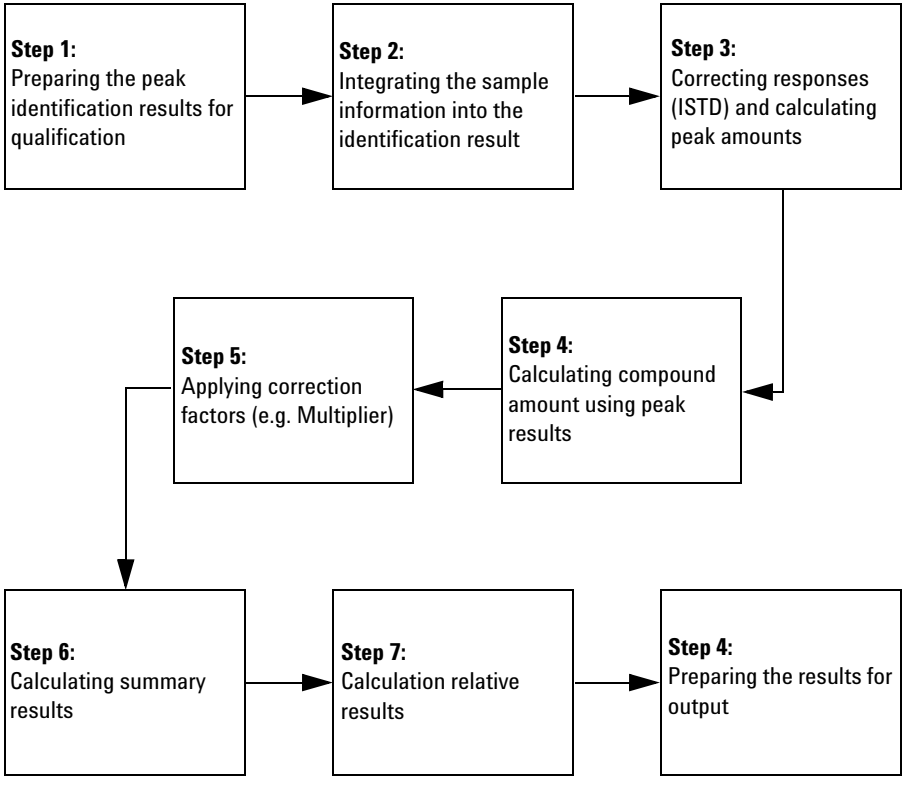


Figure 61 Quantitation Flow Diagram

Step 1: Preparing the Peak Identification results for quantitation

The first step of the quantitation process copies the essential parameters (Calculation Base and Calculation Type) from the calibration information into the quantitation results.

Step 2: Integrating the Sample Information into the identification results

In the second step of the quantitation process, the sample information is integrated into results of the peak identification process.

Step 3: Correcting responses (ISTD) and calculating peak amounts

Step 3 is divided into two parts: in the first part, each peak response is corrected by reference to the relevant internal standard response. In the second part, the peak amounts are calculated from the corrected responses.

The signal is first searched for the ISTD reference peak. If it is not found in this signal, the main peak of the ISTD reference compound is used to make corrections.

In the second part, the amount of each peak is calculated. The calculations are based on the sample information, the response of the peak (height or area) and the corresponding calibration curve.

The peak amounts of unknown peaks are calculated first; the quantitation parameters specify if the unknown peaks are calculated with a fixed response factor, the factor of a known peak or not at all.

The peak-specific parameters are usually retrieved from the calibration curve. However, it is possible to use the calibration data of a different compound and peak, or to use a fixed factor.

Step 4: Calculating compound amounts using peak results

In step 4, the compound amounts are calculated from the results of the main peak.

Step 5: Applying correction factors

The sixth step takes the calculated peak and compound amounts and applies all relevant correction factors from the sample data, for example multipliers, dilution factor and sample amount calculations.

Step 6: Calculating summary results

In step 7, the summary results, for example area, height and amount sums, are calculated based on the corrected results. The ISTD compounds are not included in the calculations.

Step 7: Calculating relative results

Step 8 calculates the relative results, Area%, Height% and Norm% based on the peak responses (area or height), compound amounts and summary results from step 7. Results for ISTD compounds are always zero.

Step 8: Preparing the results for output

In the final step, the ESTD% and ISTD% results are prepared for output by scaling the amount results by the Sample Amount.

Custom Calculations

You access Cerity NDS for Pharmaceutical QA/QC custom calculations through a familiar spreadsheet-style interface, similar to Microsoft® Excel. The number and type of worksheets for which you can set up calculations depends on the type of method — single sample or sequence — and the type of result. The variables available from the database also depend on the result type.

Result types available for custom calculations

A *result type* is a category of result based on an injection, a group of samples or standards, or a sequence.

For single samples, custom calculations can be set up for single injection results and for multiple-injection summaries. You use method variables, including custom sample variables set up in the method, and compound and peak quantitation results to set up the calculations.

A *sample-type group* is a set of sequence results grouped together according to the sample type, such as calibration standard, QC sample, or sample groups. You can also define your own custom sample groups.

For sequences, custom calculations can be set up for single injection results, multiple injection summaries and *sample-type groups*. You can also set up cross-sample-group calculations using **group identifier** and **sub-group identifier** worksheets.

The process of setting up custom calculations

During custom calculation setup you add columns to the worksheet to contain fields, variables and results already in the database and then add new columns to contain the formulas to calculate the new variables that you define.

A variety of mathematical operators and conditional statements are available to operate on the variables. The syntax for combining the variables with these functions is essentially the same as that of Microsoft Excel. See the Reference online help to find descriptions of all the available functions.

Note that if you add compounds to the method at a later date, you need to rework the custom calculation worksheets in order for the additional compound results to be calculated.

Custom calculation generation

To help you understand the setup process, look at how custom calculations are generated. As you view this figure, note that the system uses single injection custom calculation results to calculate multiple injection summary results. These, in turn, can be used to calculate sample-type group results. All results are stored to the database and taken from the database.

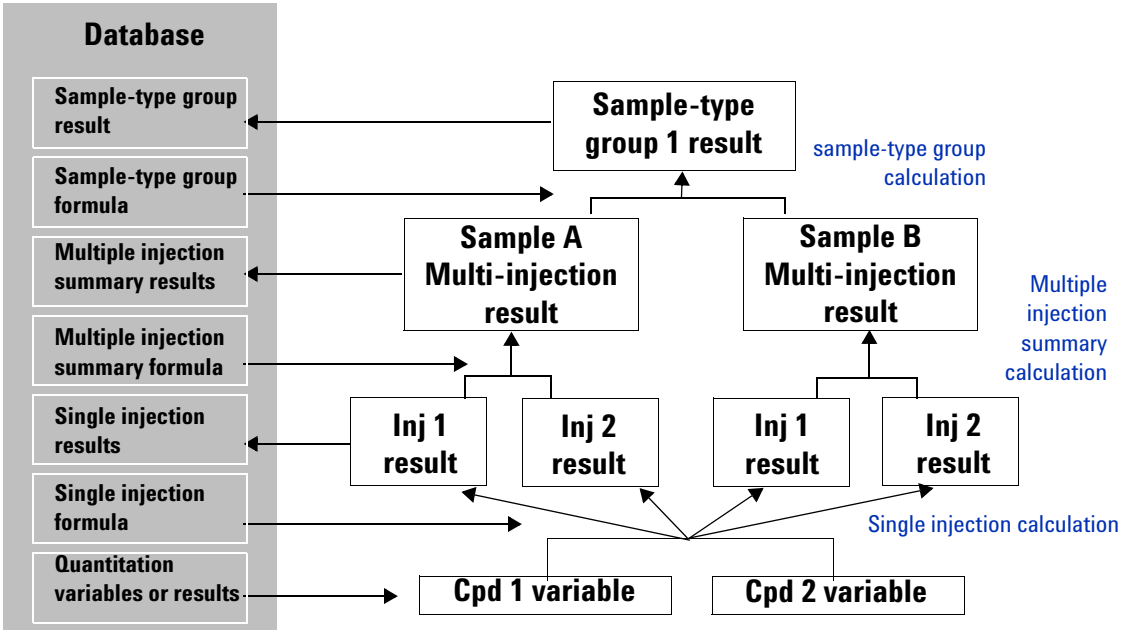
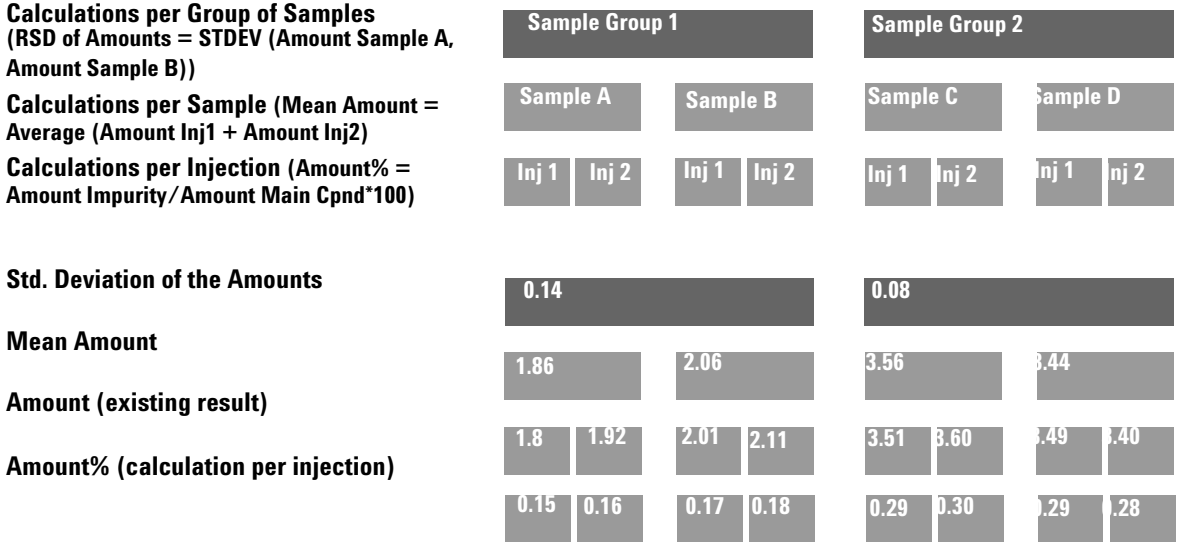


Figure 62 Hierarchy of generated calculations

Example of calculation generation



Calculation worksheet setup

You set up custom calculations through a familiar spreadsheet-style interface, similar to Microsoft Excel. These worksheets enable you to set up and perform calculations on the result types for each stage of the calculation process.

- The **Single injection** worksheet, operating after quantitation, enables you to set up a single injection calculation for all sample types. (Figure 64)
- The **Multi-injection** summary worksheet enables you to set up calculations for multiple injections of the same sample (one calculation for all sample types). (Figure 65)
- The sample-type group worksheet enables you to set up calculations for a group of the same sample type and for custom sample groups. (Figure 66)

- The **Group Identifier** worksheet allows you to make calculations on selected samples in a sequence, for example, a set of samples designated for system suitability tests. (Figure 67)

Existing variable/result addition

In the calculation worksheets, you first add a column that contains an existing variable or result before you can set up a new formula or calculation that uses this variable or result. The existing variables or results available depend on the result type.

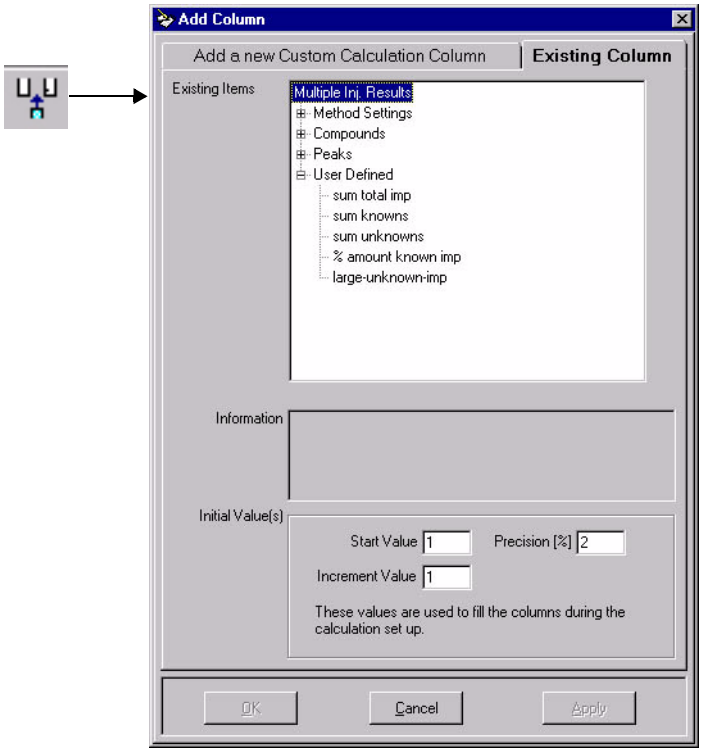


Figure 63 List of existing variables/results for multi-injection summary calculations

Single injection variables or results

- Method and sample variables
- Compound integration and quantitation results

- Peak integration and quantitation results
- Custom sample variables (set up in the Sample Variables section of the method)

Multi-injection summary variables or results

- Method variables
- Compound integration and quantitation results
- Peak integration and quantitation results
- User-defined variables or results — these are the results of the custom calculation from the formula set up in the single injection worksheet

Sample-type group variables or results

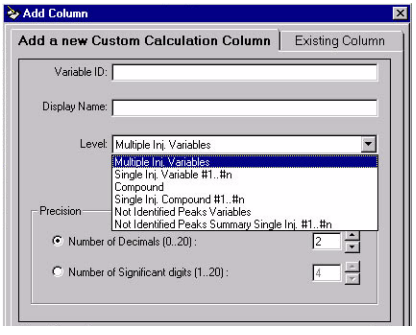
Only the user-defined results of the custom calculations set up in the multi-injection summary worksheet are available as variables to set up a calculation for the sample-type group.

Group Identifier variables or results

All results and variables of the custom calculations set up in the multi-injection summary worksheet are available as variables to set up a calculation for the group identifiers.

The user interface of the Cerity **Report Template Editor** and the Glossary in online help contain descriptions of all the variables and results that are available for custom calculations.

New custom calculation setup You also add a worksheet column to set up a formula for a custom calculation whose result can be used as a variable for other calculations. You enter both the **Display name** and the system ID for the calculation that you want to set up.



A *level* is a row on the worksheet that contains the formula or result of the new calculation

You also select a *level* for the calculation. Calculation levels for the worksheet depend on the result type. See examples of the worksheets below and on the following page to view the level that you choose for the calculation.

Levels for single injection worksheet

The figure below describes levels for single injection.

Single inj. variable level — This row contains the formula to produce a summary result for the single injection.

Identified compound or unidentified peak summary levels — These rows contain the formulas to produce summary results for all identified compounds or unidentified peaks.

Identified compound or unidentified peak #1...#n levels — These rows contain formulas for individual compound or peak calculations.

	A B C	D	E	F	G	H
1				New	New	New
2		Amount	Peak Area	Perc. of Nicotin	Sum Metabolites	AreaSum not ident. Peaks
3	-			%	mg/kg	
4	Single Inj. Results					
5	Single Inj. Variables				2.996	
6	- Identified Compounds					
7	Nicot. Metabolit I	0.9993	1.0097	24.885		
8	Nicot. Metabolit II	1.9968	1.9896	49.724		
9	PCH	3.0126	2.9811			
10	Nicotin	4.0158	3.9833			
11	- Not Identified Peaks					18.005
12	Unknown 1		5.0455			
13	..		6.0103			
14	Unknown n		6.9492			

Figure 64 Single injection worksheet

Levels for multi-injection summary worksheet

The figure below describes levels for a multi-injection summary.

Multiple inj. variable level — This row contains the formula to produce a summary result for all the single injections.

Single inj. variable #1..#n level — These rows contain the formulas for calculations on the single injection result from the single inj variable calculation set up in the single injection worksheet.

Identified compound or unidentified peak summary levels — These rows contains the formulas to produce summary results for all the single injections for a compound or peak.

Identified compound or unidentified peak #1..#n levels — These rows contain formulas for calculations for individual single injections for each compound or peak.

	A B C	D	E	F	G	H	I
1				New	New		New
2		Amount	Sum Metabolites	Mean Amount	RSD of Sum Amount Metabolites	AreaSum not ident. Peaks	Mean of AreaSum not ident. Peaks
3	-		mg/kg	mg/kg	%		
4	Multiple Inj. Results						
5	- Multiple Inj. Variable				12.58		
6	Single Inj. #1		2.996				
7	..		3.182				
8	Single Inj. #n		3.978				
9	- Nicot. Metabolit I			1.777			
10	Single Inj. #1	0.9993					
11	..	1.9496					
12	Single Inj. #n	2.3811					
13	- Nicot. Metabolit II			3.018			
14	Single Inj. #1	1.9968					
15	..	3.0455					
16	Single Inj. #n	4.0103					
17	+ PCH			7.975			
21	- Nicotin			5.347			
22	Single Inj. #1	4.0158					
23	..	5.9183					
24	Single Inj. #n	6.1065					
25	- Not Identified						18.78
26	Single Inj. #1					18.005	
27	..					17.345	
28	Single Inj. #n					20.999	

Figure 65 Multi-injection summary worksheet

Levels for sample-type group worksheet

The Figure 66 describes levels for sample-type groups.

Sample-type group variable level — This row contains the formula to produce a summary result for each group of samples in the tab.

Multi-injection summary (sample) variable #1..#n level — These rows contain the formulas for calculations from the multiple inj variable calculation set up in the multi-injection summary worksheet.

Identified compound or unidentified peak summary levels — These rows contains the formulas to produce summary results for all the group samples for a compound or peak.

Identified compound or unidentified peak #1..#n levels — These rows contain formulas for calculations for individual group samples for each compound or peak.

	A B C	D	E	F	G	H	I
1			New		New		New
2		Mean Amount	Mean Amount per Lot	RSD of Sum Amount Metabolites	Mean of RSD Metabolites	Mean of AreaSum not ident. Peaks	Mean AreaSum per Lot
3	-	mg/kg	mg/kg	%	%		
4	User Sample Groups						
5	- Sample Group Variable				12.59		
6	Sample Inj. #1			12.58			
7	..			12.02			
8	Sample Inj. #n			12.97			
9	- Nicot. Metabolit I		2.002				
10	Sample Inj. #1	1.777					
11	..	1.996					
12	Sample Inj. #n	3.002					
13	- Nicot. Metabolit II		4.995				
14	Sample Inj. #1	3.018					
15	..	4.988					
16	Sample Inj. #n	5.982					
17	+ PCH		8.003				
21	- Nicotin		10.933				
22	Sample Inj. #1	5.347					
23	..	10.980					
24	Sample Inj. #n	11.883					
25	- Not Identified						22.295
26	Sample Inj. #1					18.78	
27	..					22.02	
28	Sample Inj. #n					22.97	

Figure 66 Sample-type group worksheet

Group Identifier worksheet

The **Group Identifier** worksheet allows you to assign samples to different groups so that you can perform different calculations on them. For example, you might want to include a set of suitability-testing samples in your sequence. These samples will need to be treated differently from the other samples; they will need a different set of calculations. You set up the system suitability samples as a group, and perform the system suitability calculations in the **Group Identifier** worksheet. The **Group Identifier** worksheet bases its calculations on values in the **Multi-Injection** worksheet; values in other worksheets have no influence.

The **Group Identifiers** are set up in the custom calculator worksheet during method setup. You allocate samples to the groups when you set up the sequence table. The sequence table

also offers a further level of classification, the **Sub-group Identifier**. **Sub-group Identifiers** are not set up during method development, but are a part of the sequence definition. This gives you great flexibility in the use of **Sub-group Identifiers**, since they can be specified and allocated afresh for each sequence. Figure 66 shows the layout of the **Group Identifier** worksheet.

Sample group variable level — This row contains the formula to produce a summary result for each Group Identifier.

Identified compound level — Each compound level contains all the Group Identifiers.

Group Identifier level — These rows contain formulas to produce results for the Group Identifiers for individual compounds.

Sub-group Identifier level — These rows contain formulas to produce results for Subgroup Identifiers within individual Group Identifiers for each compound.

	A B C D	E	F	G
1				New
2			Mean Resolution	Mean Resolution overall
3	-			
4	Group Identifier			
5	-	Sample Group Variable		
6	-	Group Identifier 1		
7	-	Sub group identifier #1		
8		Sample #1		
9		..		
10		Sample #n		
11	-	...		
12		Sample #1		
13		.		
14		Sample #n		
15	-	Sub group identifier #n		
16		Sample #1		
17		.		
18		Sample #n		
19	+	Group Identifier 2		
32	-	Cmpd 1		
33	-	Group Identifier 1		2.00
34	-	Sub group identifier #1		
35		Sample #1	1.00	
36		..	2.00	
37		Sample #n	2.99	
38	-	...		
39		Sample #1	4.02	
40		..	5.02	
41		Sample #n	5.96	
42	-	Sub group identifier #n		
43		Sample #1	6.95	
44		..	7.99	
45		Sample #n	8.91	
46	+	Group Identifier 2		
59	-	Cmpd 2		
60	+	Group Identifier 1		
73	+	Group Identifier 2		
86	-	Cmpd 3		
87	+	Group Identifier 1		

Figure 67 Group Identifiers worksheet

See the Reference section in the online help for definitions of all the functions and conditional statements available to you.

Functions and conditional statements

To set up a formula, enter a mathematical function or conditional statement and the rows that it operates on into a single cell. A calculation must begin with an equals sign (=). For example, the cell entry to calculate the Mean Amount per Lot of Nicotine Metabolite I as in Figure 66 on page 203 would look like this: =AVERAGE(D10:D12)

You can access a complete list of mathematical functions in the Custom Calculations workspace when you click the **Function** button on the Tools toolbar.

Values displayed during setup

During the setup of the calculation, Cerity NDS for Pharmaceutical QA/QC produces random numbers to populate the cells, since results may not always be available.

Examples of custom calculations

See the Getting Started Exercise, "Set up a method to identify impurities", to practice setting up a custom calculation.

You can find instructions in the online help (HowTos/Setting Up Methods/Set up custom calculations) to set up the following custom calculations:

- Peak area statistics for multiple injections
- % of a known impurity
- % of total known impurities
- % of an unknown impurity
- % of total unknown impurities
- Average response factors for multiple injections
- Average response factor for each compound in the calibration standard group
- Standard deviation for the average response factor for each compound in the standards
- Relative standard deviation (RSD for the average response factor for each compound in the standards
- Relative response factor (RRF) between peaks

- Precision of check standards compared to calibration standards
- Concentration and real amount of a sample
- Adjusted amounts for individual compounds

Relationship between worksheets

The calculation worksheets are inter-related, as shown in the above example and in Figure 68 and Figure 69. The results from the single injection worksheet are used in the multi-injection summary worksheet; these results are in turn used in the sample-type group worksheet.

Single Injection Worksheet

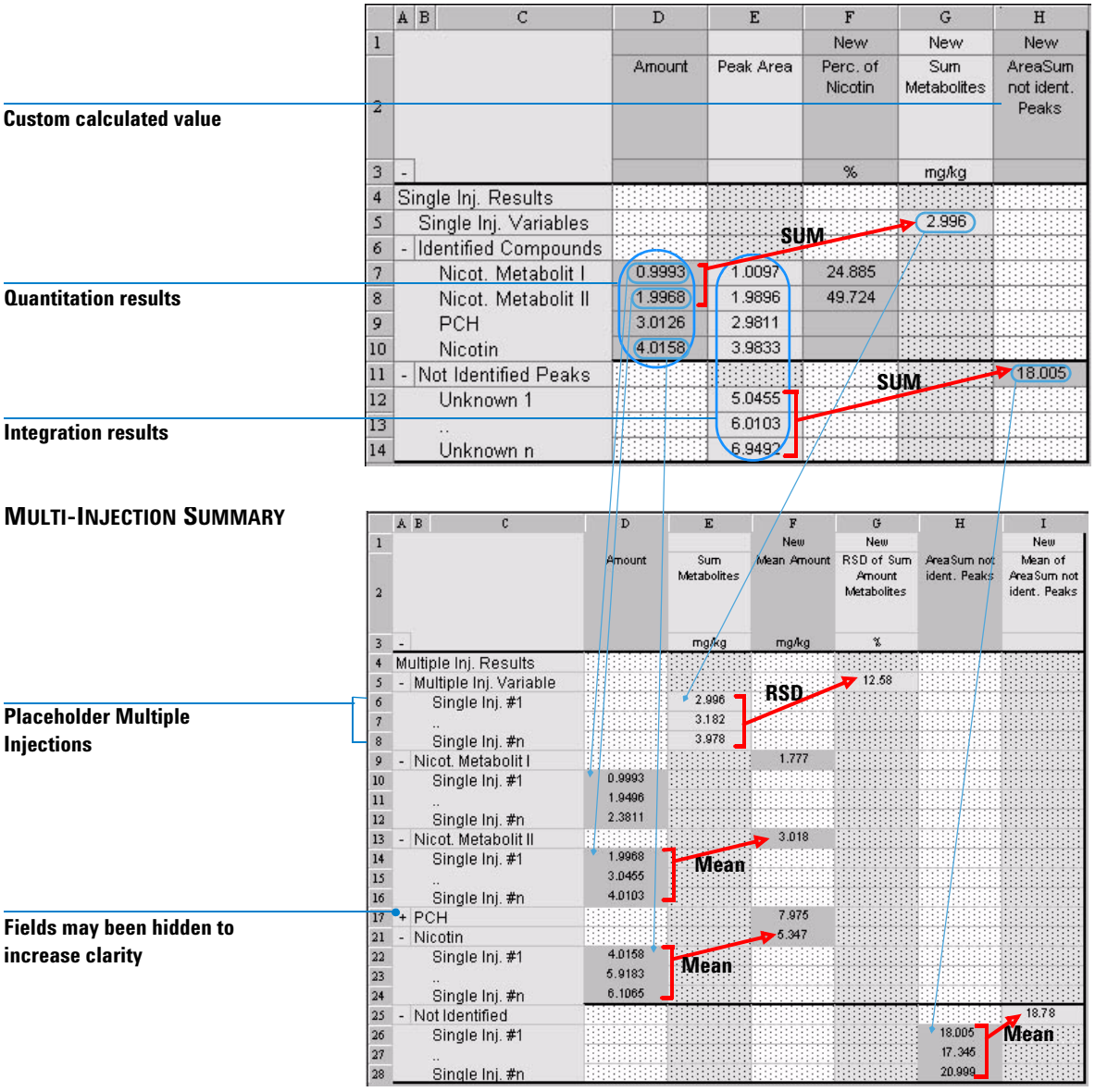
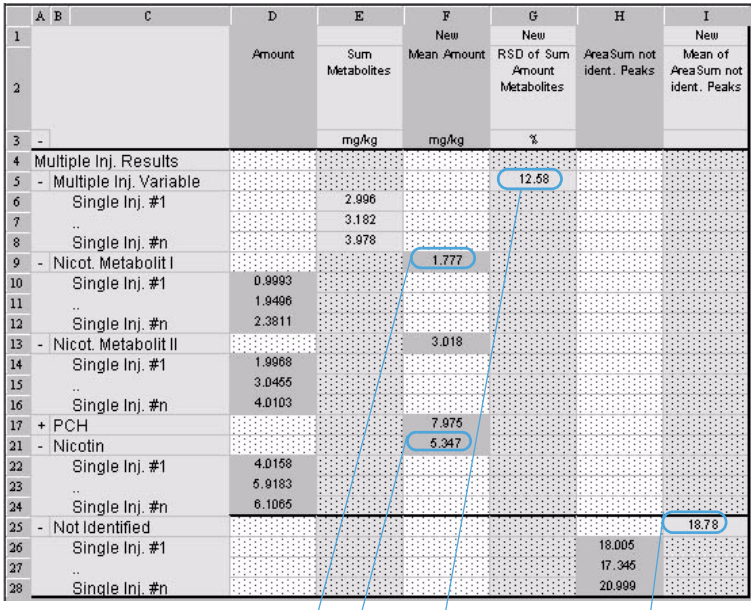


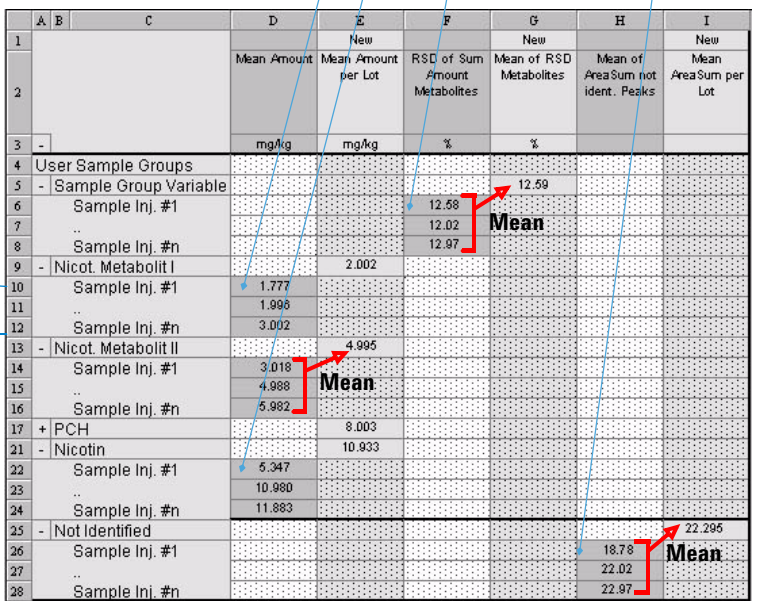
Figure 68 Relationship between the Single injection worksheet and the Multi-injection summary worksheet

Multi-injection summary worksheet



	A	B	C	D	E	F	G	H	I
1						New	New		New
2				Amount	Sum Metabolites	Mean Amount	RSD of Sum Amount Metabolites	AreaSum not ident. Peaks	Mean of AreaSum not ident. Peaks
3	-				mg/kg	mg/kg	%		
4	Multiple Inj. Results								
5		-	Multiple Inj. Variable				12.58		
6			Single Inj. #1		2.996				
7			..		3.182				
8			Single Inj. #n		3.978				
9		-	Nicot. Metabolit I			1.777			
10			Single Inj. #1	0.9993					
11			..	1.9496					
12			Single Inj. #n	2.3811					
13		-	Nicot. Metabolit II			3.018			
14			Single Inj. #1	1.9968					
15			..	3.0455					
16			Single Inj. #n	4.0103					
17		+	PCH			7.975			
21		-	Nicotin			5.347			
22			Single Inj. #1	4.0158					
23			..	5.9183					
24			Single Inj. #n	6.1065					
25		-	Not Identified						18.78
26			Single Inj. #1					18.005	
27			..					17.345	
28			Single Inj. #n					20.999	

Sample-Type Group Worksheet



	A	B	C	D	E	F	G	H	I
1					New		New		New
2				Mean Amount	Mean Amount per Lot	RSD of Sum Amount Metabolites	Mean of RSD Metabolites	Mean of AreaSum not ident. Peaks	Mean AreaSum per Lot
3	-			mg/kg	mg/kg	%	%		
4	User Sample Groups								
5		-	Sample Group Variable				12.59		
6			Sample Inj. #1			12.58			
7			..			12.02	Mean		
8			Sample Inj. #n			12.97			
9		-	Nicot. Metabolit I		2.002				
10			Sample Inj. #1	1.777					
11			..	1.998					
12			Sample Inj. #n	3.002					
13		-	Nicot. Metabolit II		4.995				
14			Sample Inj. #1	3.018					
15			..	4.988	Mean				
16			Sample Inj. #n	5.982					
17		+	PCH		8.003				
21		-	Nicotin		10.933				
22			Sample Inj. #1	5.347					
23			..	10.980					
24			Sample Inj. #n	11.883					
25		-	Not Identified						22.295
26			Sample Inj. #1					18.78	Mean
27			..					22.02	
28			Sample Inj. #n					22.97	

Placeholder Samples in Sample-Type Group

Figure 69 Relationship between the Multi-injection summary worksheet and the Sample-type group worksheet

Result Approval/Rejection

Cerity NDS for Pharmaceutical QA/QC lets you approve, reject, send to rework and lock or unlock results according to the procedures in your organization. You confirm the review of each result using the **Accept/Reject Results** dialog box.

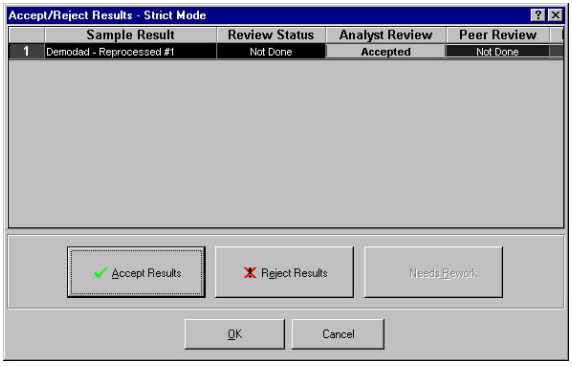


Figure 70 **Accept/Reject Results** dialog box

The review applies to all results of a sample, that is, individual injections are reviewed individually, and the summary result is assigned to the sample or sequence.

Sample acceptance levels

There are three Cerity NDS for Pharmaceutical QA/QC acceptance levels defined for all results:

1. Analyst review (Level 1) required
   Acceptance may be performed by users with Level 1, 2, or 3 review rights.
2. Peer review (Level 2) required
   Acceptance can only be performed by users with Level 2 or 3 review rights.
3. Managerial review (Level 3) required
   Acceptance can only be performed by users with Level 3 review rights.

User review rights

Users can be allocated one of four review rights by the system administrator in the Cerity NDS Administration application. These rights permit users to accept or reject results at a defined acceptance level.

0	Not permitted to do a review
10	Permitted to do an analyst review (Level 1)
20	Permitted to do a peer review or an analyst review (Level 2)
30	Permitted to do a managerial review or an analyst or peer review (Level 3)

Review Modes

At installation the system administrator defines the review mode as strict or non strict.

Strict Review

Strict Review is a system-specified policy, where the laboratory can choose only the number of levels of approval. Strict Review mode uses the following rules:

- For a result to attain an overall status of **Accepted**, all review levels of the result must be set to **Accepted.**
- Each level must be signed off before the next level review can be carried out (that is, Level 1 acceptance must be set before Level 2, and Level 2 before Level 3).
- Only a reviewer with the highest approval level defined for the result can change the state of the result from **Accepted** to **Needs Rework**.

Non-Strict Review

Non-Strict Review is a laboratory-defined policy. Non-Strict Review mode uses the following rules:

- Not all acceptance levels need be set; a higher level may accept for a lower level or overrule a lower-level rejection.
- Acceptance levels may be carried out in any order.
- All reviewers may change the review status from **Accepted** to **Needs Rework**, but only the highest level may reset the overall review status to **Needs Rework**.

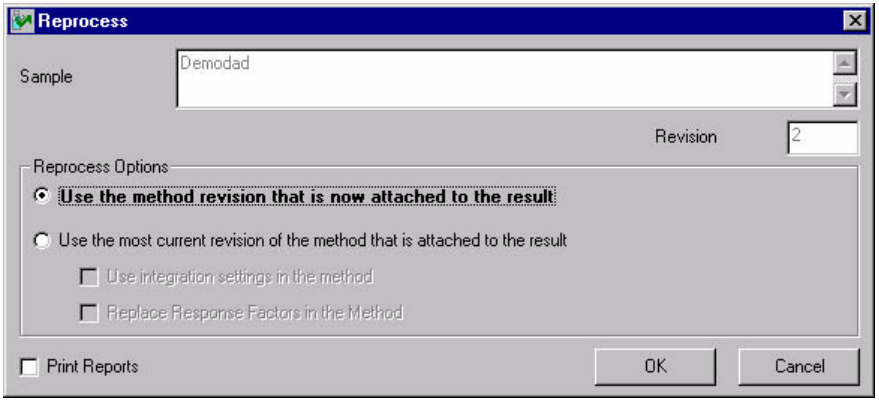
Reprocessing Calibrated Methods

Reprocessing is the action of recalculating analysis results based on modified processing parameters. You can only reprocess a selected single sample or sequence. You cannot reprocess single injections or individual samples in a sequence.

If a sample or sequence needs rework, you can make changes to the results or to the method and then reprocess the result.

Available reprocessing options

All method parameters and sample information used to produce a result are attached to the result. This design structure determines the options for reprocessing.



Reprocessing option selection

The reprocessing options that you select depend on the reasons for reprocessing. When you are reprocessing calibrated

methods, you need to consider carefully what you are trying to achieve. Use the following guidelines to make your selection:

- **For Calibration Standards using instrument specific calibration Methods:**

  When you are reprocessing a single sample calibration standard or instrument-specific sequence containing calibration standards, and want your changes to have impact on future quantitations select the option **Use the most current revision of the method that is attached to the result** and (important!) check the box **Replace Response Factors in the Method**.

  If your recalibration should not update the method keep the checkbox **Replace Response Factors in the Method** unchecked, and Select the option **Use the method revision that is now attached to the result.** This branches out the recalibration effects from the method. Only if you need to roll in method changes to the sample/ sequence quantification you MUST select **Use the most current revision of the method that is attached to the result**.

- **For 'Non calibration standards' single samples and sequence using specific calibration methods:**

  When reprocessing single sample blanks, samples or QC controls, non recalibrating instrument specific sequences, or sequence-specific calibrated sequences, select the option **Use the method revision that is now attached to the result**,

  Only in the case that you want to use calibration or other method parameter changes - select the option **Use the most current revision of the method that is attached to the result**.

- **Replay of old data:**

  The option **Use the method revision that is now attached to the result** is also usable to replay the exact same calculations as they were previously done. It is useful to show historical results from many years ago being re-evaluated again. Also proves that nothing in the result was modified since then.

  Use Table 9 to find the reprocessing option you need for more specific cases.

Table 9 Use this table to help you select the reprocessing options in specific situations

.If your reason for reprocessing is:	Then do this.	Cerity NDS for Pharmaceutical QA/QC does this.
• To change some of the integration settings for individual injections, or • To enter new values for the sample entry fields, or • To remove calibration standards from the calibration data, or • To reprocess a sample or sequence that has been acquired with no processing or only partial processing.	• After you make your changes, select the reprocessing option, **Use the method revision that is now attached to the result.**	**a** Initializes the calibration table with the initial calibration table of the sample or sequence. **b** For instrument-specific methods, if the calibration table is current the method is updated according to the settings and calibration standards. In all other cases, a new calibration node, separate from the method is created. The standards marked invalid in the calibration workspace are NOT used. **c** Calculates quantitation, custom calculations and limits.
• To use new integration settings in the most current revision of the method for all injections, or • To reprocess old sequence data using a new calibration table in the most current revision of the method.	• Select the reprocessing option, **Use the most current revision of the method that is attached to the result.**	**a** Initializes the calibration table with the most current calibration table revision of the method. **b** If the reprocess data is from a previous calibration revision, or if the method is sequence-specific, and you want to update the method, mark the **Replace the response factors in the method** check box. In all other cases, the method is updated automatically. The standards marked invalid in the calibration workspace are NOT used. **c** Quantifies calibration standards with the most current calibration table revision. **d** Calculates quantitation, custom calculations and limits with the new settings from the method.
• To reprocess the data with an updated method revision that includes new sample variables (does not affect calibration).	• After you make your method changes, set up reprocessing for new sample entry fields. • Enter values for the new sample variables, and select the option, **Use the most current revision of the method that is attached to the result.**	• Does the same steps as above. • Any other changes are also used both for this selection and above. Because Cerity NDS for Pharmaceutical QA/QC attaches the most current revision of the method to the result when you set up processing for new sample entry fields, you select Use the method revision that is now attached to the result

Table 9 Use this table to help you select the reprocessing options in specific situations (continued)

.If your reason for reprocessing is:	Then do this.	Cerity NDS for Pharmaceutical QA/QC does this.
• To reprocess the data with an updated method revision that includes new compounds (affects the calibration).	• After you make your method changes, set up reprocessing for new sample entry fields. • Enter values for the new sample variables, and select the option, **Use the most current revision of the method that is attached to the result.**	**a** Reintegrates single injection results with the method settings. **b** Updates the calibration table according to the method settings and calibration standards in the sequence. The standards marked invalid in the calibration workspace are used. **c** Calculates quantitation, custom calculations and limits with the new settings from the method. Any other changes are also used.
• To reprocess with a different method.	• Set up reprocessing for a different method. • Enter any values for the sample variables or compound amounts in the new method, and select the option, **Use the method revision that is now attached to the result.**	**a** Reintegrates single injection results with the method settings. **b** Updates the calibration table according to the method settings and calibration standards in the sequence. The standards marked invalid in the calibration workspace are used. **c** Calculates quantitation, custom calculations and limits with the new settings from the method. Any other changes are also used.

CAUTION When you reprocess with a different method, an additional calibration node with exactly the same name is inserted into the selection tree.

Reintegration

The Pharmaceutical QA/QC provides tools for reintegration. You can reintegrate modified initial events and timed events for results or use autointegrate to let the system set the parameters for the integration. You can also manually integrate individual peaks with your own baselines. You save the new settings and results to the database. You must still reprocess the result in order to recalibrate and requantitate.

Result and Calibration Table Revisions

To follow the reprocessing of results, you must understand the result and calibration table revision numbering system.

Result revisions

When a single sample or sequence is created, its revision number is set to 1. The revision number is incremented when the single sample or sequence is saved to the database. Running the single sample or sequence increments the revision number by one.

The result that is produced has the same revision number as the single sample or sequence that was run. This is because the result contains the revision of all the sample, sequence and method information in the single sample or sequence that was run. The result revision number is incremented if one or more parameters is changed in the result.

Revision changes in the Result context

Single update sequence (no bracketing)

Table 10 Revision changes for a single update sequence

Step	Action (always using *Save to database*)	View	Revision numbers		
			Sequence	Sample	Injection Chromatogram
1	Create a sequence	Sample	1	N/A	N/A
2	Add a sample to the sequence table	Sample	2	N/A	N/A
3	Change compound amounts for a sample in the sequence table	Sample	3	N/A	N/A

Table 10 Revision changes for a single update sequence (continued)

Step	Action (always using *Save to database*)	View	Revision numbers		
			Sequence	Sample	Injection Chromatogram
4	Run the sequence acquisition on the instrument		4	1	1
5	Change a sample entry to different amounts	Result	5	1	1
6	Manually integrate the chromatogram of an injection	Result	6	2	2
7	Reprocess the sequence	Result	8*	3	3
8	Change a sample entry to different amounts	Result	9	3	3
9	Manually integrate the chromatogram of an injection	Result	10	4	4
10	Reprocess the sequence	Result	12*	5	5

* The action of reprocessing increments the revision by two, due to internal processes.

Bracketed sequence

For a bracketed sequence, revisioning differs as follows:

Revisioning of calibration standards:

- Standards of an **opening** bracket have the revision of the sample and chromatogram incremented by one.
- Standards used in a **close and open** bracket have the revision of the sample and chromatogram incremented by two.

Revisioning of calculated unknowns (including QC and Blank samples):

- The revision is incremented by one when the result is calculated.

Overall bracketed sequence

Revisioning of calibration standards:

- The standards are revision 1 after acquisition.

Revisioning of calculated unknowns (including QC and Blank samples):

- The revision is incremented by one when the result is calculated, for example, they become revision 2 after initial acquisition.

Calibration table revisions

When a calibration table is created, its revision number is set to 1. The revision number is incremented when the calibration table is updated. The following examples illustrate the revision control of the calibration table. In all cases, the tables assume only one injection per standard. The revision number of the calibration table is incremented each time a calibration sample is run. For sequence-specific calibrations, n is always 1.

Table 11 Single update calibration

Sequence Order	Sample Name	Revision of Calibration Table	
		Used	Generated
1	Standard 1, run 1	n	n+1
2	Standard 2, run 1	n+1	n+2
3	Sample 1a	n+2	
4	Sample 1b	n+2	
5	Standard 1, run 2	n+2	n+3
6	Standard 2, run 2	n+3	n+4
7	Sample 2a	n+4	
8	Sample 2b	n+4	
9	Standard 1, run 3	n+4	n+5
10	Standard 2, run 3	n+5	n+6

Table 12 Bracketing calibration

Sequence Order	Sample Name	Revision of Calibration Table		Bracket
		Used	Generated	
1	Standard 1, run 1	n	n+1	1 Open
2	Sample 1a	n+2		1
3	Sample 1b	n+2		1
4	Standard 1, run 2	n+1	n+2/n+3*	1 Close, 2 Open
5	Sample 2a	n+4		2
6	Sample 2b	n+4		2
7	Standard 1, run 3	n+3	n+4	2 Close

* Revision n+2 at the closing of Bracket 1, Revision n+3 at the start of Bracket 2.

The revision number of the calibration table is changed with every modification. For bracketing, intermediate versions of the calibration data are generated, which are not directly used for the calibration of samples (for example, revision 3 in Table 12).

Table 13 Overall bracketing calibration

Sequence Order	Sample Name	Revision of Calibration Table	
		Used	Generated
1	Standard 1, run 1	n	n+1
2	Sample 1a	n+3	
3	Sample 1b	n+3	
4	Standard 1, run 2	n+1	n+2
5	Sample 2a	n+3	

Table 13 Overall bracketing calibration (continued)

Sequence Order	Sample Name	Revision of Calibration Table	
		Used	Generated
6	Sample 2b	n+3	
7	Standard 1, run 3	n+2	n+3

In overall bracketing, the samples are not quantified until all standards have been analyzed. This means that the calibration table is initialized at the start of the sequence, then updated twice (lines 4 and 7) to produce revision numbers 2 and 3. The samples are quantified using revision 3, which is the average of all calibration points.

To track consistent chromatographic performance of the system, calibration standards should be distributed equally throughout the sequence. Problems with calibration precision can be detected using appropriate statistics, or response factors.

8
Reporting

Chapter 8 gives a description of the Report Template Editor, which is the basis of the production of Cerity reports.

Cerity Report Template Editor

The Cerity **Report Template Editor** lets you create and modify report templates. You use the Cerity **Report Template Editor** to customize and format Cerity NDS for Pharmaceutical QA/QC reports to suit your laboratory needs.

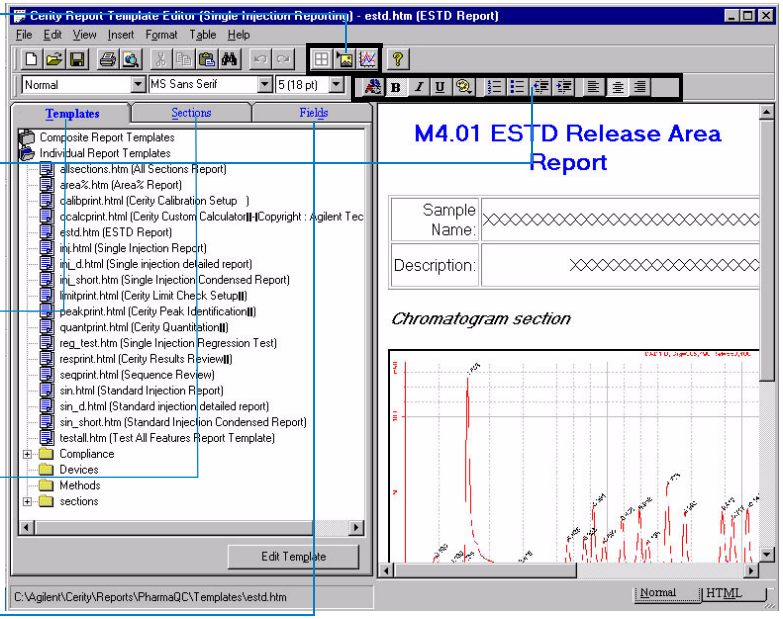
Insert Toolbar - Use these tools to insert a table, image or chromatogram into the template.

Format Toolbar - Use these tools to format the text of the template and/or report.

Template Tab - Select a template to edit from the Templates tab. The templates appear in the Workspace.

Sections Tab - Select a section to insert into the template from the Sections tab.

Fields Tab - Select a field or variable from the Fields tab to insert into the template.



Selection Tree **Workspace**

Report templates

A *report template* is a framework that contains the layout of fields, plots, images and tables whose values you want in the report.

Each report type is linked with a default report template that generates a report of the type selected. When a sample or sequence is run, the report template gives instructions to the database to populate the report with the values of the fields and variables set up in the layout and content of the template.

You can make one of three choices to select a report template:

- Use the default template already linked with the report type
- Select a different default report template for the report type
- Create a new report template or edit an existing one before you select it as the template for the report type

When you choose to edit a template for a report type, the templates for only that type appear in Cerity **Report Template Editor**.

New report templates

You can begin to create a new report template when you click the **New** button in the Cerity **Report Template Editor**.

The Cerity **Report Template Editor** provides two types of templates, the **Individual Report Templates** and the **Composite Report Templates**.

Individual report templates

Use the **Individual Report Templates** to insert simple elements, such as tables, chromatograms, images or fields.

Individual Report Templates include:

- Single Injection Reports
- Method reports
- Compliance reports
- Devices reports

After you select “new.htm” to create a new individual report template, a report template appears in the workspace with the heading **Report Title**. You need to name and save the new report template for a template title to appear under the **Individual Report Templates** folder.

Composite report templates

The **Composite Report Template** lets you insert more than one existing individual template into the final report template.

Composite Report Templates include:

- Multi-injection reports
- Sequence reports.

You can create *multi-injection templates* from individual templates using the following report components:

- Cover Page
- Instrument
- Multi-injection summary
- Single Injections
- Standard Injections

The saved report template appears as an XML file under the **Composite Report Template** folder.

You can create *sequence templates* from individual templates using the following report components:

- Cover Page
- Sequence
- Instrument
- Custom Sample Group
- Sample Group
- QC Sample Group
- Calibration Standards Group
- Multi-injection Summary
- Single Injections
- Standard Injections

The saved report template appears as an XML file under the **Composite Report Template** folder.

Template titles

The template title appears in the following places after you save the file:

- A description for the template file name or section file name
- On the title bar of Microsoft Internet Explorer when you preview a template
- The name of the file when you save the template for the first time

The template title and the report heading that appears in the new template are not the same. You can change the report heading to any heading you need for the report.

New templates from existing templates

You can create new report templates from Cerity NDS default report templates, or your own report templates. All templates appear under the **Templates** tab. After you select and modify an existing report template, you need only to save the report template to a new file name. The new report template appears under the Individual or Composite Report Templates folders.

Text editor

The text editor for the Cerity **Report Template Editor** uses common tools you can find in most word processing programs. You start editing your new report template with the cursor ready to edit the report heading. If you need to insert an element into the report, you must put the cursor below the report heading.

You can do the following tasks to enter your own text into the report:

- Enter the names of fields and descriptions.
- Change the font and size of the text
- Change the position of the test
- Change the emphasis on the text
- Create a numbered or bulleted list
- Set background properties

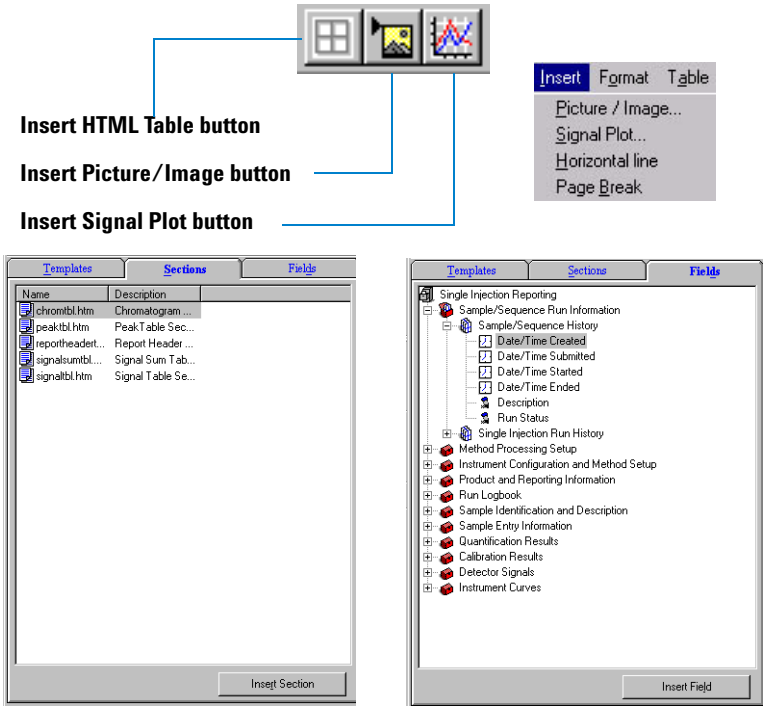
- Change alignment of text
- Change paragraph style
- Change text color
- Restore normal formatting
- Create or edit a header or footer

Report template elements

The Cerity **Report Template Editor** provides Sections and Fields for inserting into a report template. You can insert saved individual report templates as sections. These sections appear under the **Sections** tab of the Cerity **Report Template Editor.**

The **Fields** tab provides all the fields available in the **Sample**, **Method**, **Instrument** and **Result** Views.

You can insert individual fields, tables, images, signal plots, and other report elements into a report template.



Report Element Formats

You can set up formats in the **Picture/Image**, **Signal Plot** and **Table** dialog boxes. Use each dialog box to select your format options. You do not set up formats for sections or individual fields.

Preview or print report templates

In the **Report Template Editor** workspace, you can only print the report template that appears there. When you select the **Preview template** item in the **File** menu, you can make sure the report template is complete and ready to print. You can print the template from the Microsoft Internet Explorer program.

Save a report template

There are several options to save a report template:

- Save the report template with the same name after you edit a report.

The Cerity NDS for Pharmaceutical QA/QC provides default templates that are Read Only. You cannot edit these templates unless the Cerity NDS administrator changes the report template's directory attribute to Read/Write.

- Save a report template as a new file after you edit the report template. Use the **Save As** command under the **File** menu.
- Save the report template as a section.

  You need to change the report template title before renaming the report template file name. The new template appears in the **Sections** tab and **Sections** folder under the **Templates** tab. You can now add the section to another template.

Report Template Creation and Storage

The following information explains how report templates are created and stored:

- The Cerity data dictionary, displayed under the Fields tab in Cerity Report Template Editor, defines the fields and their format information in a report template.
- You can create a report template layout in the method when you edit the report template layout in the Cerity Report Template Editor.
- Cascading Style sheets (CSS) provide report template style parameters that establish a consistent display of fonts and font sizes for every report.
- Cerity data formats apply to numeric data.
- You can store their reports in the Cerity reports directory that resides under the CerityReports shared directory. You can also set up your own reports directory under the CerityReports shared directory. The Pharmaceutical QA/QC application stores reports under CerityReports share\PharmaQC\Reports.

Data Dictionary

The Cerity data dictionary describes the contents of the Cerity relational database that stores and organizes Cerity data from multiple data sources. All data items are available for inclusion in reports. The Cerity NDS describes a particular data item using the term Field. The **Fields** tab, located in Report Template Editor, displays the data dictionary. Result data, formatted according to data dictionary definitions, display within generated reports.

The data dictionary provides:

- display of field names

- access information for report generation
- format information for formatting results

For example, the Multi-injection Summary template displays the following folders and field names in the Cerity Report Template Editor:

- Sample/Sequence Run Information
  - Sample/Sequence History
  - Multi-injection Run History
- Method Processing Setup
  - Method Information
  - Single and Multi-injection Setup
  - Sequence Setup
- Instrument Configuration and Method Setup
- Product and Reporting Information
- Run Logbook
- Accept/Reject Review
- Sample Identification and Description
- Sample Entry Information
- Integration Settings
- Multi-Injection Summary Results
  - Multi-injection Variables
  - Compounds
  - Unidentified Peaks
  - Results for each Injection

The Sequence Reporting template displays the following folders and field names in the Cerity Report Template Editor:

- Sample/Sequence Run Information
- Method Processing Setup
- Instrument Configuration and Method Setup
- Product and Reporting Information
- Run Logbook

- Accept/Reject Review
- Sequence Information
- Sequence Execution
- Sequence Entry Information
  - Overall Sequence Settings
  - Sequence Sample Information Table
  - Sequence Template Sample Table
  - Sample Entry Information
- Calibration Standard Group
  - Standard Group Variables
  - Compounds
  - Unidentified Peaks
  - Results for each Standard
- QC Sample Group
- Sample Group
- Custom Sample Groups

You can find the data dictionary file, pharmaqc.dd, in the **CerityReports** share\PharmaQC\ directory.

Template Layout

Cerity default report templates provide for the layout of generated reports. The Reporting workspace in the **Method** View lets you select the appropriate report types from the Cerity default report templates to generate a report. Optionally, the Cerity **Report Template Editor** lets you edit Cerity default report templates or create a new report template. You can access the Cerity **Report Template Editor** during Method creation or modification from the **Reporting** workspace.

Individual Report Templates and **Composite Report Templates** provide report components you can edit or add to a new report template. When you insert a results field into a report template, a `<SPAN> Hypertext Markup Language (HTML)` element

that uses an ExpandTo attribute along with a field text identifier is inserted into the HTML. The value of the ExpandTo attribute references the field definition in the Data Dictionary. For example, the data dictionary element **Single Injection Reporting** under **Method Processing Setup**, field **method name** displays in HTML:

<SPAN expand to=
“Method.Method.Title”>XXXXXXXXXXXXXXXXXXXX</SPAN>

The data field displays in the report template as:

XXXXXXXXXXXXXXXXXXXX

When the report is generated, the data field above is replaced by the actual value.

NOTE The ExpandTo attribute for the <SPAN> HTML definition is not a standard HTML attribute. The ExpandTo attribute is a Cerity attribute.

You can also insert method-specific fields such as custom calculations, custom sample variables, and device-specific items for a method in the Cerity Report Template Editor.

Template Style

For clarity within the report, you must be aware of the relationship between the screen style and the print style. Cascading Style Sheets (CSS2), an extension of HTML 4.0, provide style parameters for establishing a consistent layout for a report. The Cerity NDS defines the screen style in the file ScreenStyle.css and the print style in the file PrintStyle.css.

Reports that display in the Cerity **Report Viewer** apply the screen style set by the ScreenStyle.css. The screen style provides a format that displays the report properly. The print style, set by the PrintStyle.css, provides a format that prints the report properly. The screen style and print style apply different formats. You can modify the PrintStyle.css to correspond to the ScreenStyle.css. The screen style requires the fixed font MS

Sans Serif for proper alignment of the decimal point inside column cells of a table. Text outside of the table that provides the titles, headings, headers, footers, and caption of a table can use the default proportional font, Arial with fixed width digits.

The Cerity hardware requirements for proper display of reports require a video display card set to 1024x768 pixels for screen area and High Color for colors. The Cerity **Report Viewer** provides the required format settings to display and print a report.

NOTE

For regulatory requirements, you must use the Cerity **Report Viewer** to print reports printed to a file. Any report that uses Microsoft Internet Explorer (MSIE) to print the report displays a page header/footer different then the page header/footer for the Cerity **Report Viewer**. The MSIE printed report is not considered a valid report.

Data Formats

The **Cerity Software Administration** application lets you, with the assigned role capability, define the Cerity data formats for result data that appears in a report. The Pharmaceutical QA/QC application enforces default field formats every time you display a field unless method specific formats overwrite default formats. You can only modify fields defined to have a **Format Type** as defined in the **Cerity Software Administration** application under **System Wide Settings** for **Numeric Format** and **Date and Time Format**. Any user other then the Cerity administrator must not have the capability to modify **System Wide Settings**. For more detail see the System Reference Chapter in the Cerity Reference Guide.

Cerity data format specifications apply only to numeric data. All textual data appears in the report, such that report generation does not truncate textual data if the textual data exceeds the field width.

Report templates can provide default field placeholders with no corresponding results data in a report. Default placeholders for textual data appear as a series of X characters. Default

placeholders for numeric data appear as defined by Cerity format specifications. For example, a numeric field can display as `####.DDD`.

Report Template Storage

The Cerity Network Data System (NDS) stores report templates on the server file system and creates a shared directory, **CerityReports**, during the installation of the Cerity NDS client-server system. The Cerity NDS creates the **CerityReports** share on the local computer during the installation of the Cerity NDS Professional system. The **CerityReports** share provides access to:

- report template files
- reports stored in a file
- view a report in the Report Viewer

The Cerity installation lets the installer set up the **CerityReport** share directory location. See the Installation Guide for more information.The **CerityReport** share creates the following directories:

Table 14 CerityReport share

File Directory	Contains
Pharmaqc	the pharmaqc.dd file
Pharmaqc\Reports	generated report files
Pharmaqc\Templates	Individual Report Templates (HTM, HTML)
Pharmaqc\Templates\Compliance	templates for IQ/OQ/PV reports
Pharmaqc\Templates\Composite	Composite Report Templates (XML)
Pharmaqc\Templates\Images	report images
Pharmaqc\Templates\Sections	templates you can insert into other templates

Table 14 CerityReport share

File Directory	Contains
Pharmaqc\templates\New	basic templates for you to create new templates
Pharmaqc\Templates\Preview	templates to print a view or table from the user interface
Pharmaqc\templates\Methods	templates to print method contents only
Pharmaqc\templates\Devices	templates to print device settings
Pharmaqc\templates\Compliance	templates for compliance reports
Pharmaqc\templates\Preview	templates to print views or tables interactively

Users can create additional subdirectories to organize their reports. Users create the additional subdirectories in the **Sample Entry** or **Sequence Sample Entry Report Destination** box. you do not need to create the report destination subdirectories in the file system since the system creates the subdirectories during the generation of reports. During the generation of reports, the directories and their contents are set to read-only. To avoid overwriting of directories, a numeric suffix (-####) is appended to the destination directory to make it unique.

The Cerity NDS limits access to **CerityReport** share directories. See “Cerity Reports Access” on page 25 for more information.

Report generation

The **Reporting** workspace for a method lets you select a default report template for each report type. You can enable or disable a report type such that only the enabled reports generate during a single sample or sequence run. The Cerity Pharmaceutical QA/QC application generates enabled reports for a single injection, sample, or end of a sequence run. The exact order depends on the exact calibration or bracketing for the sequence. For example, standards may be reported more then once with bracketing.

Order of report storage

An example of how a sequence report stores individual reports on the file system appears as follows:

MySeqReport\

\001 Multi-injection Summary Group\
default.htm, *.gif, *.css, report.xml
\01 Standard Single Injection\default.htm, *.gif, *.css, *.wmf, report.xml
\02 Standard Single Injection\default.htm, *.gif, *.css, *.wmf, report.xml

\002 Multi-injection Summary Report\
default.htm, *.gif, *.css, report.xml
\01 Sample Single Injection\default.htm, *.gif, *.css, *.wmf, report.xml
\02 Sample Single Injection\default.htm, *.gif, *.css, *.wmf, report.xml

\003 Multi-injection Summary Report\
default.htm, *.gif, *.css, report.xml
\01 Standard Single Injection\default.htm, *.gif, *.css,

*.wmf, report.xml
\02 Standard Single Injection\default.htm, *.gif, *.css, *.wmf, report.xml

\Sequence
default.html, *.gif, *.css

\QC Sample Group
default.html, *.gif, *.css

The report can use the Agilent logo GIF file or you can insert your own image file. The Cerity NDS stores image files in the Images folder under the **Templates** directory folder. All image files copied into a report template must be stored in the **Images** folder. The Cerity NDS stores the Cascading Style Sheet files (CSS) in the **Templates** directory folder. Every report folder must include the ScreenStyle.css and the PrintStyle.css to create consistent reports. The Windows Meta File (WMF) is a chromatogram image file that provides the image of the chromatogram. Reports that generate a chromatogram also store the WMF file in the injection report folder. The report.xml provides report file information that includes the template file name, the server name, the printer, the application, and meta information.

Default report templates

The Cerity NDS provides default templates for a single sample or a sequence to generate a report. you can access the default report templates from the **Reporting** workspace of a method. For each report type, you can choose the standard report template or choose a condensed or detailed version of the standard report template. The file names for the three levels of a default report type are:

- Standard template - <template name>.html
- Condensed template - <template name_short>.htm
- Detailed report template - <template name_d>.html

For each report type, a selection of individual report templates is available for you to put into a report. You can also choose to create a composite report template. The composite report can include all of the report templates for a sequence. You can select which report templates to include in the composite report.

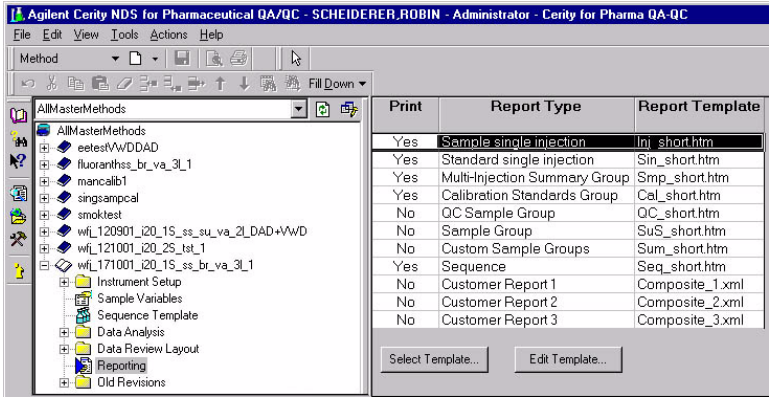


Figure 71 Reporting workspace

Individual report templates

Individual Report Templates specify a report type that includes **Single Injection templates** for sample injections and **Standard Injection templates** for calibration injections. **Individual report templates** for groups and summaries include **Multi-Injection Summary**, **Calibration Standard Group**, **QC Sample Group**, **Sample Group**, **Custom Samples Group**, and **Sequence Report**. Individual templates can display the following information:

- The sample identification contains identification of the sample, which includes the sample name, date and time of injection, and name of the instrument.
- **Method Reference** identifies the method you apply. The **Method Reference** should provide sufficient information to reproduce the test. Optional information can include sample logbook, method parameters, system suitability results, instrument history, sequence reference, column properties, and limits. You identify the operator and instrument along with any changed parameters.
- The **Results** section can provide a result in a table with a single index for compounds or peaks and injection or sample name as the secondary index. The **Results** section can contain amount data and statistical summaries that includes a report on limit checks.
- The **Chromatogram** section contains the chromatogram of the injections overlaid or in separate graphs with the same time axis.
- The instrument module provides basic instrument information that includes model number, manufacturer, serial number, version, and firmware.

Sample single injection

Default template file names: Inj.html, Inj_Short.htm, Inj_D.html

Sample single injection templates provide a single injection report for every injection except calibrations.

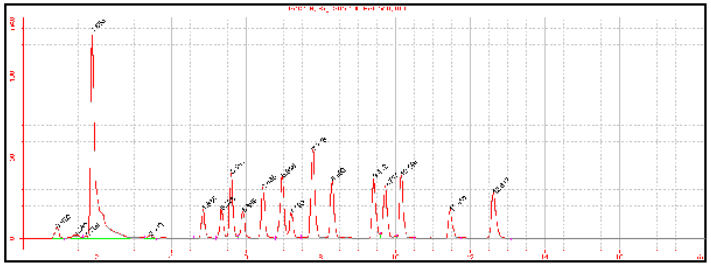
Sample single injection

Sample identification

Sample name		XXXXXXXXXXXXXXXXXXXX
Sample type		XXXXXXX
Date	Start	sys_date, sys_time
	End	sys_date, sys_time
Instrument		XXXXXXXXXXXXXXXXXXXX
Acquisition		sys_date, sys_time
Injection		## of ##

Sample method description

Method (rev.)	XXXXXXXXXXXXXXXXXXXXXXXXXXXX (###)	Calibration created	sys_Date, sys_Time
Sample scheduler	XXXXXXXXXXXXXXXXXXXXXXXX	Calibration modified	sys_Date, sys_Time
Instrument	XXXXXXXXXXXXXXXXXXXXXXXX	Instrument rev.	sys_Date, sys_Time



Sample single injection compounds

RT	Compound	Peak area	Amount	Unit	Resp. f.	Tailing f.
##### .##	XXXXXXXXXXXXXXXXXX	X.DDDD	### .##	XXXXX	X.DDDD	##### .###

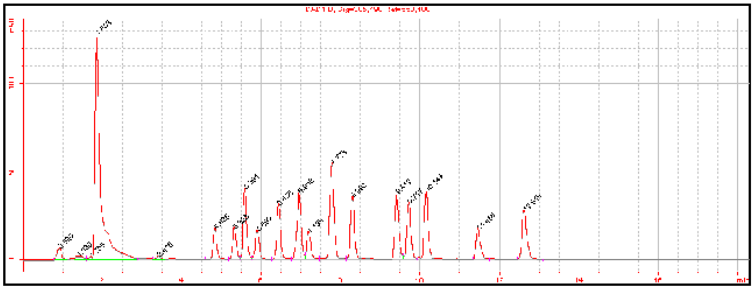
Sample single injection report

Sample identification

Sample name		XXXXXXXXXXXXXXXXXXXX
Sample type		XXXXXXX
Date	Start	sys_date, sys_time
	End	sys_date, sys_time
Instrument		XXXXXXXXXXXXXXXXXXXX
Acquisition		sys_date, sys_time
Injection		## of ##

Sample Method Description

Method Name	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	Calibration Creation	sys_Date, sys_Time
Sample scheduler	XXXXXXXXXXXXXXXXXXXX	Calibration Modification	sys_Date, sys_Time
Instrument Name	XXXXXXXXXXXXXXXXXXXX	Instrument Revision	sys_Date, sys_Time



Sample single injection compounds

Retention Time	Compound Name	Amount	Unit	Response Factor	Tailing Factor
##### .##	X	### .##	XXXX	X.DDDD	##### .###

Instrument: XXXXXXXXXXXXXXXXXXXX
Info: XXXXXXXXXXXXXXXXXXXXXXXX
Acquisiton Server: XXXXXXXXXXXXXXXXXXXXXXX
Acq. Server Name: XXXXXXXXXXXXXXXXXXXXX

Instrument Description

ID: XXXXXXXXXXXXXXXXXXXXX
Name: XXXXXXXXXXXXXXXXXXXXX
Revision: #####
Information: XXXXXXXXXXXXXXXXXXXX

Instrument Module Description

Model	Manufacturer	Serial #	Version	Firmware
XXXXXX	XXXXXXX XXXXXXXXXX	XXXXXXXXX	XXXXXXXXXXXXX	XXXXXXXXX

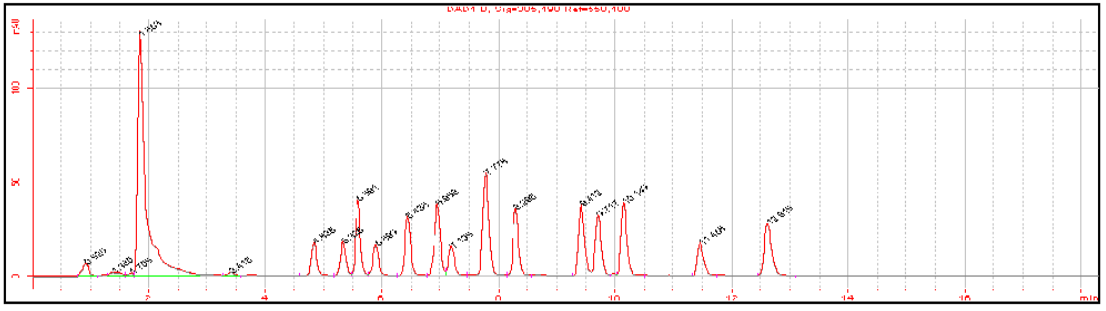
Sample single injection detailed report

Sample identification

Sample name		XXXXXXXXXXXXXXXXXX
Sample type		XXXXXXX
Date	Start	sys_date, sys_time
	End	sys_date, sys_time
Instrument		XXXXXXXXXXXXXXXXXX
Acquisition		sys_date, sys_time
Injection		## of ##

Sample method description

Method name	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	Method revision	###
Calibration creation	sys_Date, sys_Time	Calibration modification	sys_Date, sys_Time
Instrument name	XXXXXXXXXXXXXXXXXX	Instrument revision	###



Sample single injection compounds

Compound	RT	Amount	Units	Area %	Tailing	Limit Check (Compound)
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	X.DD	X.DDDD	XXXXX	X.DDDD	##.###	XXXXXXXXXX

Instrument: XXXXXXXXXXXXXXXXXXXX
Info: XXXXXXXXXXXXXXXXXXXXXXXX
Acquisiton server: XXXXXXXXXXXXXXXXXXXXXXX
Acq. server name: XXXXXXXXXXXXXXXXXXXXXX

Instrument module reports will replace this section. Don't edit this box.

Six templates for detailed reports that also include various spectral plots are also available.

Standard single injection template

Default template names: Sin.html, Sin_short.htm, Sin_D.html

Standard single injection templates provide injection results of calibration samples. Each calibration injection provides one standard injection report.

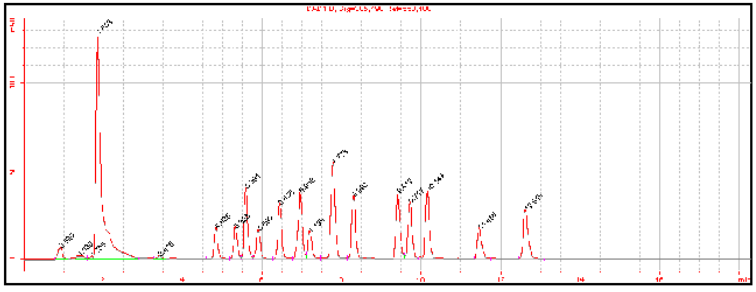
Standard single injection condensed report

Sample identification

Sample name		XXXXXXXXXXXXXXXXXXXX
Sample type		XXXXXXX
Date	Start	sys_date, sys_time
	End	sys_date, sys_time
Instrument		XXXXXXXXXXXXXXXXXXXX
Acquisition		sys_date, sys_time
Injection		## of ##

Sample method description

Method (Rev)	XXXXXXXXXXXXXXXXXXXXXXXXXXXX (###)	Calibration created	sys_Date, sys_Time
Sample scheduler	XXXXXXXXXXXXXXXXXXXXXXXX	Calibration modified	sys_Date, sys_Time
Instrument	XXXXXXXXXXXXXXXXXXXXXXXX	Instrument rev.	sys_Date, sys_Time



Compound calibration info

Compound	Area	Amount	Unit	RF Rsp/Amt	Amt calc. method	Calib.
XXXXXXXXXX	X.DDDD	X.DDDD	XXXXX	##.DDDD	XXXXXXXXX	XXXX

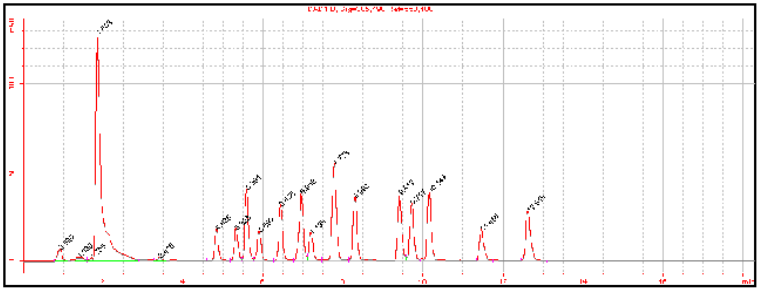
Standard single injection report

Sample identification

Sample name		XXXXXXXXXXXXXXXXXXXX
Sample type		XXXXXXX
Date	Start	sys_date, sys_time
	End	sys_date, sys_time
Instrument		XXXXXXXXXXXXXXXXXXXX
Acquisition		sys_date, sys_time
Injection		## of ##

Sample method description

Method name	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	Calibration created	sys_Date, sys_Time
Sample scheduler	XXXXXXXXXXXXXXXXXXXX	Calibration modified	sys_Date, sys_Time
Instrument name	XXXXXXXXXXXXXXXXXXXX	Instrument revision	sys_Date, sys_Time



Quantification results of compounds

Compound	Amount	Unit	RF (Rsp/Amt)	Limit check (Compound)	Used for cal.
XXXXXX	X.DDDD	XXXXX	X.DDDD	XXXXXXXXXX	XXXXXXXX

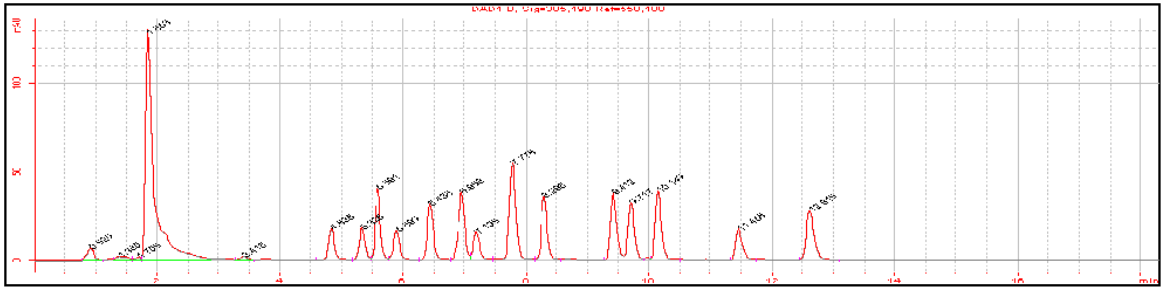
Standard single injection detailed report

Sample identification

Sample name		XXXXXXXXXXXXXXXXXXXX
Sample type		XXXXXXX
Date	Start	sys_date, sys_time
	End	sys_date, sys_time
Instrument		XXXXXXXXXXXXXXXXXXXX
Acquisition		sys_date, sys_time
Injection		## of ##

Sample method description

Method name	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	Method revision	###
Calibration creation	sys_Date, sys_Time	Calibration modification	sys_Date, sys_Time
Instrument name	XXXXXXXXXXXXXXXXXXXX	Instrument revision	###



Quantification results of compounds

Compound	Amount	Unit	RF (Rsp/Amt)	Limit Check (Compound)	Used for cal.
XXXXXX	X.DDDD	XXXXX	X.DDDD	XXXXXXXXX	XXXXXXX

Quantification results of peaks

Compound	RT	Height	Area	Area %	Width	Tailing	Symmetry
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	X.DD	X.DDDD	X.DDDD	X.DDDD	X.DDDD	##.###	##.###

Quantification results of peaks

Compound	RT	Plate # USP	Plate # BP	Plate # JP	Peak resolution EP/JP/BP/DAB	Peak resolution USP
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	X.DD	##.###	##.###	##.###	##.###	##.###

Multi-injection Summary Group template

Default template file names: Smp.html, Smp_Short.htm, Smp_D.html

Multi-injection Summary group templates provide for multiple injections of one sample.

Multi-Injection summary group

Sample Condensed Identification

Sample Name		XXXXXXXXXXXXXXXXXXXX
Date	Start	sys_Date, sys_Time
	End	sys_Date, sys_Time
Instrument		XXXXXXXXXXXXXXXXXXXX
Sample Type		XXXXXXXXXXXXXXXXXXXX

Sample method description

Method (rev.)	XXXXXXXXXXXXXXXXXXXXXXXXXXXX (###)	Calibration created	sys_Date, sys_Time
Sample scheduler	XXXXXXXXXXXXXXXXXXXXXX	Calibration modified	sys_Date, sys_Time
Instrument	XXXXXXXXXXXXXXXXXXXXXX	Instrument rev.	sys_Date, sys_Time

Compound	Amount (known)	Unit	Signal Short Description	Limit Check (Compound)
XXXXXXXXXXXXXXXXXXXXXXXX	X.DDDD	XXXXX	XXXXXXXXXXXX	XXXXXXXXXX

Multi-Injection summary group

Sample identification

Sample name		XXXXXXXXXXXXXXXXXXXX
Date	Start	sys_Date, sys_Time
	End	sys_Date, sys_Time
Instrument		XXXXXXXXXXXXXXXXXXXX
Sample Type		XXXXXXXXXXXXXXXXXXXX

Method identification

Method name	XXXXXXXXXXXXXXXXXXXXXX	Calibration creation	sys_Date, sys_Time
Sample scheduler	XXXXXXXXXXXXXXXXXXXXXX	Calibration modification	sys_Date, sys_Time
Instrument name	XXXXXXXXXXXXXXXXXXXXXX	Instrument revision	sys_Date, sys_Time

Retention time	Compound name	Amount	Units	Limit Check (Compound)
X.DD	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	X.DDDD	XXXXX	XXXXXXXXXX

Multi-Injection summary group

Sample identification

Sample name		XXXXXXXXXXXXXXXXXX
Date	Start	sys_Date, sys_Time
	End	sys_Date, sys_Time
Instrument		XXXXXXXXXXXXXXXXXX
Sample type		XXXXXXXXXXXXXXXXXX

Method identification

Method name	XXXXXXXXXXXXXXXXXX	Calibration creation	sys_Date, sys_Time
Sample scheduler	XXXXXXXXXXXXXXXXXX	Calibration modification	sys_Date, sys_Time
Instrument Name	XXXXXXXXXXXXXXXXXX	Instrument revision	sys_Date, sys_Time

Multi-Injection compound results

Compound	RT	Amount	Units	Limit check (Compound)	Limit check (Peak)	Signal
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	X.DD	X.DDDD	XXXXX	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXXX

Calibration Standard Group template

Default template file names: Cal.html, Cal_Short.htm, Cal_D.html

Calibration Standard Group report templates provide for group of calibration samples.

Calibration standards group (condensed)

Sequence name:	XXXXXXXXXXXXXXXXXX
Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXX (###)

Number of unidentified Peaks: ##

Standard sample results

#	Sample	Position	Inj. vol.	Limit (Standard)
##	XXXXXXXXXXXXXXXXXX	XXXXXXX	###.DD	XXXXXXXXX

Calibration standard group

Sequence name:	XXXXXXXXXXXXXXXXXXXX
Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXXXX (###)

Number of unidentified Peaks: ##

Standard sample group variables

#	Standard name	Amount	Position	Inj. vol.
##	XXXXXXXXXXXXXXXXXXXX	##.DDDD	XXXXXXXX	###.DD

Standard sample group limit results

#	Standard name	Compound	Limit (Calib Sample)
##	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXX

Calibration standard group report

Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method:	XXXXXXXXXXXXXXXXXXXX

Sample	Seq. order	Compound name	Limit check (Sample)
##	##	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXX

Sample	Seq. order	Compound name	Limit check (Compound)
##	##	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXX

Number of Unkowns: ##

QC Sample Group template

Default template file names: QC.html, QC_Short.htm, QC_D.html

QC Sample Group report templates provide for a group of QC samples.

QC sample group (condensed)

Sequence name:	XXXXXXXXXXXXXXXXXXXX
Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXXXX (###)

Number of unidentified peaks: ##

QC sample results

#	Sample	Position	Inj. vol.	Limit (Sample)
##	XXXXXXXXXXXXXXXXXXXX	XXXXXXXX	###.DD	XXXXXXXXXX

QC sample group

Sequence name:	XXXXXXXXXXXXXXXXXXXX
Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXXXX (###)

Number of unidentified peaks: ##

QC sample group variables

#	QC name	Amount	Position	Inj. vol.
##	XXXXXXXXXXXXXXXXXXXX	##.DDDD	XXXXXXXX	###.DD

QC sample group limit results

#	QC name	Compound	Limit (QC Sample)
##	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXX

QC sample group (detailed)

Sequence name:	XXXXXXXXXXXXXXXXXXXX
Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXXXX (###)

Number of unidentified peaks: ##

QC sample group variables

#	QC name	Amount	Position	Inj. vol.
##	XXXXXXXXXXXXXXXXXXXX	##.DDDD	XXXXXXXX	###.DD

QC sample group limit results

#	QC name	Compound	Limit (Compound)	Limit (QC Sample)
##	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX

Sample Group template

Default template file names: Sus.html, Sus_Short.htm, Sus_D.html

Sample Group report templates provide for a group of samples.

Sample group (condensed)

Sequence name:	XXXXXXXXXXXXXXXXXXXX
Sequence start:	sys_Date, sys_Time
Sequence end:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXXXX (###)

Number of unidentified peaks: ##

Sample results

#	Sample	Position	Inj. vol.	Limit (Sample)
##	XXXXXXXXXXXXXXXXXXXX	XXXXXXXX	###.DD	XXXXXXXXXX

Sample group

Sequence name:	XXXXXXXXXXXXXXXXXXXX
Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXXXX (###)

Number of unidentified peaks: ##

Sample group variables

#	Sample name	Amount	Position	Inj. vol.
##	XXXXXXXXXXXXXXXXXXXX	##.DDDD	XXXXXXXX	###.DD

Sample group limit results

#	Sample name	Compound	Limit (Sample)
##	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXX

Sample group (detailed)

Sequence name:	XXXXXXXXXXXXXXXXXXXX
Sequence Start:	sys_Date, sys_Time
Sequence End:	sys_Date, sys_Time
Method (rev):	XXXXXXXXXXXXXXXXXXXX (###)

Number of unidentified peaks: ##

Sample group variables

#	Sample name	Amount	Position	Inj. vol.
##	XXXXXXXXXXXXXXXXXXXX	##.DDDD	XXXXXXXX	###.DD

Sample group limit results

#	Sample name	Compound	Limit (Compound)	Limit (Sample)
##	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX

Custom Sample Group template

Default template file names: Sum.html, Sum_Short.htm

The Custom Sample Group templates provides for a user-defined group of samples.

Custom sample groups

Number of Custom Groups: ##

Samples in Group	Group Name	Limit (Compound)
##	XXXXXXXXXXXX	XXXXXXXXXX

Custom sample groups

Number of Custom Groups: ##

Samples in Group	Group Name
##	XXXXXXXXXXX

Group	Sample	Amount	Position	Inj. Vol.
XXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	X.DDDD	XXXXXXXX	###.DD

Compound	Limit (Compound)	Sample	Position	Limit (Sample)
XXXXXXXXXXXXXXXXXXX	XXXXXXXXX	XXXXXXXXXXXXXXXXXXX	XXXXXXXX	XXXXXXXXX

Sequence template

Default template file names: Seq.html, Seq_Short.htm, Seq_D.html

The Sequence template provides for all sample injection and calibration injection reports.

Sequence report (condensed)

Sequence Name (rev):	XXXXXXXXXXXXXXXXXXX	Revision:	###
Sequence description:	*		
Start:	sys_Date, sys_Time	End:	sys_Date, sys_Time
Instrument ID:	XXXXXXXXXXXXXXXXXXX	Instrument name:	XXXXXXXXXXXXXXXXXXX

Method parameters

Method: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

Revision: ### Last modified: sys_Date, sys_Time

Reporting

Destination: XXXXXXXX

Printer: XXXXXXXXXXXXXXXXXXX

File: XXXXXXXXXXXXXXXXXXX

Sequence rollout

	Sample Type	Calibration Level	Bracketing
##	XXXXXXXXXXX	XXXX	XXXXXXXXXXX

Sequence samples

	Name	Position	Modified inj. volume	Amount	Unit	Cal. level
##	XXXXXXXXXXXXXXXXXXX	XXXXX	###.DD	##.DDDD	XXXXXX	XXXXXXXX

Sequence report

Sequence Name (rev):	XXXXXXXXXXXXXXXXXXXX	Revision:	###
Sequence description:	*		
Start:	sys_Date, sys_Time	End:	sys_Date, sys_Time
Instrument ID:	XXXXXXXXXXXXXXXXXXXX	Instrument name:	XXXXXXXXXXXXXXXXXXXX

Method parameters

Method: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Revision: ### Last modified: sys_Date, sys_Time
Description: xxxxxxxx

Reporting

Destination: XXXXXXXX
Printer: XXXXXXXXXXXXXXXXXXXX
File: XXXXXXXXXXXXXXXXXXXX

Report	Enabled	Report type	Template
##	XXX	XXXXXXX	XXXXXXXXXXXX

Instrument

Module	Model	Ord #	Manufacturer	Serial #	Version	Firmware version
##	XXXXXX	#	Xxxxxx Xxxxxxxxxx	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX

Sequence rollout

	Sample Type	Calibration Level	Bracketing
##	XXXXXXXXXXX	XXXX	XXXXXXXXXXX

Sequence samples

	Name	Position	Modified inj. volume	Amount	Unit	Cal. level
##	XXXXXXXXXXXXXXXXXXXX	XXXXX	###.DD	##.DDDD	XXXXXX	XXXXXXXX

Sequence report (detailed)

Sequence Name (rev):	XXXXXXXXXXXXXXXXXXXX	Revision:	###
Sequence description:	*		
Start:	sys_Date, sys_Time	End:	sys_Date, sys_Time
Instrument ID:	XXXXXXXXXXXXXXXXXXXX	Instrument name:	XXXXXXXXXXXXXXXXXXXX

Method parameters

Method: XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Revision: ### Last modified: sys_Date, sys_Time
Description: xxxxxxxx

Reporting

Destination: XXXXXXXX
Printer: XXXXXXXXXXXXXXXXXXXX
File: XXXXXXXXXXXXXXXXXXXX

Report	Enabled	Report type	Template
##	XXX	XXXXXXX	XXXXXXXXXXX

Instrument

Module	Model	Ord #	Manufacturer	Serial #	Version	Firmware version
##	XXXXXX	#	Xxxxxxx Xxxxxxxxxxx	XXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXX

LogBook name: XXXXXXXXXXXXXXXX

	Event Description	Entity	Audit Comment	Time Value (local)	ESig Auth.
##	Description	XXXXXXXXXXXXXXXX	Comment	Time Stamp	XXXX

Sequence rollout

	Sample Type	Calibration Level	Bracketing
##	XXXXXXXXXXXX	XXXX	XXXXXXXXXXXX

Sequence samples

	Name	Position	Modified inj. volume	Amount	Unit	Cal. level
##	XXXXXXXXXXXXXXXXXXXX	XXXXX	###.DD	##.DDDD	XXXXXX	XXXXXXXX

Composite report templates

Composite report templates combine a group of individual report templates into one report with a cover page. For example, composite reports can combine the results that start with a single injection report and ends with a sequence report. **Composite report templates** are XML files that organize the report templates you selected to print to a file or a designated printer.

The file names for the three levels of composite reports are:

- Customer Report 1: Composite_1.xml
- Customer Report 2: Composite_2.xml
- Customer Report 3: Composite_3.xml

You can create a new **Customer Report** only for a sequence. The file name for the new default **Customer Report** for a sequence is sequence.xml.

The **composite report template** is set up separately from individual reports. An example **composite report template** sets up the following report order:

- Cover
- Sequence
- Instrument
- Custom Sample Groups
- Sample Group
- QC Sample Group
- Calibration Standards Group
- Multi-Injection Summary Group 1
  - Sample Single Injection 1
  - Sample Single Injection 2
  - Sample Single Injection n
- Multi-Injection Summary Group n

Page numbering is based on the entire report.

Reporting Functions

Calibration Curve

CalibrationCurve.html is a default single-injection report template that includes the calibration curve. Calibration curves can also be added to any other single-injection template from the **Compounds** section of the **Calibration Results** node. Other calibration-related information is available from the **Calibration Points** node of the **Compounds** section.

Spectral Method Setpoints and Results

Method setpoints can be reported either from the Cerity **Report Template Editor** or from the **Method** view, using **Print Method** command. The templates are common to both reporting options. For descriptions of the available templates, see "Reporting and Reviewing of Meta-data" on page 52.

Reporting Spectral Results

Six default single-injection templates are available for reporting spectral results:

- Inj_d_3D.html is a detailed report template for reporting UV Compound Confirmation results. For each compound, it includes individual plots of the compound reference spectrum and apex spectrum, and an overlaid plot of both spectra.
- Inj_short_3D_ApexAndRawApexSpectrumOverlaid.html for reporting spectral results. For each compound, it includes an overlaid plot of the background-corrected apex spectrum and the raw apex spectrum, together with a plot of the background spectrum.

- Inj_short_3D_CompRefAndApexSpectrumOverlaid.html for reporting UV Compound Confirmation results. For each compound, it includes an overlaid plot of the compound reference spectrum and the apex spectrum, together with a plot of the background spectrum.
- Inj_short_3D_PuritySpectrumOverlaid.html for reporting UV Purity results. For each compound, it includes a plot of the peak purity spectrum, and a plot of the residual spectra. The UV Purity tables are also included in the report.
- Inj_short_3D_ResidualOfApexAndCompRefSpectrum.html for reporting UV Compound Confirmation results. For each compound, it includes a plot of the residual spectrum against the compound reference spectrum, together with a plot of the background spectrum.
- Inj_short_3D_ResidualOfApexAndPuritySpectrumOverlaid.html for reporting UV Purity results. For each compound, it includes a plot the residual peak spectra against the apex spectrum, together with a plot of the background spectrum.

In addition, the **UV Spectral Compound Purity Setpoints**, **UV Confirmation Default Setpoints** and **Spectra Handling Setpoints** and spectra are available for addition to any other single-injection report template.

Reporting Custom Calculator Results

Custom calculator results are reported using a dedicated reporting tool; reporting parameters are set in the **Custom Calculator** node of **Data Analysis** setup in the **Method** view. Custom calculator reports are set up using a tabbed dialog box that allows you to design the layout of multi-page reports, add headers and footers, and specify which elements of the custom calculator worksheet to print.

Conditional Reporting

Conditional reporting allows you to change the display of a report element based on the result of a test condition. You can change the display of a complete table, a column of a table, an individual cell in a table or a field. For example, you can apply formatting to an element (font enhancements such as bold, italic or color), or display or hide an element, depending on the result of the test condition.

Test conditions are of two types:

- An **Internal Condition** operates without operands, and is evaluated using internal states. The following operators are available:

INSEQUENCE	Tests if the report runs as a sequence report.
INSEQSUBTEST	Tests if the report runs as a sample report within a sequence.
INMETHOD	Tests if the report is a method report.

  If the result of the test is true, the element is included in the report, if the result is false, the element is omitted.

- An **External Condition** uses operands and references. The following operators are available:

IN	Tests if the **Reference** string is one of the **Operands**.
NOTIN	Tests if the **Reference** string is not one of the **Operands**.
LESS	Tests if the value of the **Reference** is less than the value of the **Operand(s)**.
LESSEQUAL	Tests if the value of the **Reference** is less than or equal to the value of the **Operand(s)**.

GREATER	Tests if the value of the **Reference** is greater than the value of the **Operand(s)**.
GREATEREQUAL	Tests if the value of the **Reference** is greater than or equal to the value of the **Operand(s)**.
EQUAL	Tests if the value of the **Reference** is equal to the value of the **Operand(s)**.
UNEQUAL	Tests if the value of the **Reference** is not equal to the value of the **Operand(s)**.

You select the **Reference** from a selection tree that includes all available references. If the result of the test is true, the element is included in the report, if the result is false, the element is omitted.

9
Administration and Maintenance

This chapter explains, among other things, the Cerity Administration and Maintenance utility.

Post-Installation Setup

After you install the Cerity NDS for Pharmaceutical QA/QC software, the Cerity NDS administrator must set up Cerity NDS users to use the Pharmaceutical QA/QC application.

The Cerity NDS administrator must complete the following tasks:

- Start the Cerity NDS Administration application
- Connect to the database
- Set the bootp configuration only if laboratory does not use DHCP for instruments
- Add licenses
- Verify successful installation
- Set a default printer for the Cerity NDS Service user
- Synchronize timestamps among Cerity NDS machines
- Add users
- Add acquisition controllers
- Add instruments
- Add a device
- Save changes to the database

See the System Administration Online Help for instructions to complete these tasks. The concepts in this section help the administrator perform these tasks.

Cerity NDS Administration Application

You use the Cerity NDS Administration configuration tools to manage the system. You select the **Cerity Software Administration** menu item from the **Start** menu to access the configuration window.

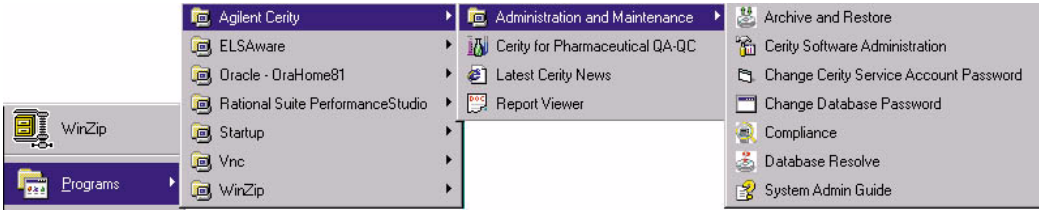


Figure 72 Cerity NDS Administration menu item

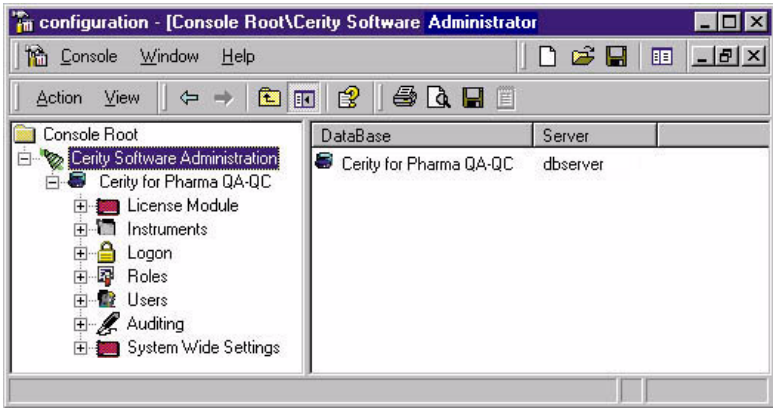


Figure 73 Cerity Software Administration configuration window

Connection to a Database

You need to add the database that the Cerity Software Administration configuration tools manage. A right-click on the Cerity Software Administration folder in the main window lets you add a database. After you add a database, expand the database folder to access its properties and settings.

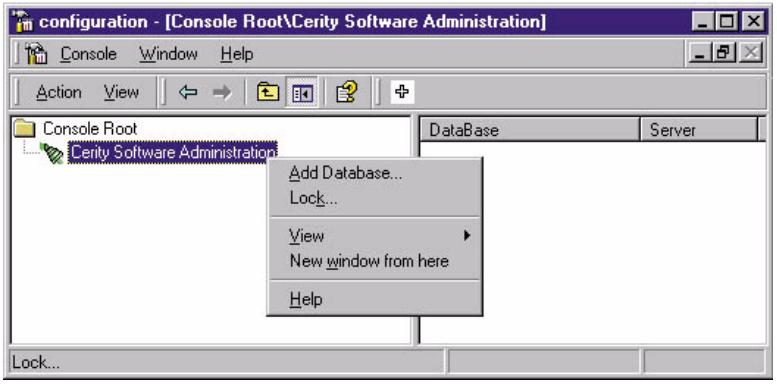


Figure 74 Shortcut menu to add database

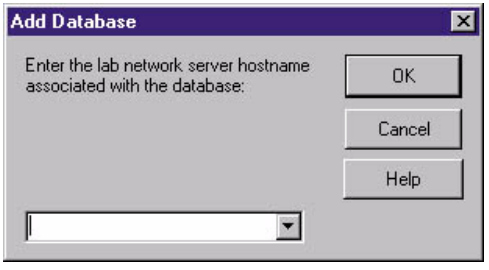


Figure 75 Add Database dialog box

If this is a standalone installation (Cerity NDS Professional), you use the name of the standalone PC.

Cerity NDS Licensing

The system authorizes a set of “demo” licenses for your instruments and Cerity NDS modules during installation. This license type is temporary. You may not use the demo license for longer than 30 days. If you require a license for longer than the 30-day demo period, you must add the required license that has been purchased from Agilent Technologies in the License Module. After you purchase a license, you need to authorize the use of your new license based on the license agreement.

The **License Module** folder lets you:

- View license usage across all installed modules
- Authorize use of a license
- Upgrade or add a Cerity NDS license

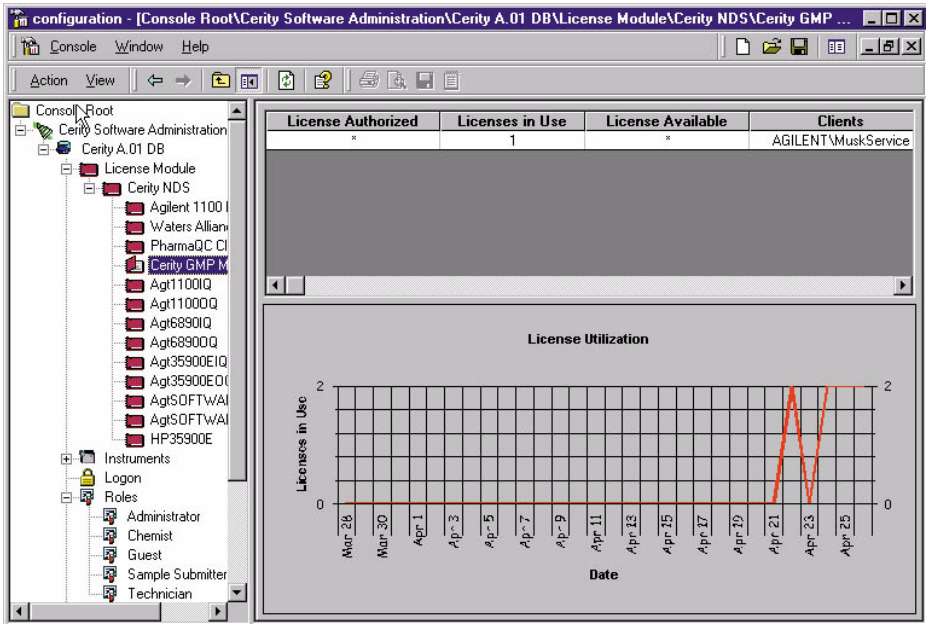


Figure 76 License item

License Types

Three license types are supported for Cerity NDS for Pharmaceutical QA/QC:

Demo This is the default license type when you install Cerity NDS software. The demo license allows an unlimited number of users to access Cerity modules and instruments. **Demo** expires on a predefined date; when it expires (or before), you must enter the license information from your Agilent license certificate.

Expiration This license type is used for Cerity Compliance validation utility (IQ and OQ/PV). The system counts the number of times users have run the Compliance utility and printed a certificate. When this number reaches a predefined limit, you must contact Agilent Technologies to purchase more licenses.

None This license type allows a specified number of concurrent users to access a module or instrument. The number of users depends on your purchase agreement with Agilent Technologies.

UV Spectral Licenses

A UV Spectral license is needed only for UV spectral acquisition; processing of spectra does not require a license. The UV Spectral license is assigned to an instrument, and allows UV spectra to be acquired on the instrument. If the license is revoked, the acquired spectra can still be processed (UV spectral compound confirmation, UV purity), but further UV spectra cannot be acquired, and methods with UV spectral acquisition cannot be created.

Managing Users

The Users folder lets you set up users in your Cerity NDS.

You can:

- Add Cerity NDS users
- Enable and disable users
- Assign users their **Current Roles**
- Assign users their Review Rights
- Assign a Default Printer for each uses
- Copy users from one database to another

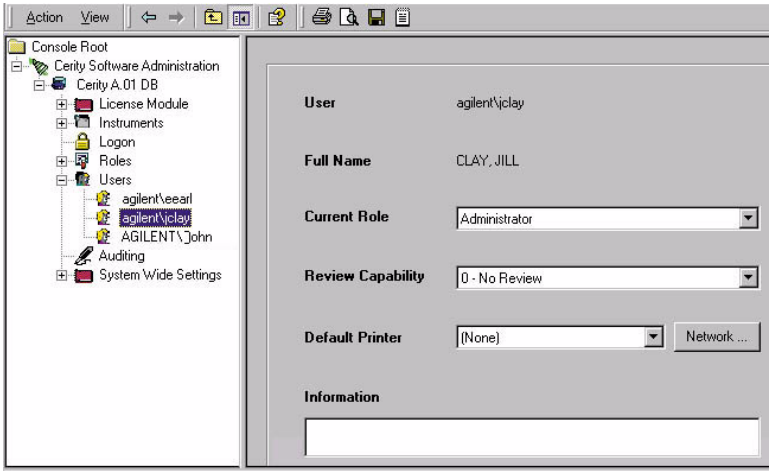


Figure 77 Users folder

Managing Instruments

You use the Instruments folder to add acquisition controllers, logical instruments, and devices. You must enter parameters for the instruments and devices in the Pharmaceutical QA/QC application.

You can:

- Add and remove acquisition controllers
- Add and remove logical instruments
- Add and remove devices
- Change connection properties of devices, instruments, and acquisition servers
- Move a logical instrument and linked devices to a different acquisition controller
- Stop and Suspend an instrument
- Resume and Start an instrument
- Add a UV Spectra license
- Revoke a UV Spectra license

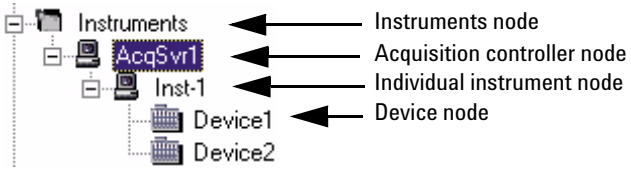


Figure 78 Instruments folder

Cerity NDS System Administration and Maintenance

After administrators perform the post-installation tasks, they must maintain the system and can exercise the option of customizing the Cerity NDS to meet their own laboratory needs. Administrators must understand how to manage the following Cerity NDS features:

Security and auditing

Administrators can do the following to make sure that the system is secure:

- Set or change logon security
- Change password of Cerity NDS Network Server account and for CAGDbAdmin
- Restrict access to the Registry Editor
- Set permissions on Cerity NDS and Oracle directories
- Assign roles to users to restrict their access to Cerity NDS for Pharmaceutical QA/QC functions
- Set up auditing so that the system tracks the change, user who made the change, date of the change and reason for the change according to your company procedures.

System-wide formats

Administrators can set up or change the numeric formats or date/time formats for the Cerity NDS as a whole.

Database maintenance

Administrators can do the following to maintain the database:

- Archive, restore or delete data
- Back up the database
- Resolve database inconsistencies after restoring data

System maintenance

Administrators can do the following to maintain the system:

- Print the Cerity NDS Software Administration setup parameters
- Display Cerity NDS host details
- Check status, start, or stop Cerity NDS services

See the System Administration Online Help for instructions to complete these tasks. The concepts in this section help the administrator perform these tasks.

Security and Auditing

Logon access

The Logon item in the Cerity Software Administration Configuration window controls logon access to your Cerity server and client systems. For example, you can control the number of users who can log on to the Cerity NDS from the same Windows Workstation.

You can:

- Enable and disable logon security
- Allow one user per computer
- Allow multiple users for a client computer
- Set idle time to automatically lock the application for user sessions that share the same client computer
- Specify the Cerity NDS application(s) that can access the database

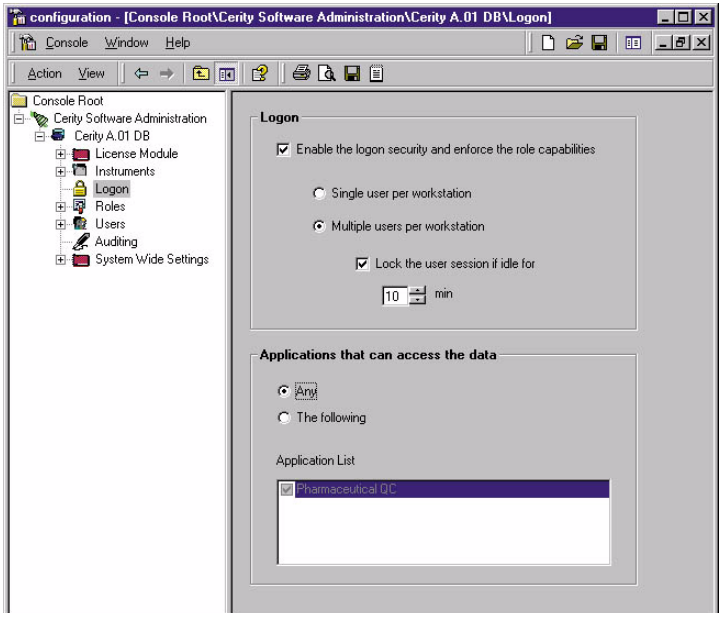


Figure 79 Logon item

Password changes

You can change passwords for the server account and for the database in the Administration and Maintenance list of tools. You access these two tools from the **Start** menu. When you select the **Change Password** menu items, their respective dialog boxes appear.

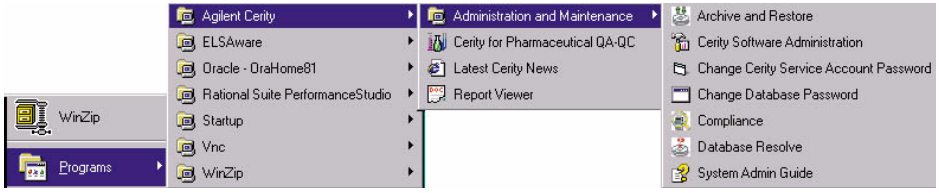


Figure 80 Change Password menu items

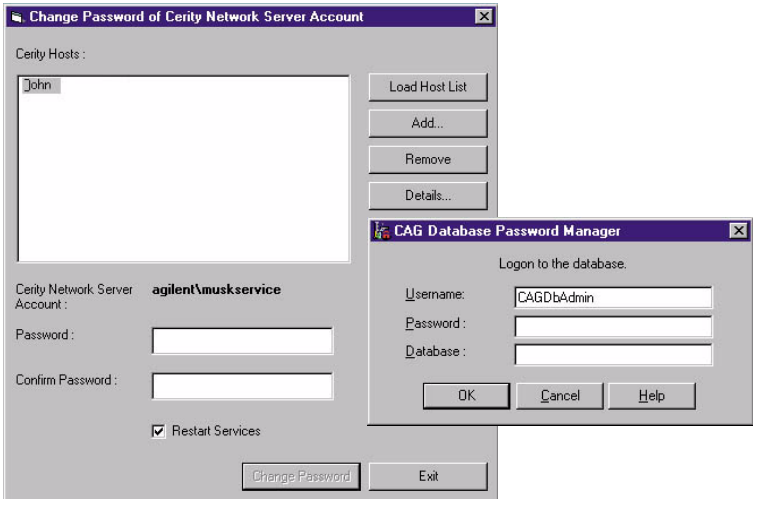


Figure 81 Change Password dialog boxes

Permissions for Cerity NDS and Oracle directories

The table below provides a brief summary of important Cerity NDS and Oracle directories and the recommended Windows permissions for accessing them.

Table 15 Windows Directory Permissions

Directory Name	User or Group	Recommended Permissions
Cerity NDS registry entry (HKeyLocalMachine\Agilent\Cerity)	Administrators group; EVERYONE	Share and file system permissions: Full Control Share permissions: Read-only
Oracle\Ora81\Bin	SYSTEM	Directory system permissions: Full Control
	Administrators group	Directory system permissions: Read-only
Oracle\...\Oradata	SYSTEM	Directory system permissions: Full Control
	All other users	Directory system permissions: None
Oracle registry entry (HKeyLocalMachine\Software\Oracle	SYSTEM	Directory system permissions: Full Control
	All other users	Directory system permissions: None
System Temp directory (e.g., C:\Temp), if certain services do not start.	All users	Directory system permissions: Full Control
Cerity\Reports	EVERYONE	Share permissions: Read-only
	• Any Windows user that will use Cerity NDS • All Cerity NDS clients • Cerity NDS administrator	Share permissions: Full Control
Cerity\Reports\PharmaQC\Templates	EVERYONE	File system permissions: Read-only
	Any Cerity NDS user who needs to edit report templates	File system permissions: Full Control
Cerity\Reports\PharmaQC\pharmaqc.dd (Data dictionary — contains all fields, variables and results available to user)	All users and groups	File system permissions: Read-only
Cerity\Reports\PharmaQC\Reports	EVERYONE	File system permissions: Read-only
	Cerity NDS Service User	File system permissions: Full Control

Role assignment

The Roles folder lets you set up task rights for the default roles: Administrator, Chemist, Guest, Sample Submitter, and Technician. See "User roles and rights" on page 26 for more information.

Auditing

NOTE By default, the Guest role has no user rights, and therefore gets an empty application on login. The setup of the Guest role is the responsibility of the system administrator.

Cerity NDS for Pharmaceutical QA/QC provides a set of tasks that supports regulatory guidelines for auditing electronic records. The Auditing item lets you set up the auditing requirements for each task.

You can:

- Require users to enter an audit reason for a task
- Restrict users to audit reasons set up by the Cerity NDS administrator
- Require an Electronic Signature for a task.
- Create a list of audit reasons
- Remove audit reasons from the list
- Mark or clear auditing requirements for a task

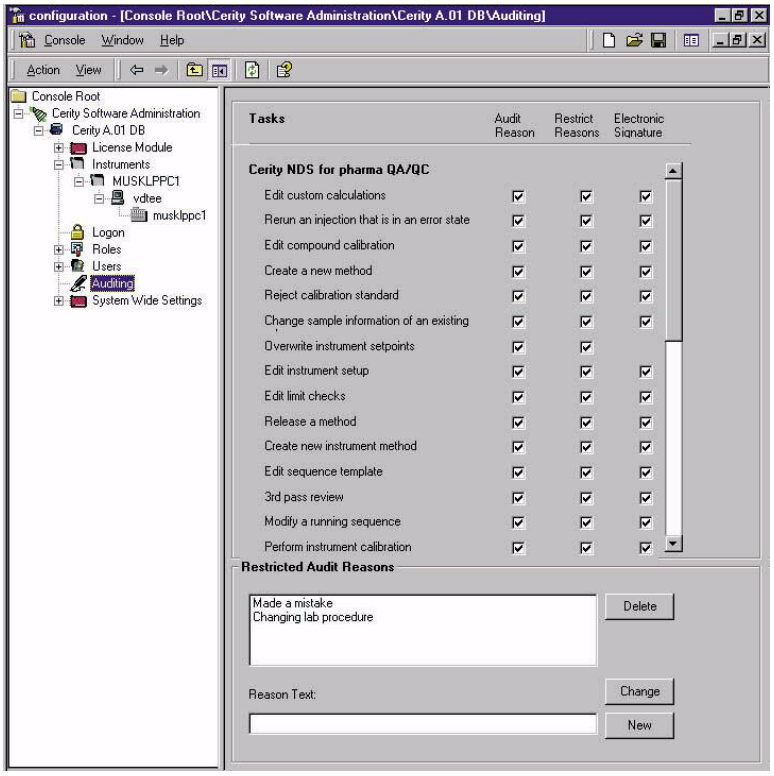


Figure 82 Auditing item

Database Maintenance

Archive and Restore

You use the Archive and Restore application to archive, restore or delete data in the database. You select the **Archive and Restore** menu item from the **Start** menu to access the first panel of the Archive and Restore application.

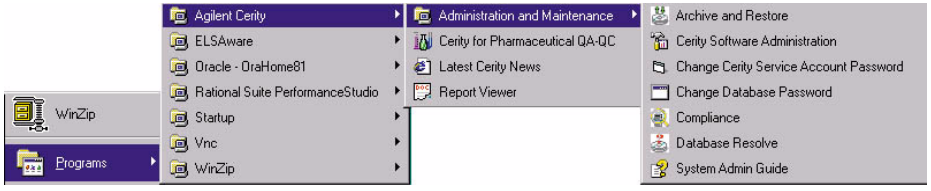


Figure 83 Archive and Restore menu item

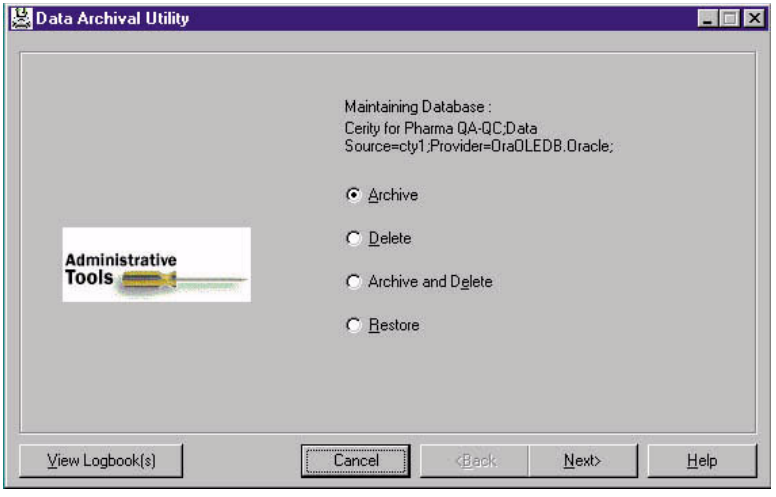


Figure 84 First panel of the Data Archival Utility

Search the database to archive or delete "objects" The Cerity NDS Data Archive Utility lets you save database "objects" such as entered samples and sequences, sample and sequence results, instrument and method information to an archive media (disk or other storage). You use the archive utility for long-term storage. You also use this tool to move data from one database to another. Once you archive your data, you can remove old data from your database. You need to prune your database on a regular basis to maintain good performance of your system. The Cerity NDS stores the archived objects in the directories of the Windows file system.

The Data Archival Utility uses the same **Query Wizard** to find these objects to archive that the Pharmaceutical QA/QC application uses to find the objects to set up or edit. See "Database Searches" on page 72 to learn more about the Query Wizard.

Restore "objects" to the database The Data Archival Utility restores objects in the Windows file system onto any drive on the network to the same or a different database on the network.

When the Data Archival Utility restores objects archived from one database to a different database, the Database Resolve utility starts by itself to resolve inconsistencies between the databases. You must decide which versions to use if there are duplicates.

Cerity NDS backup

For details of cold and hot system backups using standard Oracle tools (for example, RMAN), see the documentation on the Cerity Application CD-ROM. Backup and restore scenarios using third-party backup/restore programs such as those by Veritas Software can be developed and provided by the Agilent Professional Services Organization (PSO) as a service.

Work with your Agilent Cerity NDS representative to establish backup, archive, and delete schedules that are appropriate for your system.

Resolution of database name conflicts

You can resolve database name conflicts when you run the Database Resolve utility. Select the **Database Resolve** menu item from the **Start** menu to start the utility.

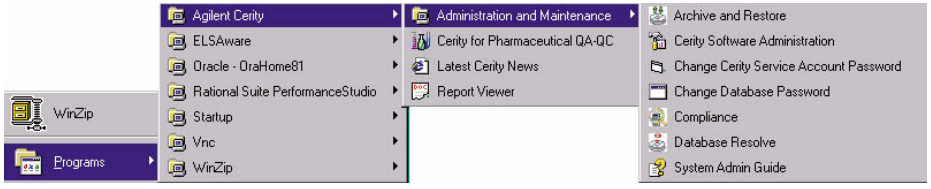


Figure 85 Database Resolve menu item

After you log on, the system runs the utility and displays either a message that declares no name conflicts or a panel that displays the name conflicts that you must resolve. If duplicate names are found, you can resolve the name of the role or user and you can choose to enable an instrument.

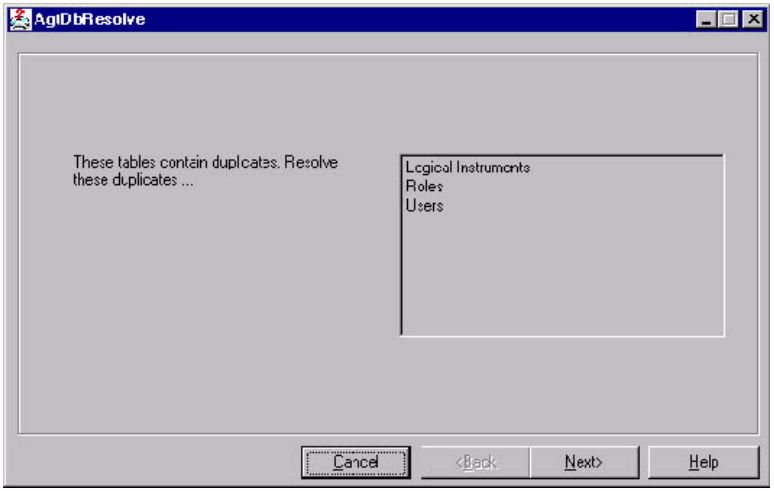


Figure 86 Database Resolve panel

The utility, **Archive and Restore**, automatically launches the **Database Resolve** utility when it attempts to restore data from one database to a different database.

Object locking

When an application accesses an object in the database, for example, a sample or method, the object is locked automatically. Should the system crash, the lock is not broken, and the object remains unavailable to other computers on the network. Restarting the application from the computer where the crash occurred recovers the locked objects in most cases. However, in cases where the object is not recovered by restarting the application, execution of one of the commands in the *lockedobjects.sql* query will recover the object.

10
Definitions of Terms

Chapter 10 explains the terms that are used in Cerity NDS for Pharmaceutical QA/QC.

Integration

Cardinal Points

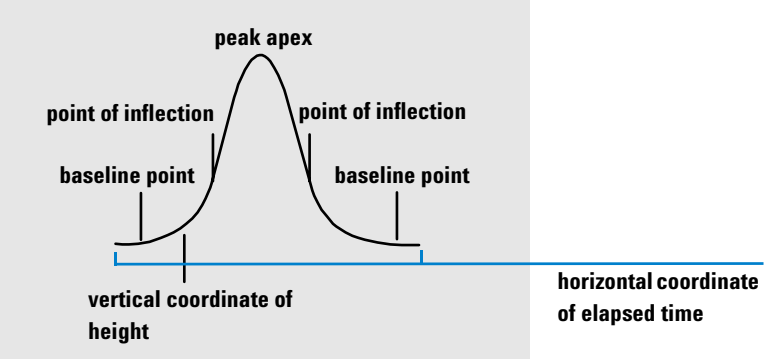


Figure 87 Cardinal points

Cardinal points are the points chosen by the integrator to define and quantify a peak. Baseline points, valley points, peak apex, and points of inflection are designated cardinal points and saved. Each cardinal point has a horizontal coordinate of elapsed time, a vertical coordinate of height from the baseline, and other parameters, such as peak type, separation codes, start/end values of potential peaks, and corresponding height, area and slope readings, that the integrator uses to calculate the peak areas.

Solvent Peak

The solvent peak, which is generally a very large peak of no analytical importance, is not normally integrated. However, when small peaks of analytical interest elute close to the solvent peak, for example, on the tail of the solvent peak, special integration conditions can be set up to calculate their areas corrected for the contribution of the solvent peak tail.

Shoulder (front, rear)

Shoulders occur when two peaks elute so close together that no valley exists between them, and they are unresolved. Shoulders may occur on the leading edge (front) of the peak, or on the trailing edge (rear) of the peak. When shoulders are detected, they may be integrated either by tangent skim or by drop-lines.

Slope

The slope of a peak, which denotes the change of concentration of the component against time, is used to determine the onset of a peak, the peak apex, and the end of the peak.

Spectra Handling

Spectrum extraction

When not all acquired spectra are needed for a spectral processing task, a reduced number of spectra (3, 5, 7 or 9) can be extracted from the data set.

Apex spectrum

The spectrum at the apex of the chromatographic peak. The apex spectrum is always included in all spectral processing calculations.

Reference spectrum

A known spectrum, extracted from a previous analysis, that is used for comparison in spectral compound confirmation.

Background spectrum

A spectrum that contains only background absorbance, that is subtracted from the peak spectrum to give a background-corrected spectrum containing absorbance due to the sample only.

Background correction

Removal of background absorbances from the peak spectrum by subtraction of one or two background spectra.

Spectral compound confirmation

Comparison of the apex spectrum with a reference spectrum, and calculation of a similarity value.

UV purity

Comparison of all extracted spectra in a peak with the apex spectrum to check peak homogeneity.

Similarity value

A measure of how similar two spectra are; identical spectra give a similarity value of 1000.

Identification

Peaks and Compounds

A peak is an integrated chromatographic envelope in a signal. A compound can consist of a single peak, or several peaks, for example from multiple signals or different detectors.

Main peak

Where a compound consists of more than one peak, one peak (usually the largest) is specified as the main peak for compound identification. All other peaks are then classified as secondary peaks.

Peak identification table

The peak identification table is a database containing the expected retention times and a signal identifier (either signal name or description) of the compounds in the analysis.

Expected retention time

The expected retention time is the time at which the peak is expected to elute. It is the retention time of the peak in the peak identification table, corrected by any drift correction determined by time reference peaks (if present).

Relative retention time

Relative retention times are specified in many regulatory methods for the identification of minor components. The relative retention times are calculated relative to a main reference peak.

Time reference peaks

A time reference peak is a peak whose retention time is used to correct for any drift.

Time window

The time window is the window around the expected retention time of a peak, within which the peak is expected to appear. Time windows can be asymmetrical about the expected retention times of the peaks.

Signal

A signal is the measured response of the detector against time throughout the run. Where a detector can be configured to give multiple measurements (for example, diode-array or multi-wavelength detectors), each response is considered to be a different signal.

Signal correlation

Signal correlation assigns two peaks measured in different detector signals within a defined time window to the same compound. When signal correlation is off, peaks eluting at the same retention time in different detector signals are treated as different compounds.

Calibration

Calibration

Calibration is the process of determining response factors used to calculate absolute component concentrations, by injecting specially-prepared calibration standards.

Recalibration

Recalibration is the process of updating the calibration information (responses and retention times) in the calibration table based on new injections of the calibration standards. Recalibration can be carried out at any time, and the updating of the calibration information can either include or exclude the existing calibration data.

Compound

A chemical compound can comprise several peaks, in a multi-signal calibration, typically one per signal. In a single signal calibration, a compound refers to one peak.

Calibration Level

A calibration level comprises the calibration points for one calibration standard concentration. In a multi-signal calibration the calibration points can be distributed over several signals.

Calibration Point

A calibration point refers to an amount/response pair for a peak on the calibration curve.

Calibration Standard

A calibration standard is a sample containing a known amount of the compound to quantify. In the software, the calibration standard is referred to as an injection from the calibration standard vial.

Calibration standards may be purchased from chemical suppliers or they may be prepared using an accurately-measured amount of the pure compound. The amount of the compound in the calibration standard is usually expressed as a concentration, for example in ng/µl.

Single-level Calibration

For a single-level calibration, the response of the detector is assumed to be linear over the working range of concentrations for the samples of interest. A single calibration standard is analyzed, and a linear calibration curve is constructed using the response of the calibration standard and the origin. The slope of the calibration curve gives the response factor.

Multi-level Calibration

For a multi-level calibration, the calibration curve is characterized using the responses of multiple calibration standards analyzed at different concentrations. The calibration curve, which may be non-linear, is constructed by fitting the curve to all the points.

Calibration Table

The calibration table is a multi-dimensional matrix that defines the response of each different analyte at each different concentration.

Calibration Curve

The calibration curve defines the response of the detector to different concentrations of an analyte.

$$Response = f(Amount)$$

It is a graphical representation of the amount and response information for the analyte in the calibration table.

Relative Response Factor

The relative response factor of an analyte is the response relative to another, usually major, compound whose response factor is well characterized. Relative response factors are used when calibration standards are not available.

Calibration Precision

In variable-amount calibrations, the calibration precision can be calculated as the relative standard deviation (RSD) of the response factors.

Fixed-amount Calibration

In fixed-amount calibrations, the amounts of calibration standards injected are the same as the entry in the calibration table at each level each time the calibration is run. Response factors can be replaced or averaged during recalibration.

Variable-amount Calibration

In variable-amount calibrations, the individual weights or concentrations of the calibration standards are entered for each calibration. Variable-amount calibrations allow the calibration history to be maintained, and the calibration precision to be calculated.

Quantitation

Response

The response is the magnitude of the signal provided by the detector. Response can be measured either as the height of the signal at the highest intensity, or as the area of the signal above the baseline.

Response Factor

The response factor is the ratio of the response (the magnitude of the signal as either height or area) to the concentration of the analyte:

$$\text{Response Factor} = Response/Amount$$

Area Percent and Height Percent

Area percent (Area%) calculates the area of each peak as a percentage of the total area of all peaks in the run.

Height percent (Height%) calculates the height of each peak as a percentage of the total height of all peaks in the run.

ESTD

ESTD (External Standard) quantitation is the basic quantitation procedure in which the response of the unknown is compared with the response of one or more calibration standards analyzed under the same conditions.

Norm%

The Norm% calculation calculates the amounts by applying response factors before calculating the result for each peak as a percentage of the total amounts of all peaks in the run.

ISTD

In the ISTD (Internal Standard) quantitation method, a known amount of a component is added to all samples and standards. This component is used as a normalizing factor to compensate for changes in, for example, detector response.

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In This Book

The Concepts Guide contains descriptions of the concepts of the Cerity Networked Data System (NDS) for Pharmaceutical QA/QC to help you understand the Cerity NDS for Pharmaceutical QA/QC components, and how they work.

It contains information about the design principles, the system behavior, and the control and information flow of the Cerity Networked Data System (NDS) system.

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