Ingo Green

Understanding Empower 3

(English translation of the German original edition)

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Compendium of the well-known

Chromatography Data System

Including Topics on Regulatory Compliance

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Disclaimer

This manual for the Empower 3 software does not represent official manufacturer documentation. The information in this book is based on the author's personal experience, research and assessment and is free from manufacturer interests. Despite careful preparation and the author's many years of expertise with the system, no guarantee can be given for the accuracy of all information provided.

In order to keep costs low when producing this book, professional editing and proofreading were not used. Despite careful and extensive checking of spelling and grammar, no guarantee can be given that the text is error-free.

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Why Such a Book?

If you want to find out more about using Empower 3 on your own, there are many sources available. The manufacturer itself already provides numerous instructions and documents on a wide range of topics. There is also a special ‚Empower Tip of the Week' section on the Waters website, which provides useful information on specific use cases, and the manufacturer regularly organizes events to discuss Empower 3 topics. Many presentations on the software can also be found via a search engine on the Internet. Last but not least, the software itself offers extensive online help.

But one thing also becomes clear: working your way through this is time-consuming and requires initiative. There is usually a lack of resources to deal intensively with the software and Empower users have other priorities to pursue in their day-to-day work. As the sources are diverse, you can never be sure that you have found and reviewed all information on a specific topic. Many Empower users gain their knowledge mainly through an introduction by experienced colleagues or by trying things out for themselves in their day-to-day work. There is usually no systematic and structured introduction to the software.

After more than 18 years as an independent Empower consultant, I have therefore regularly experienced the desire for a centralized and up-to-date documentation. This should give Empower newcomers quick access to the software, but also be an easy-to-understand reference work for the essential topics of everyday laboratory work. Due to the focused use of Empower 3 in the pharmaceutical sector, issues related to the mapping of business processes that go beyond the actual functionality of the software should also be addressed. Admittedly, this is not an easy undertaking.

I had already compiled an initial manual in 2007 for my employer at that time, which also drew on existing documents from other sources. This received little attention, which was certainly due to an unfavorable presentation, but also to the lack of a marketing concept. A revised version was finally published in 2015. I even trained in graphic design and text layout so that I could have a direct influence on the promotion. And this book really became an unexpected and ground-breaking success. In terms of content, it differed little from its predecessor. An English-language version followed in the same year and I am still regularly asked about this manual by my customers today. At least in German-speaking countries, it seems to have established itself as a kind of standard work on Empower. However, many people are not aware who the actual author of this book was, as it was distributed under the brand of my former employer. When I left the company, the book remained there as I had failed to secure the necessary rights to the book, but it has not been updated since then and is no longer available on the market.

I am now the owner of my own company and after 10 years I look at this book with a different perspective. Through ongoing customer contact, my own experience and time-consuming research, I have noticed many gaps and inaccuracies. I wouldn't write many things the same way today. And of course the software itself has also developed in 10 years.

That's why there has long been a desire for a new edition, not an addition to the existing one, which would also be legally questionable, but a real new version. In summer 2024, I made the decision to get started. Again, everything was to be done on my own, from the rough draft to the finished print template. This time, however, I had a lot more time at my disposal, as it didn't have to be created after work.

The book is not based on a specific release status, but attempts to summarize the release statuses Empower FR5 to Empower 3.8. In addition, the topics are generally presented under the assumption that you have all the required privileges. It is therefore quite possible that you will be presented with functions that you cannot execute with your privilege level in your own system. Furthermore, the content of the chapters builds on each other. Functions that have already been described are not explained again in the same level of detail. These must then be assumed to be known. However, references are used wherever necessary. When describing individual processes, self-evident facts are also avoided as far as possible. It is therefore not mentioned every time that you save an object with ‚OK' or that the next window in a wizard is displayed with ‚Next'. Nevertheless, I have attached great importance to extensive illustrations. This is one of the reasons why the use of online help in pure text form is considered difficult. With images, we can grasp relationships much faster and more precisely.

Now I hope that this book is a work that fulfills its purpose. The intention is not only to offer it to corporate customers, but also to make it available for private purchase directly from bookshops at a significantly lower price. The self-publishing print-on-demand process opens up new possibilities. It offers the advantage of being able to offer updated versions easily and without major investment costs. I am aware that there will continue to be wishes that this book does not cover to the extent expected or other topics that are currently still excluded. I would like to respond to this as best I can in the future.

Special options such as dissolution, mass spectrometry, GPC. CE are not yet included in this edition. Furthermore, the presentation is limited to the Pro interface. The original book has been published in German. In addition to this English-language translation, extensions are also planned in this regard.

My offer to you should therefore also be understood as a request: Write to me directly if you have any questions or suggestions. I guarantee you an answer that will help you, and it will also help us to develop this work. (info@cromingo.com)

Empower has become so well established in recent decades that it has become part of everyday life for hundreds of thousands of employees worldwide. Just like Microsoft Office products at the computer workstation, Empower has become indispensable, at least in the pharmaceutical-analytical laboratory. I therefore also see it as justified to offer support free of manufacturer interests. An independent position also makes it possible to address the pitfalls of the software in a different way and to formulate constructive suggestions for dealing with these pitfalls.

My experience shows that such a work can lead to greater acceptance of the Empower software in user circles. Even today, there is still a certain rejection of the system, especially among users who are already familiar with other systems. This can usually be explained by the fact that Empower follows its own, very individual logic and is therefore difficult to compare with systems that are already familiar. This makes it more difficult to understand Empower. Nevertheless, it is repeatedly confirmed that the possibilities of Empower are gratefully accepted once the initial hurdles in understanding the software have been overcome.

Not least because of its uniqueness, it is an incomparably strong and powerful program in the world of chromatographic data systems. Empower has therefore quite rightly been able to maintain its market leadership, particularly in the pharmaceutical sector, over the last few decades.

I would like to expressly thank Dr. Britta Kupfer, who has made a valuable contribution to the success of this book with many suggestions, a differentiated view of the subject matter and a meticulous review of the individual chapters.

Let us now embark on a journey together with this book to explore and better understand the Empower 3 world.

Ingo Green

This book is an English translation of the German original „Empower 3 Verstehen“ published in January 2025.

1. General Information

1.1. Special Features of the Empower Software - Benefits in Regulated Environment

The special feature of Empower lies in its architecture, which is mainly based on a relational database in which almost all data is stored. Only the recorded measurement signals, such as chromatograms and pressure curves, are stored file-based in a Windows directory structure. This means that the actual raw data is not stored in the database, but is available in the form of files consisting of a series of data points. The metadata, on the other hand, which contains information on methods, settings and versions, for example, is managed in the Oracle database.

The advantage of this structure lies in its efficiency and clarity. An object, such as a method element, only needs to be saved once and can be used again and again by means of references. This reduces redundancies, as the same object can be called again and again without additional storage. This means that it is always possible to trace which Method Settings were used when creating data. It also prevents data from being accidentally overwritten, as updating Method Settings leads to the creation of a new version, while the previous versions remain accessible. This form of versioning also makes it possible to access older data and trace its creation.

However, this type of networking of information leads to a certain level of complexity, which is particularly difficult for users who expect their processes to be more linear. Empower uses a non-linear but clearly structured data organization, which is presented in the form of a „data cluster“ that has a defined internal logic. For example, if you know the name of a method, you can be sure that the latest version of this method is always used, regardless of where in the Project this method is called.

In practice, working with Empower usually requires a longer familiarization phase, as you first have to familiarize yourself with this structure. However, once the necessary orientation has been gained, working with the system and especially its advantages for regulated areas is greatly appreciated, as great importance has been attached to traceability and data integrity.

1.2. Login and Start Window

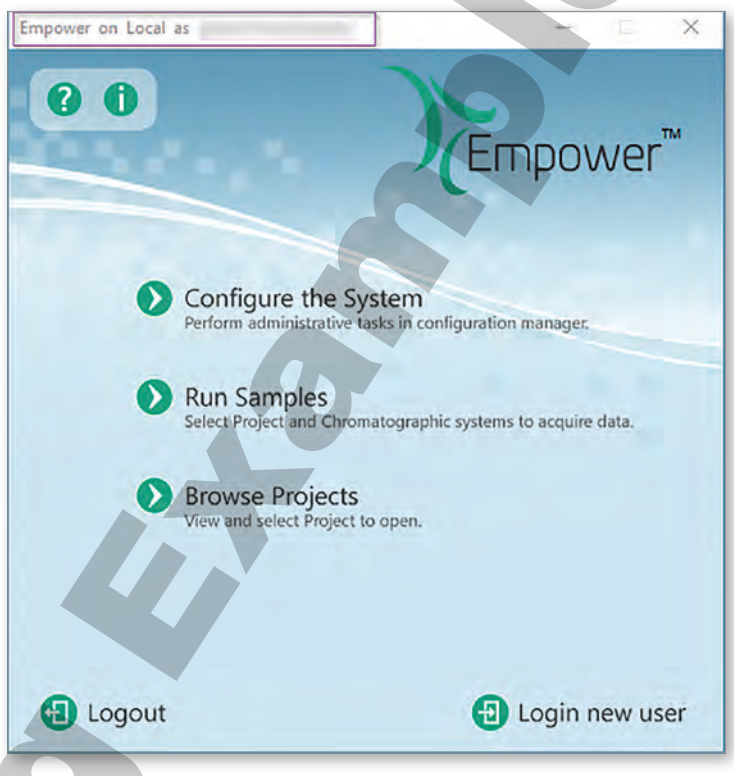
Depending on the installation mechanism, the login differs. If Empower is installed locally on your computer, there should be an Empower icon on your desktop that you can use to call up the program.

Alternatively, Empower can be called up via the Start menu (the selection here depends on the Windows version used; if in doubt, a search function can also be used).

In the case of a terminal server installation, adhere to the company-specific specifications. A generally valid representation is not possible in this case.

After starting the program, the Empower login screen appears. Here you must first authenticate yourself by entering a user name and password.

Depending on which authentication mechanism is configured for your installation, it may be that your login data is set specifically for Empower or that your user account is synchronized with a company LDAP server. In the latter case, your login data for Empower is identical to the login data for your Windows operating system.



In an Empower network, a database must also be selected under ‚Database'. This describes the closed instance. In other words, an environment with its own database and therefore its own system specifications and its own user management. Depending on the architecture of your network environment, there may be several entries to choose from. Many customers differentiate between GMP, non-GMP, validation, training and test instances. In such cases, it should be known how the desired instance is designated at this point.

Once you have successfully confirmed your login data by clicking ‚OK', the Empower start window will appear.

The header will show you which User Account and User Type you have logged in with. You will now be offered three login options:

Configure the System

Click on 'Configure the System' to open the Configuration Manager. Administrative activities can be carried out here. This function is of little relevance for users who are only responsible for measuring and evaluating analyses. However, it does provide a good overview of Projects, systems and LAC/Es that can be accessed.

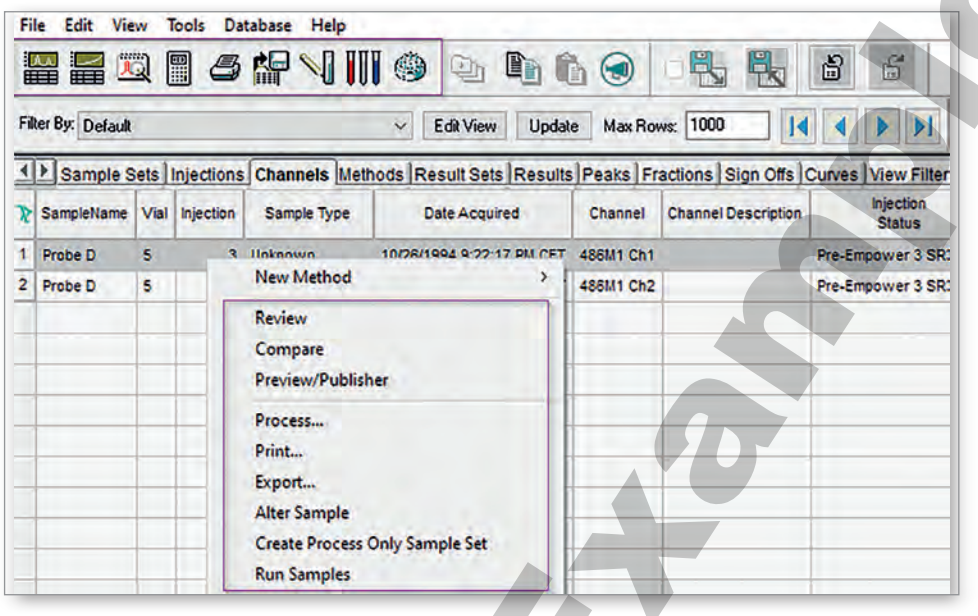
Run Samples

With 'Run Samples' you can access directly to a measuring device.

Calling up this command also gives you a view of all measuring devices and Projects to which you have been granted access. To be able to open 'Run Samples', you must also select an Empower Project without this Project opening itself. By selecting a Project, the software knows from which Project the required methods should be taken and in which Project the measured data should be saved.

2.2. Functions in the Project Window

Further functions can be called up in the Project window via commands, which open a new window. These commands can be called up context-sensitively by selecting an entry with the right mouse button or using the icon buttons in the ribbon.



2.2.1. The Commands at a Glance

The most important buttons on the toolbar in the Project window are:

1 Review

The ‘Review’ function allows you to view chromatograms and all available metadata. It can be used to view chromatograms or to check results electronically. The Review window is also used to create Processing Methods or to compare them with existing chromatograms. Review can be called up for Sample Sets, Injections, Channels, Result Sets and Results.

2 Compare

With ‘Compare’, chromatograms and calibration curves can be viewed and compared with each other. Further processing is not possible in this view

3 Preview/Publisher

This command is required to create or customize reports, but also to display data on the screen using a ready-made report template.

In your own system, it may be that a number of user-defined columns (Custom Fields) are offered at this point. In these cases in particular, it makes sense to compile corresponding table views.

The table views can be called up later by any user and are therefore not user-specific. However, it is not possible to distribute ready-made table views to other Projects.

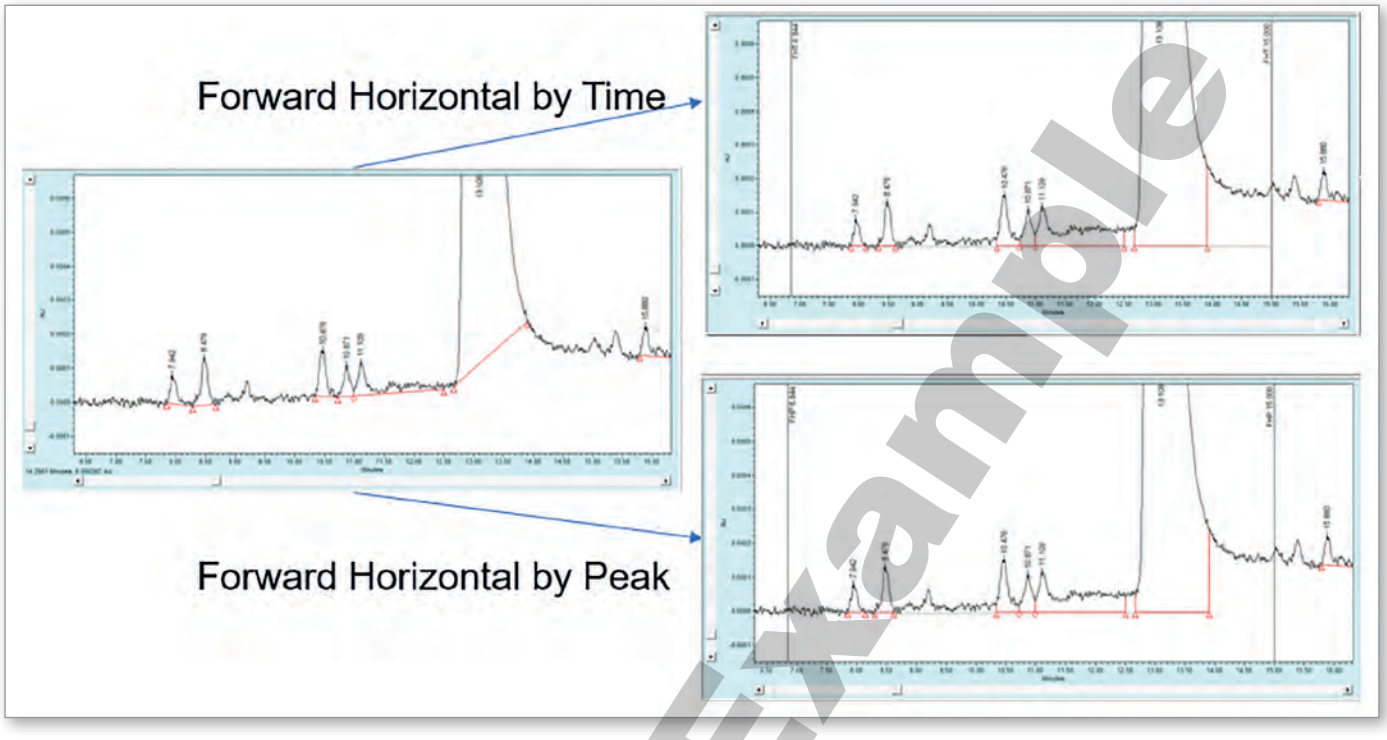
Below you will find a detailed overview of the different columns and their functions. Some columns are dependent on certain options that can be activated for a Project.

3.8. Sample Set Fields

Table 1: Sample Set Fields

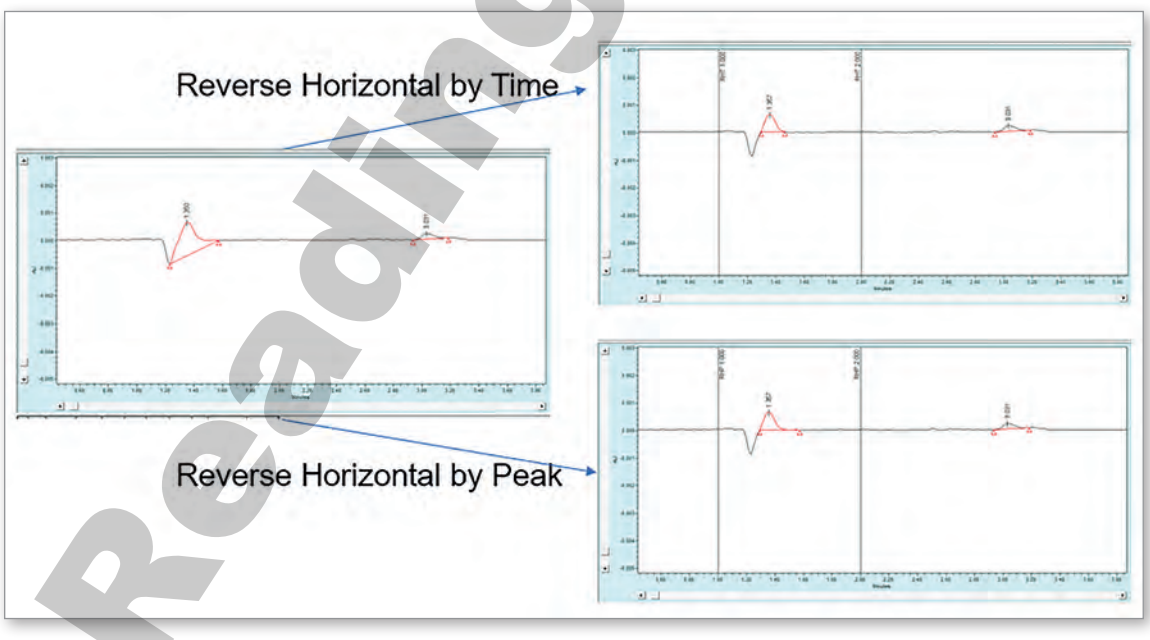
Field Name	Option	Explanation
Vial	--	Specification of the vial position on the sample plate, field name and description of the position depends on the selected plate type.
Inj. Col (µl)	--	Specification of the injection volume
# of Injs	--	Number of injections per injection line
Label	--	Specification of a freely selectable label for the sample line. Required for calibration and quantification functions as well as for Custom Field calculations.
SampleName	--	Specification of a sample designation
Level	--	Specification of a calibration level. Only required if weight values for calibration standards are specified in the Processing Method (tab 'Default Amounts')
Function	--	A long selection list is offered here. The selection options are explained in „Table 2: Field ‚Function' in the Sample Set" .
Method Set/ Report or Export Method	--	Specification of a Method Set, a Report Method or an Export Method
Label Reference	--	Specifies the labels that are to be processed with this line. Is required for the 'Calibrate' and 'Quantitate' functions. If empty, there is no restriction to specific labels.
Processing	--	Usual specifications: 'Normal', or 'Don't Process or Report'. See the creation of complex Sample Sets in chapter „13. Structure of Sample Sets/ Sample Set Methods".
Run Time (Minutes)	--	Duration for which the measurement signal is to be acquired.
Data Start (Minutes)	--	Delay after the injection before the run time is to be started.
Next Inj. Delay (Minutes)	--	Duration after the run time for which a method should continue to run without data being acquired, e.g. for equilibrating the column.

By Peak: In contrast to the ‘by Time’ approach, the starting point for the horizontal is set from the starting point of the baseline of the first peak.



Reverse Horizontal

This event works in the same way as the corresponding forward event, except that the horizontal line is drawn from the end of the event, not from the start of the event.



The example shows how this behavior can be used, for example, to record a peak before a negative deflection in the injection peak.

» If no Result Set is created and the results are generated by direct saving, it is recommended that all results are labeled in a uniform manner. This can be done using the nomenclature of the Sample Name, or using an additional Custom Field in which, for example, the batch number is entered. It is only important that all results that were generated during the control of the production batch can be clearly identified on the 'Results' tab so that they can be reported in context.

» If it becomes apparent during the measurement that further sample injections are required, it is advisable to call up the 'Alter Running Sample' command during the last measurement in order to add further sample lines. („3.13. Editing Current Sample Sets and Sample Set Queue“ on page 43) This ensures that all samples are still running in the same Sample Set. Once a Sample Set has reached the status 'Completed', no further samples can be added. Further Sample Sets would then have to be created.

14.3. Use in a Development Laboratory

The main characteristic of the work in method development is that a large number of measurements must be carried out under different method conditions. The following will show you how this can be implemented in Empower.

Method Set

If you still work traditionally according to a 'One-Factor-At-a-Time' approach (OFAT), you can make use of the Method History of the Instrument Method.

- You can always select the same Method Set that refers to your development method.
- You can use the Instrument Method from the previous attempt as a template and save the change for the next run using 'Save'. This creates a new version entry in the History.
- You can return to an earlier version at any time via 'Save as Current' and edit the method in a different direction based on this template if necessary.
- Using the History and the 'Differences' function, you always have an overview of the development process and the differences between the methods under consideration.

Sampe Set Method

If you need something more extensive and would like to set up a complete screening with different method conditions, Empower's on-board tools offer little support. Such a Sample Set must be set up manually. Note the necessary phases for conditioning and/or equilibrating the separation column between the runs with different method conditions. In particular, if the chemistry of the method changes, these should last long enough to avoid misinterpretations. Repeat measurements are unavoidable with this approach, but also with an OFAT approach due to random error.

Sample Set Generator

To automate the creation of such Sample Sets, Waters offers the Sample Set Generator (SSG) as additional software. This can be used to create screening protocols in which the investigated factors can also be transferred to corresponding Custom Fields. The respective method conditions are already visible in the Sample Set view, but it is also possible to wonderfully create suitable reports by arranging the chromatograms according to these factors or presenting them in an overlay display. According to the manufacturer,

the SSG supports the current development machine of the UPLC and UHPLC model series from Waters (Acquity, ARC).

Fusion QbD

If you also want to automate the evaluation of your study, the Fusion QbD® software from S-Matrix® Corporation is the right choice. Similar to the SSG, study protocols can be created smoothly based on a statistical Design of Experiments (DoE) approach and exported to Empower as ready-to-run Sample Set Methods. The evaluated results can then be imported back into Fusion QbD for further data modeling.

For central European countries, Cromingo represents S-Matrix Corporation in its entirety and also provides operational support for all Fusion QbD customers. You can find more information about this product at www.cromingo.com

14.4. Use for Instrument Qualification

In a regulated environment, there is really no alternative to having the device qualification performed in the same validated software environment in which the GXP samples are measured. An approach in which a service technician carries out the measurements with their own notebook and then either provides a report, imports the data for further processing or imports the fully evaluated data into the validated environment is prohibited for reasons of data integrity alone. This is because it is not possible to trace how this data was generated and whether all the data that was generated during qualification, including the failed measurements, was actually delivered. Please refer to the notes on the ALCOA++ principle in chapter 22 on page 367 ff.

Of course, this also requires that the service technicians in Empower are appropriately trained, both practically and formally, with a recognized training certificate.

In principle, Projects should be prepared that already contain all methods and reports required for qualification and, if necessary, Custom Fields. If the qualification is carried out by Waters, the manufacturer supplies the required SQT Projects and it is only necessary to ensure that these are also available in the system at the time of qualification.

The following specific tips and recommendations should be made at this point:

- **Noise:** Use the ‘Inject Immediate Samples’ function to determine the detector noise. This records the pure detector signal without any injection taking place.
- **Noise:** The ‘Average Peak to Peak Noise’ field is used to calculate the noise according to the ASTM* standard.
- **Drift:** The ‘Detector Drift’ field is used to calculate the drift according to the ASTM* standard.
- **Injector linearity:** There are two options here:
  - When selecting ‘Amount’ for ‘Sample Value Type’ in the Processing Method, the injection volume of each level must be specified. It is recommended to store this value in the Processing Method on the ‘Default Amounts/Purity’ tab, as it is an unchangeable value. (10.6 on page 134)

average mass per tablet. The value is only output for the last injection in the case of multiple injections.

CF_Amount_AVE_Z

Type: Peak/Real/Calculated

All or Nothing: Yes

Formula:

```
NEQ(Injection Id,SAME.%..MAX(Injection Id))*-1*50000+
EQ(Injection Id,SAME.%..MAX(Injection Id))*SAME.%..
AVE(CF_Amount_AVE_Vial)
```

Function: The field calculates the mean value from the results in the CF_Amount_AVE_Vial field, i.e. the content values from a multiple injection for a sample series with an identical label. The value is only output for the last injection of a sample series.

CF_Label_Claim_Pct_Vial

Type: Peak/Real/Calculated

All or Nothing: No

Formula:

```
CF_Amount_AVE_Vial/CF_Label_Claim*100
```

Function: Output only for injection lines for which an average content value from a multiple injection is output in µg/tablet.

CF_Label_Claim_Pct_Z

Type: Peak/Real/Calculated

All or Nothing: Yes

Formula:

```
CF_Amount_AVE_Z/CF_Label_Claim*100
```

Function: Output only for injection lines for which an average content value for a sample series is output in µg/tablet.

CF_M_CU

Type: Sample/Real/Keyboard

Function: The formula contains a chain of six conditions according to which the mean value is to be output as described in the table below. To make the formula expressions for the different conditions recognizable, they are marked accordingly in the formula.

Formula:

```
LTE(CF_T_CU,101.5)*
(GTE(ROUND(CF_Label_Claim_Pct_Z,-1),98.5)
```

20. Data Import and Export

Empower offers a wide range of options for importing and exporting data. In summary, the following options are offered and discussed in more detail in this chapter.

Importing Data

- Project Restore
- Import of chromatograms (AIA or ASCII format)
- Copy&Paste
- Drag&Drop
- Waters Data Converter
- Importing Plate Types

Exporting Data

- Project Backup
- Export Method
- Export to Text
- Copy&Paste
- Archive options (AutoArchive and SDMS)

In addition, the import and export using toolkit applications is addressed below and a procedure for the migration of spectrum libraries is presented.

20.1. Importing Data

20.1.1. The Restore Function

With the Restore function, Empower Projects can be imported into your Empower installation. This may be necessary, for example, if you need Default Projects from the manufacturer, want to migrate Projects you have created yourself from another Empower instance or need to review Projects that have already been archived. You can import all Projects from previous Empower releases and even old Millennium Projects to Empower3 via ‘Restore’. However, if you want to import Projects from future higher release levels, this is not possible. Only downward compatibility can be offered. How the restore process works is explained in more detail in section „21.8.2. Restore“ on page 346.

20.1.2. The Import Function

If you would like to import chromatograms that were created in other data systems, this is possible with the import function. The prerequisite is that this data is available in AIA (*.cdf) or ASCII (*.asc) format. You can access this function from the Project window via the menu command ‘Database > Import’.

20.1.3. Copy&Paste

You can create entire Sample Sets in Excel and then copy them into the ‘Samples’ table in the Run Samples window or into the Sample Set Method Editor. Please note that the row numbers must also be specified in

21. Administration in the Configuration Manager

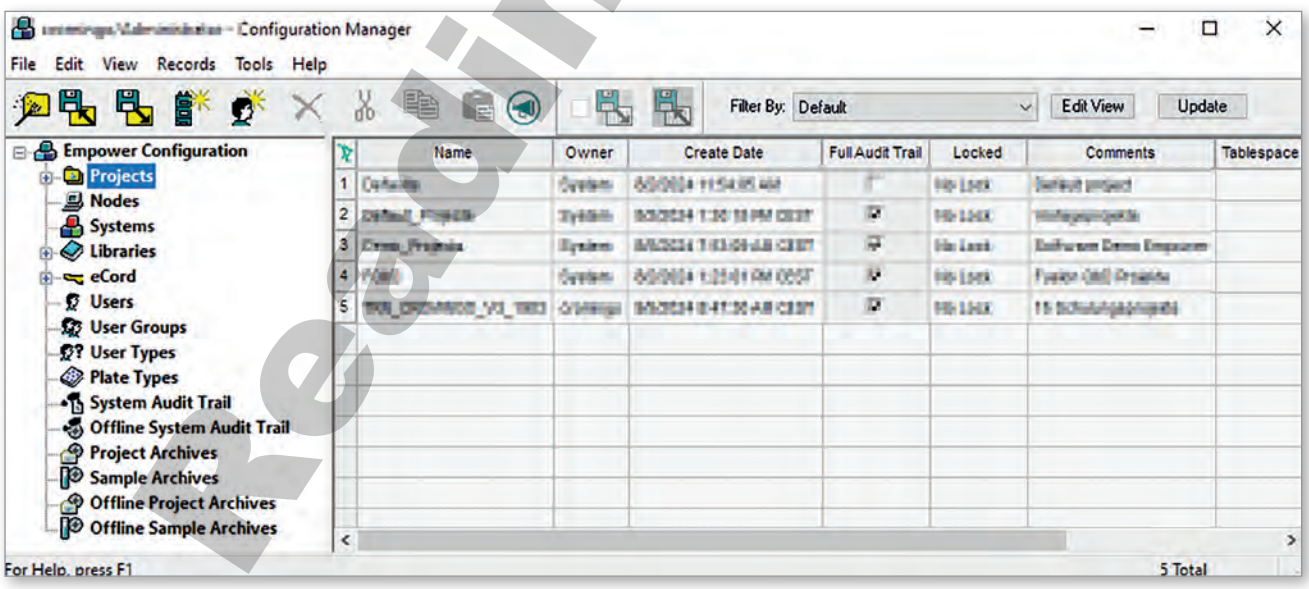
In the Configuration Manager, you can view and, if necessary, edit all system-wide settings accessible to you. Systems, data acquisition computers and Projects are also created and configured here, and Users and User Groups are managed.

This topic is very extensive. For this reason, this manual can only cover the basics of configuring and administering Empower. We will limit ourselves to the basic, purely technical application of the Configuration Manager and, where necessary, provide some useful tips for practical use.

21.1. Launching Configuration Manager

After logging in to Empower, select 'Configure the System' in the start window.

The Configuration Manager opens.



22. Procedure for Data and Audit Trail Review

Thanks to its data structure, Empower software makes it easy to track the creation, processing and deletion of data. Empower is therefore very popular for use under regulatory conditions. Many functions are adapted to the requirements of the pharmaceutical sector in particular. The consistent verifiability of data integrity and the easily readable audit trails should be emphasized here.

Nevertheless, this topic continues to cause headaches for many customers, both in terms of the selection of test objects and the routine implementation of the inspection. A separate chapter will therefore be dedicated to this topic.

First, the special requirements regarding data integrity will be discussed before practical recommendations are given for checking them as part of an operational data and audit trail review.

22.1. Requirements and Definitions

22.1.1. Objective

To ensure the integrity of GMP-relevant data in Empower 3, it is necessary to check the original electronic data and all associated audit trail entries to determine whether any unauthorized changes have been made to the data, consciously or unconsciously. The measures defined for this purpose are aimed at obtaining certainty as to whether the data generated has remained intact and provides truthful results.

22.1.2. Definitions

Data Integrity

The extent to which the data corresponds to the ALCOA++ principle. The acronym stands for:

- Attributable - Who performed the action and when?
- Legible - Can the electronic record be read over its entire life cycle and are the records easy to read?
- Contemporaneous - Record at the time of the activity with date and time stamp
- Original (original) - Original acquisition or certified copy
- Accurate - No errors or editing without documentation of the changes
- Complete - All data including performed and canceled tests and repetitions, no deletions
- Consistent - All elements of the analysis, such as the sequence of events, are provided in chronological order with the corresponding date and time stamp.
- Enduring - Recording in laboratory journals or validated systems over the entire lifecycle while retaining legibility
- Available - The data can be used at short notice during the entire life cycle for checks, audits or inspections.
- Traceable - Data should remain traceable throughout its lifecycle. Any changes to data or metadata should be explained and traceable without obscuring the original information. Timestamps