SIEMENS

SIMATIC IT Unilab 6.7

Stability Module

Concepts and User Manual

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Guidelines

This manual contains notices intended to protect the products and connected equipment against damage. These notices are graded according to severity by the following texts:

Caution

Indicates that if the proper precautions are not taken, this can result into property damage.

Notice

Draws your attention to particularly important information on handling the product, the product itself or to a particular part of the documentation.

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Preface

Where is this manual valid?

This manual is valid as of release 6.7 of SIMATIC IT Unilab.

Basic knowledge required

This guide is intended for SIMATIC IT Unilab users who are responsible for system configuration, such as application managers and system integrators (consultants). To be able to understand the concepts and examples discussed in this guide, the reader should at least have taken the SIMATIC IT Unilab Basic Training.

In order to understand this manual, general knowledge of the concepts and architecture of Unilab is required.

Purpose

This Concepts and User Manual explains how the **Stability module** integrates the concept of stability studies in Unilab.

The present guide includes several scenarios that illustrate how stability testing can be used to implement specific laboratory procedures.

Important

The **Stability module** is a Unilab Component that needs to be activated with a specific 21 CFR Part 11 license key.

Related documentation

The following documents contain information related to the content of this Concepts and User Manual.

- Unilab Concepts Guides (part 1, 2 and 3)
- The presentation Unilab Stability Module Concept

These documents are all available online from the SIMATIC IT Unilab Documentation Library.

Conventions

The table below describes the specific typographic conventions that are used throughout this manual:

Symbol/Convention	Indicates...
E.g.	Where examples are given.
Text in bold	The names of menus, commands, dialog boxes and toolbar buttons and, in general, all strings (e.g. **File** menu; **Save** command).

Symbol/Convention	Indicates...
KEY1+KEY2	Shortcut keys, which permit rapid access to commands (e.g. CTRL+C).
UPPERCASE	The names of keyboard keys (e.g. RETURN key).
Italics	Noun with special importance or significance for which emphasis is needed. The names of parameters that must be replaced with a specific name or value.
>	A succession of commands in which the command preceding the symbol must be selected before the command following it.
`Code example`	Code example.

SIMATIC IT Documentation Library

The SIMATIC IT Documentation Library provides you with a comprehensive and user-friendly interface to access the overall product documentation where manuals and helps online can be browsed by functionality or by component.

Readme

The installation includes a readme file, which contains information on upgrade procedures and compatibility with previous releases. This file is supplied both in standard text (**Readme**.**wri**) and in Acrobat PDF (**Readme**.**pdf**) format.

This file is available in folder \ReleaseNotes of the setup DVD and is available from the SIMATIC IT Unilab Documentation Library.

Stability concepts

The table below lists the stability concepts that are use in this document.

Concept	Explanation
Protocol	A plan for stability studies, including points in time, storage conditions, number of samples, test plans etc.
Stability study (Study)	Stability testing in operational sense, including related objects like samples
Sample (sc)	Common Unilab sample
Study sample	Operational sample (sc), linked to a study
Sampling	Taking material (from storage or production areas) for analysis
Pulling	The removal of study samples from storage
Zero-time	The starting point of (a part of) the study
Condition	Aspect or state of storage or study material, e.g. temperature, humidity, light
Condition set	Combined storage conditions e.g. temperature of 25 C, upright position

SIMATIC IT Training Center

Siemens IA AS MES offers a number of training courses to familiarize you with the SIMATIC IT product suite. To successfully achieve this goal, training consists of lessons in both theory and practice.

Courses are held year-round, according to a program that is published well in advance of the first scheduled session.

The material on the basis of which our courses are conducted reflects the result of years of experience in process, LIMS, quality control and production management.

All courses are held by expert personnel that are aware of the developments and innovations in the Siemens IA AS MES product suite.

Courses are held in English at the Siemens IA AS MES Training Centers.

Upon request, training courses can also be organized on the customer's premises.

For more information on the training course calendar, please visit our technical web site (http://www.siemens.com/simatic-it/training).

SIMATIC IT Service & Support

A comprehensive Software Maintenance program is available with SIMATIC IT products. Software Maintenance includes the following services:

- **Software Update Service** (SUS): automatic distribution of upgrades and service packs
- **Technical Support Service** (TSS): support on technical problems with SIMATIC IT software (standard support and other optional services)
- **Online Support**: a technical web site, providing information such as Frequently Asked Questions and technical documentation on SIMATIC IT products

Software Update Service (SUS)

This service provides automatic shipment of new versions and service packs when released. When a new version / service pack is available for shipping, it is typically shipped within one month.

One copy of the installation DVD is shipped for each Server covered by Software Maintenance.

Hot fixes (officially tested and released) are not shipped and must be downloaded from the Technical Support Service web site.

Technical Support Service (TSS)

Siemens provides a dedicated technical support team for SIMATIC IT products.

The following options are available:

Bronze support: 9 hours/day, 5 days/week

Silver support: 24 hours/day, 5 days/week

Gold support: 24 hours/day, 7 days/week

The principal language of the SIMATIC IT hotline is English.

SIMATIC IT partners and customers covered by the Software Maintenance program are entitled to direct access to the TSS.

Access to TSS

To be able to access TSS, the customer needs to register as a user on the Technical Support web site. Connect to http://www.siemens.com/mes-simaticit/ and follow the **Technical Support Service** link.

The registration form must be completed with:

- Personal data
- The required company and plant information
- The Contract Number provided by Siemens Back Office when the contract is agreed.

Online Support

A customer who is a registered TSS user, can access the Technical Support web site (http://www.siemens.com/mes-simaticit/tss), which contains technical information such as:

- Service conditions (Phone numbers, Working hours, Reaction times,…)
- SIMATIC IT knowledge base: a technical support database that includes practical service solutions from Technical Support or the SIMATIC IT community
- SIMATIC IT software (e.g. hot fixes, software examples) and release notes that can be downloaded
- SIMATIC IT cross-industry libraries that can be downloaded (limited access to SIMATIC IT certified partners)
- SIMATIC IT product documentation that can be downloaded
- Frequently Asked Questions and useful tips.

Table of Contents

1 Introduction

Stability testing is a routine procedure performed on drug products, active ingredients and excipients in order to understand the long-term effects of the environment on the drugs. It is used at various stages of product development. In the early stages, accelerated stability testing (high temperatures and relative humidity) is used to evaluate the stability of the drug and to determine what types of degradation products may be found after long-term storage. Testing under normal conditions (those recommended for long-term shelf storage) can be used to determine a product's shelf life and expiration date. In these types of studies, the product is analyzed at predetermined intervals for various parameters.

Remark: An excipient is an inert drug substance used as a medium or carrier for an active drug.

Definition of stability testing

ICH defines stability testing as follows:

> The purpose of stability testing is to provide evidence on how the quality of a substance (drugs, food) varies with time under the influence of a variety of environmental factors(conditions) such as temperature, humidity, and light, and enables recommended storage conditions, retest periods, and shelf lives to be established.
> Stability testing can be done as part of the introduction of new substances (e.g. drugs) (R&D) but also in case of a new dosage form, e.g. a different administration rout (oral, parenteral), new specific functionality/delivery systems and different dosages forms (QA/QC).

The purpose of the Unilab **Stability module** is to support users in defining and executing stability studies and analyzing the results of stability studies.

The stability functionality focuses on the extra functionality needed for stability studies. As already available, standard Unilab functionality is used for configuration, analyzing, calculations etc. on samples and parameters of stability studies. This functionality is not described in this document and presumed to be known to the reader.

2 Conceptual Overview

General

To define the functionality of the **Stability** module, the functionality is divided into 2 major parts:

- A configuration part, which consists of:
  - A condition set
  - A location
  - A protocol

  Defined by making use of the defined condition sets and time points. These dimensions can easily be derived from the ICH definition.
- An operational part: a **Stability Study**

  The operational blueprint of the protocol, also containing locations next to the time point and condition sets.

Configuration data versus operational data

The building blocks **Condition Sets**, **Locations** and **Protocols** are the configuration objects. They are (like e.g. request types, sample types) templates for future operational objects. A protocol is a template for a study. The study itself and all related objects are to be considered as operational objects (like e.g. requests, samples). The relation between a study and a protocol is equal to the request and request type relationship.

The study itself and all related objects like info cards and parameter profiles will be created as configured in the protocol. At the creation of a study, assignment rules are evaluated and samples are created with the status ‘planned’.

Samples that are part of a study are put into storage under a certain condition for a specific period of time. After this period, the samples are removed from the storage location (pulling) and are analyzed in the laboratory. It is clear that all operational samples that are part of a study can only be planned after filling in the zero-time. At pulling time (or pulling time-warning period), the sample will switch from status ‘planned’ to its status ‘available’ based on its life cycle.

Interaction with existing Unilab modules

So as to limit the number of different modules, the implementation of the functionality should be part of existing modules:

- **Condition Sets** and **Locations** config.: part of **Configuration**
- **Protocol** builder: part of **Configuration**
- **Stability Study** management: part of **Analyzer**

A protocol is considered to be a special kind of request type, with comparable but some specific properties. A study is a special kind of request.

The samples that are part of a study are ordinary samples. Result entry on these samples is done in the current operational **Analyzer** tasks: Request, Sample or Worklist tasks.

Standard properties of protocols and studies can be used for:

- Viewing
- Searching

21 CFR Part 11

The **Stability module** also supports 21 CFR Part 11, which means a comprehensive, extended audit trail, compliant logon procedure and version control is applied.

License key

The **Stability module** is a separate module, which has to be activated with a specific 21 CFR Part 11 license key.

3 Configuration Data

General

To be able to create protocols, some additional configuration objects are required: **Condition Sets** and **Locations**.

Condition sets

A condition set consists actually of one or more conditions with a fixed value. A condition might be for example “T=40°C”, a set “T=40°C / RH = 40%”. These conditions that are part of the condition sets should be selectable on sample level. In this way, it is also possible to show all samples stored in 30°C, not looking at the relative humidity or position.

It is possible to assign attributes to condition sets to make it possible to have user defined properties for e.g. custom logic, grouping of condition sets.

The **Conditions** table consists of 2 columns. In the first one a condition can be selected from a so-called existing list. This is a combo box where the list shows already assigned conditions in the system. This prevents typing errors or case-sensitivity errors (“Temperature” is different from “temperature”). This makes the selection also more user-friendly.

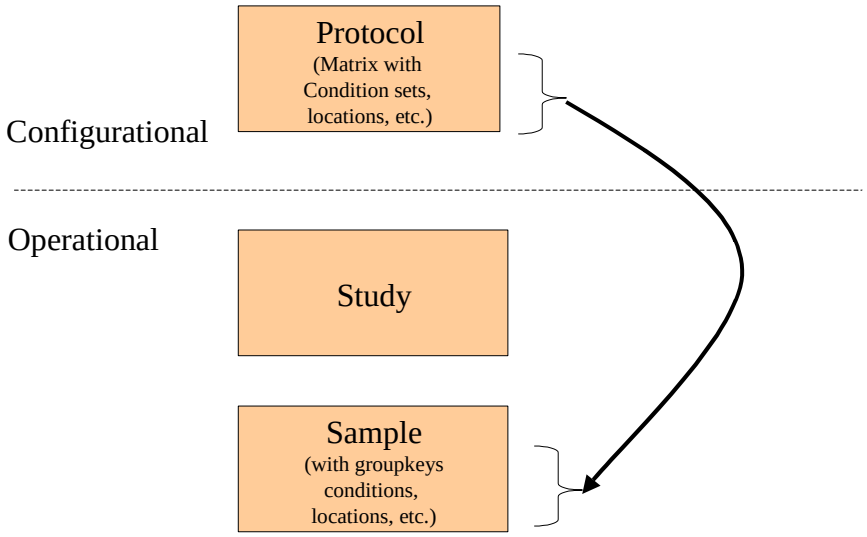
A **Condition Set** has the following properties:

- Name (e.g. “30_75_TD”)
- Description (e.g. “30°C / 75% / TD”)
- Description 2
- Tab **Attributes**

Storage locations

In this configuration object, the specific locations for the storage of samples are defined. For each sample, it is possible to assign such a storage location. In this manner, samples can be found easily, and it is possible to have a basis for storage management (which can be done by custom functionality).

The picture below illustrates the relation between **Protocol** condition sets and locations and **Sample** group keys.



Locations can have a hierarchy, but it is assumed that it is not necessary to have different levels of locations (e.g. location = “Freezer 1”, sub location = “Shelf 2”). Each distinctive physical location must get a unique name (e.g. “F1S2” meaning “Freezer 1, Shelf 2”). For storage location management, standard properties **maximal number of samples**, **current number of samples** are foreseen.

It is possible to assign attributes to locations in order to have user-defined properties for e.g. custom logic, grouping of locations.

Each location can be linked to condition sets. This is an n-n link: each location can have one or more condition sets. one condition set can be valid for several locations.

Example

Location “Freezer1” can have condition sets “T=0°C, position=top down” and “T=0°C, position=bottom down”.

Thus, a LOCATION has the following properties:

- Name (e.g. “F1S2B34”)
- Description (e.g. “Freezer 1, Shelf 2, Box 34”)
- Description2
- Tab **Attributes**

Protocol

The definition of a protocol means setting rules for operational studies. The most important rules for studies are:

- The storage time
- The condition of the samples

The time points and condition sets together form a 2-dimensional matrix.

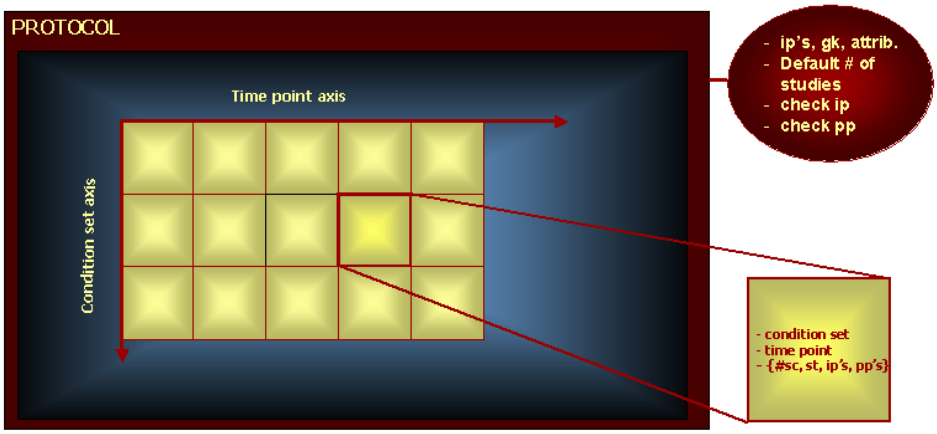
A protocol consists of a 2-dimensional matrix.

These 2 dimensions however are not sufficient for the protocol as it is commonly defined by e.g. pharmaceutical companies. A protocol can be made for several batches or packaging types. It is possible that for a different packaging type, a different matrix is needed.

So it is possible to group different protocols, using the Unilab group key principle. For instance, it is possible to assign a group key **Protocol Group** to different Unilab protocols with a certain value referring to the internal protocol definition, which mainly will consist of different matrixes. So, define each different matrix as a Unilab protocol, and group the matrixes belonging together with a protocol group key such as **Protocol Group**.

It is possible to assign and inherit group keys to protocols.

When several batches, lots, … have to be part of a study, the protocol where the study is based upon is repeated as much as needed grouping them with the protocol group keys. It is possible to define the default number of studies when a study is created based upon this protocol.



The 2-dimensional protocol matrix looks like this:

The default screen shows per cell the total number of samples that it default contains. When it is empty, no samples will be created for this condition set - time point combination.There are no tooltips implemented (the grid doesn't allow it). Double clicking on the cell opens the details, where it is possible to assign the number of samples, info profiles, parameter profiles.

Protocol properties

Each protocol consists of a matrix, with time points and condition sets. The X-axis is the **Time Point** axis relative to zero time. It is possible to delete, insert, append time points. The following details can be filled in:

- Offset time, relative to zero time. This can be defined in minutes, hours, days, weeks, months, fixed months, years etc
- A warning period for each time point to warn eventually the user of the system when a pulling is coming near or is expired.

The Y-axis is the condition set axis. It is possible to assign multiple condition sets in one protocol by means of inserting and appending rows. This is done via right clicking on the condition set axis/column. By deleting a row, a condition set is removed from the protocol. Choosing from a drop down list, containing the configured condition sets, can specify the condition set for one row. The list contains the name and the description of the condition sets. By assigning condition sets, columns representing specific conditions (see paragraph on condition set definition) are automatically filled up.

The table below lists the properties of a protocol.

• name • version • description • description2 • status • SOP • label format • planned responsible • **Can be used as template** checkbox • study life cycle (Life cycle of the operational Study) • UCM Study (Unique code mask of the study) • study sample life cycle (Life cycle of the sample in a Study)	• UCM sample (Unique code mask of the sample in a study) • an **Info Profile** tab where protocol info profiles can be assigned • a **Add st parameter profiles** checkbox (keep orig st pp or only prot. pp) • a **Add st info profiles** checkbox (keep orig st ip or only prot. ip) • a **Planning** tab with all frequency properties (nice to have) • an **Attributes** tab • an **Audit Trail** tab • an **Access rights** tab • a **Group keys** tab (inheritance flag)

Remarks

- Samples of study could have code mask = unique code mask study + counter sample within study.
- It is possible to create a new protocol based upon an existing protocol.

Protocol cell properties

The body of the 2-dimensional protocol matrix consists of **Protocol cells** (one for each timepoint/condition combination), and contains the default number of samples to be created, the sample type, parameter profiles and info profiles.

In each cell of the protocol**,** it is possible to add/remove/change the properties. The pp and ip are inherited by the operational samples that are created based upon the protocol definition.

Double-clicking a cell or a group of cells (selected by a multi-select operation) shows the actual details as already described. The **Time Points** and **Condition Sets** fields are automatically filled up with the current focus. This is not possible at protocol cell level.

Summary

- A protocol consists of one protocol matrix.
- Each protocol consists of protocol cells.
- Group keys are configured on protocol level.
- Sample types are configured on protocol CELL level.
- Parameter profiles are configured on protocol cell level.
- Info profiles can be configured on protocol and on protocol cell level.

Example typical workflow to define a protocol

Below is an example of a typical workflow to define a protocol:

1. Create new protocol or a new version of a protocol.
2. Complete protocol properties (Name, description, SOP, access rights, LC, UCM, etc.)
3. Add attributes.
4. Add group keys.
5. Add infoprofiles.
6. Insert condition sets in the 2-dimensional protocol matrix by choosing from a list of the active condition sets.
7. Add time points in 2-dimensional protocol matrix. Complete warn upfront and warn backward of time points.
8. Assign sample types, number of samples, info profiles, parameter profiles details in each cell of the protocol matrix by means of multi-select operations.
9. Save the protocol.
10. Approve the protocol.

4 Operational Data

4.1 Stability Study in General

In the operational applications, stability studies are created, based on a corresponding protocol, and maintained.

Basically, a stability study has the following structure:

Highest level: **Study** level (general information about the study) based upon a protocol, which consists of a matrix with **Time Point** and **Condition Set** axes. A study has an infocard and group keys eventually inherited from protocol level.

Second level: **Study cell** level (samples with info cards, parameter profiles, …).

Schematic representation of a Study

The table below shows a 2-dimensional **Study** matrix.

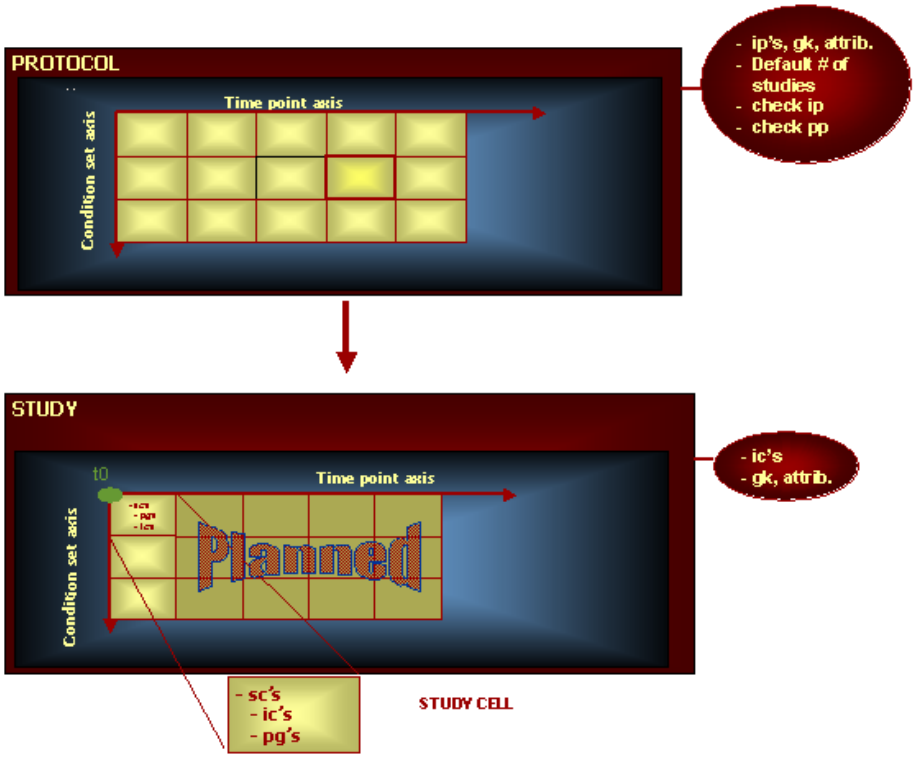
Description	6 Hours	1 Days	3 Days	1 Weeks
Condition Set 1	20050307-001	20050307-004		20050307-...
Condition Set 2		20050307-008	20050307-010	

Once a study or condition set is started, the zero time is protected. In the body of the matrix, the number of samples, as it was represented in the protocol definition, is replaced by sample codes. Each condition set row is multiplied per sample code. The condition set and its properties are only shown once, when multiple samples per time point apply for it. This matrix thus shows the sample codes. In this way it is possible to represent samples as in other Unilab applications. Right clicking on it or applying the menu makes it possible to see the sample infocards, parameter result window, properties or change a status, … The color of the sample code immediately gives an indication of the status of the sample, and makes it possible to make fast decisions.

In the matrix it is also possible to remove, add condition sets and time points (See later).

4.2 Study Creation

The picture below shows the principle of creating studies.



When creating a new study**,** a task is used to show a list of protocols. It is not possible to copy a study. The evaluation of the rules in the protocol is only done once: at study creation. A study consists of several **Study cells** for each time point – condition set combination. Each study cell contains one or more samples.

The study and the samples contains the correct infocards and parameter profiles according to all configuration settings and assignment rules. Samples obtain the condition set and time point properties as sample in study-properties. It is possible to show these properties in layout, and to select samples in sample lists based upon these properties.

After creation, the study properties and the underlying object properties can be altered according to functional access rights, new objects can be assigned etc. Extra time point values can only be added if the user has sufficient access rights to do so.

Concerning version management of protocols, the following must be taken into account:

- Apply version at study creation: At study creation, samples are created with status 'planned' with versions (i.e. sample type version, parameter profile versions, parameter versions, method versions, etc.) valid at the moment of study creation. When pulling time or near pulling time occurs, samples go to status 'available' based on their life cycle and maintain their versions valid at study creation
- Apply current version at pulling time: At study creation, samples are created with status 'planned' with infoprofiles but without parameter profiles, parameters, methods. When pulling time or near pulling time occurs, samples go to status **Available** based on their life cycle: from this point on, the current

versions of parameter profiles, parameters, methods assigned to the samples will be considered.

4.3 Zero Time

Zero time, the root point of the **Time Point** axis, can be defined at study level or condition level. If the lower level is not filled in, the system will relate to the higher level.

Zero time is the date that is used as a reference point for the calculation of the pulling-dates (sample planning dates). If Zero time is only defined at study level, then all time points in that study are calculated relative to this date.

Thus, it is possible that grouped Studies have different zero times (e.g. comparing different batches in a study, produced on different periods).

It is also possible that the study under room temperature has as zero time the production date, the testing that under acceleration circumstances has the dates assigned that the samples are stored under these conditions (and that can be on a date other than the production date).

Example

Study 1:

	Zero Time	**1 month**	**2 months**	**6 months**
Room temperature	15-4-2002	1 (15-5-2002)	1 (15-6-2002)	1 (15-10-2002)
Temperature 30°C	1-4-2002	1 (15-5-2002)	1 (15-6-2002)	

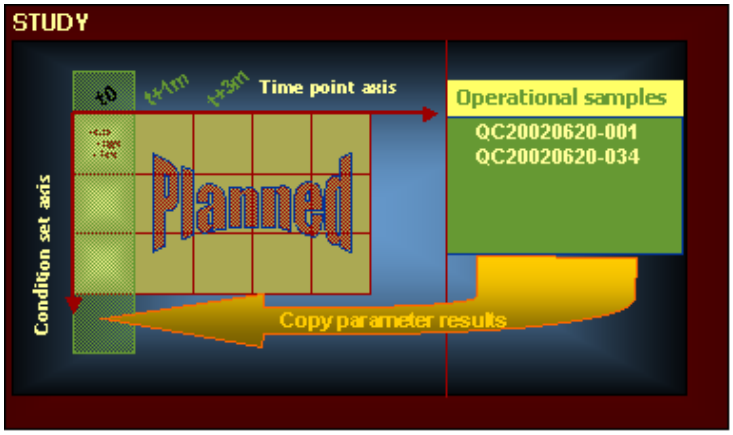
Study 2:

	Zero Time	**1 month**	**2 months**	**6 months**
Room temperature	1-4-2002	1 (1-5-2002)	1 (1-6-2002)	1 (1-10-2002)
Temperature 30°C	10-4-2002	1 (10-5-2002)	1 (10-6-2002)	

4.4 Assignment of Operational Samples

A study can be related to a certain production batch. For QC reasons, this batch has already been sampled, so it is possible to assign one or more operational QC samples to each study. The operational samples are the starting point of a study and are used for each condition of that study. These samples have to be seen as condition and time point independent.

Preferably, these operational samples are assigned via an extra window. This window tab can also be reached via a button in the toolbar.



4.5 Starting/Stopping a Study

It is possible to start and stop a study. Canceling can be done on study, time point, condition set or on sample level. Before a study or condition set within a study is started, no samples are activated yet.

When starting a study or condition set, the zero time setting is checked. This is necessary information to be able to plan the samples with their correct schedule date. A study can only start if this critical data is entered into the system. After the start of the study, the critical data cannot be altered anymore. When clicking the button, the system will ask to fill in these data when this information is not yet present.

At the start of the study or condition set, all necessary samples are planned at the pulling dates for each time point (these dates are calculated on the basis of the Start moment).

Example

20/06/2002 + 1M = 01/07/2002

20/06/2002 + 4W = 18/07/2002

20/067/2002 + 1M(fixed day) = 20/07/2002

The proposed pulling dates can be modified, provided that they have not yet expired. This can be done for each cell in the study via the cell's properties sheets. A message should appear when a date falling outside the warning period of the current time point is chosen.

From this moment on, one can easily create labels, calculate workloads and determine when samples have to be pulled for each location. Studies must be formally stopped. This can be done in the middle of a study. A stopped study will no longer accept new samples or results.

4.6 Adding/Deleting Axis Points

It is possible within a study to add a time point or condition set. This is done by right clicking on the respective axes. Samples will not automatically be created when adding columns or rows in the study matrix. This has to be performed afterwards.

It is clear that appropriate access rights are required to fine-tune this functionality according to function of a user in the lab.

4.7 Adding New Samples to Studies

Samples can be created at any time in any cell of a study.

There are 3 possible scenarios when creating samples in a study:

- One cell is selected and the cell (condition set – time point combination) is also present in the corresponding protocol where the current study was based upon
- More than one cell is selected and the cells (condition set – time point combinations) are also present in the corresponding protocol where the current study was based upon
- One or more cells are selected and the cells (condition set – time point combinations) are not present in the corresponding protocol where the current study was based upon.

4.8 Storing Study Material

The physical samples must be stored in certain locations. These locations are linked to certain condition sets (see location definition). It is possible to assign a location for each sample or condition set in a study. This is a customizable C++ function. By default, this function shows a list of locations according to the condition that is currently selected. For each condition, the user can see the maximum allowed number of locations, as well as the number of locations that are currently open at that specific moment (these are standard properties of a location).

Location	Description	# total positions	# positions left
F1S5B7	Freezer 1 Shelf 5 Box 7	10	2
T2S7	Tropical room 2 Shelf 7	20	8

As specific sample group keys based upon these locations are available, the user is able to easily retrieve a list of samples present in a certain location at any time.

The assignment of locations is done by means of a multi-select operation (selecting all samples of one condition set).

4.9 Maintaining Studies

- **Study properties**

  Standard properties like requests: ‘Description’, start date, end date, etc. An SOP should be assignable.

- **Study information window**

  Studies have (like requests) assigned info cards. General information concerning the study like the ‘reason for the study’ (e.g. a new dosage form) can be filled in. With a navigation bar, the user can switch from one study to the other study details window.

- **Study details window**

  This gives a list of all samples present in a study in a two-dimensional matrix view. With a navigation bar, the user can switch from one study to another. Gliding over a study **cell** shows a tooltip giving a short summary of what it contains. When right clicking on a sample, the sample information window or the parameter result window can be opened. A navigator gives the possibility to go to each sample in the study by choosing a condition set or a time point. From this point on, it is possible to modify each property of the sample, e.g. specifications.

- **Study operational samples window**

  This is a window showing the assigned operational QC samples. It is possible to assign samples, by means of a customizable list.

- **Alteration of Time Point Axis**

  Change, Insert, Delete time point. At the start of the study**,** the system proposes a pulling time. It is possible to alter this proposed pulling time, as long as it is not yet expired.

- **Alteration of Condition Set Axis**

  Change, Insert, Delete, cancel condition sets.

- **Alteration of matrix content**

  Create, Cancel samples. It is never possible to assign operational samples to the study cells. These are not actually part of the study and have to be assigned in a separate part of the application. It is possible to modify samples or add samples, to modify or assign parameter groups, modify or assign info cards.

- **Comment handling**

  Entering comment when a study is altered is possible. It is possible to let the system demand a userid/password (electronic signature), it is possible to force comment. Labels can be printed on study level. In this way, labels for all samples are printed, to be placed upon the physical samples stored in the various physical locations.

4.10 Life Cycle of Samples Belonging to a Study

At protocol level, it is possible to assign a sample life cycle. This life cycle is assigned to all samples created in this study. The initial samples keep their own life cycles.

Example life cycle:

- Within grace period, before pulling date
- Pulling date
- Within grace period, after pulling date
- Within margin to be pulled
- Too late to be pulled
- Planned
- Available
- In Execution

- Out of Spec
- Validated
- Cancelled

The life cycle of a study sample indicates the position of the study sample relative to pulling. Of course it is possible to send e.g. an e-mail when a sample has to be pulled (status), this is standard Unilab functionality.

4.11 Life Cycle of a Study

Studies also have a life cycle that dictates the behavior of the study. The life cycle reacts on states and properties of the samples in a study. This way it is possible to automatically stop the study on certain conditions.

Canceling a study does not automatically imply canceling all samples of that layer. This is determined in the life cycle definition, e.g.handling initial QC samples.

Example life cycle:

- Planned
- In Execution
- Ended
- Validated
- Cancelled

4.12 Example Typical Workflow to Define a Study

Below is an example of a typical workflow to create and maintain a study:

11. Create a new study with a certain unique code based on a certain selected protocol. Possibly the study is in a **planned** status.
12. Fill in study info fields.
13. Change 2-dimensional study matrix where necessary.
    - Add or cancel a time point
    - Add or cancel a condition set
    - Add or cancel samples, parameter groups, …
14. Fill in sample info fields.
15. Assign sample locations.
16. Assign operational samples (this can be done automatically in projects when e.g. the infofield representing the batchnumber is filled in).
17. Fill in zero time per condition set. Preferably the study is started for that condition set at filling in the zero time. When this is not the case, skip to the following step.Otherwise, proceed from step 9.
18. Start the study and samples will appear on pulling lists at pulling time.
19. Pull from location when sample is at pulling time (status change) and methods of the pulled samples appear on a worklist.
20. Fill in the analysis results.

21. Validate the study.