LABS Suite

# 01 Statistical evaluations at the touch of a button in LABS/Q®

Statistical evaluations at the touch of a button in LABS/Q®

Modern analytical laboratories generate a very large number of measurement results. When making decisions based on these results it is helpful to be able to present them graphically in a control chart or histogram and statistically evaluate them in this format. The information must be compiled and arranged in a straightforward way and based on a variety of criteria for this purpose.

LABSGraphic is available for use as a statistical and graphical evaluation tool with LABS/Q®. A key goal in developing LABSGraphic was to create a tool that would be very easy to use, thereby offering time-efficient graphical and statistical evaluation of final results. The most important features of LABSGraphic are described below.

Functions for quality control and in-process control

In addition to checking the results against warning, action and specification limits, it is very important to detect trends in the measurement results early on. The option is therefore provided in LABS/Q® of immediately opening LABSGraphic even while results are still being recorded. The result history is checked against the trend rules and outlier tests saved in LABSGraphic, and violations are displayed in a list and in the control chart. The user is free to change the trend rules that come with the program, and to add additional rules.
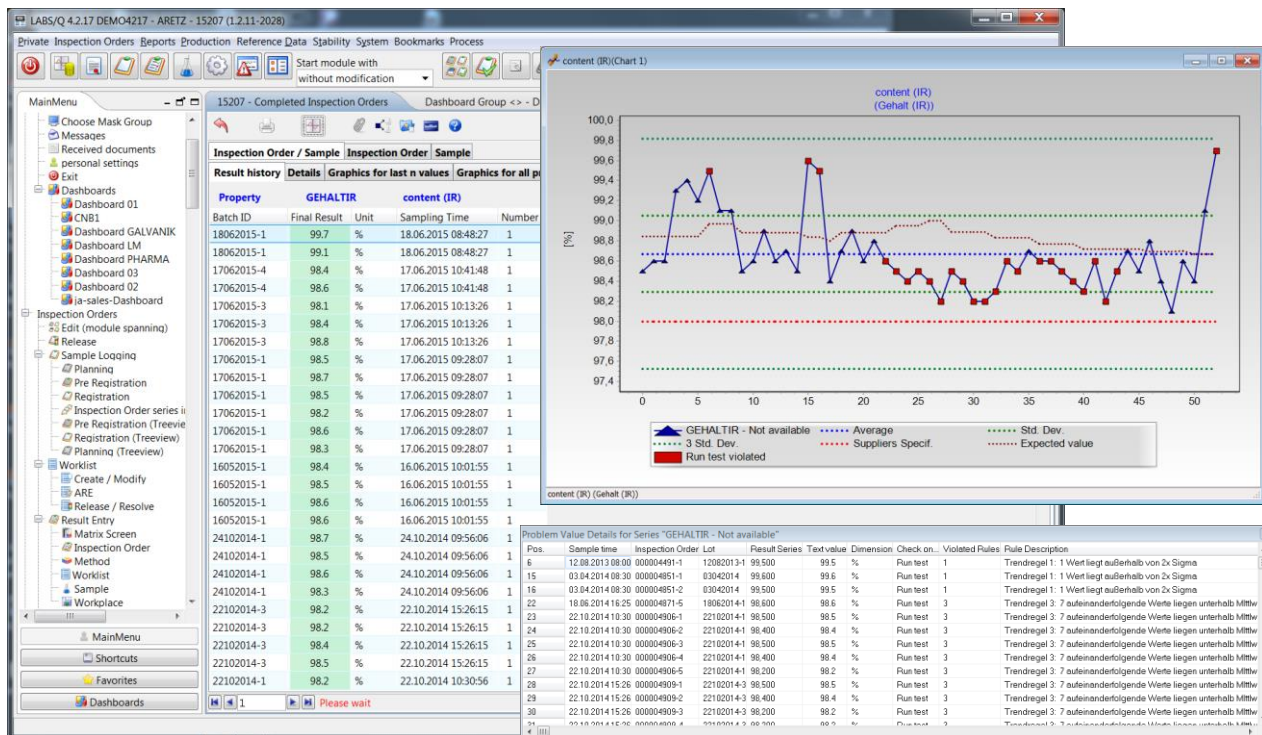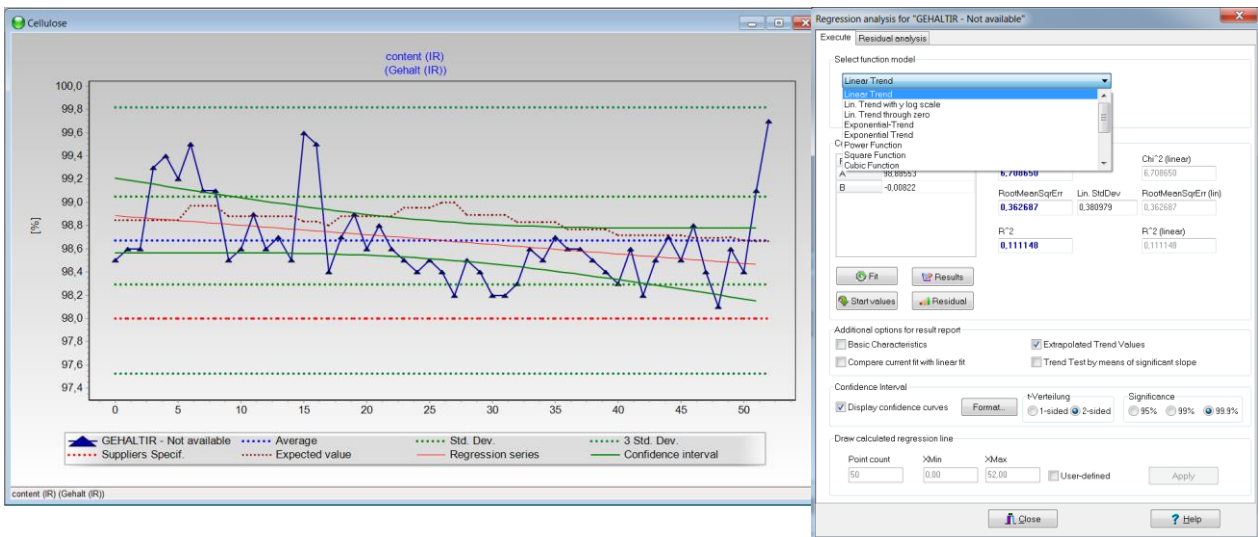
02 Functions for quality control and in-process control

The user is free to select what information they want to be presented in the control chart. The user settings are saved automatically so that they are immediately available after the user leaves and restarts the program.

Additional statistical evaluations are also offered. These include a range of regression models, a residual plot and a normal distribution test.

Key statistical data such as standard deviation, relative standard deviation and average are also provided. Depending on the limit values set, the process capability values Cp and Cp/k are also calculated. In addition, the result of an assessment of normal distribution based on a David test is also provided.
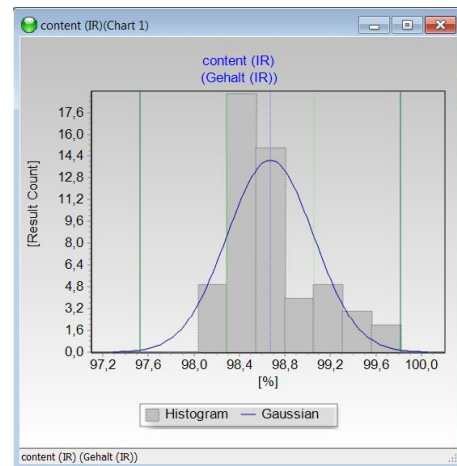
The option is also provided of displaying the results in a histogram.

03 Statistical evaluation of stability studies according to ICH guidelines

Evaluation of stability studies according to ICH

For stability and shelf-life investigations, it is also advantageous to have a tool for performing statistical and graphical evaluations on the available results that is as easy to use as possible. LABSGraphic provides a number of different options for this.

Shelf-life estimations for pharmaceutical products are performed in accordance with ICH guidelines, taking into account confidence intervals. In relation to the storage of the pharmaceutical product under defined conditions, users can choose between endurance tests and accelerated shelf-life tests (stress tests). This includes a test for poolability, which is based on an F-test including covariance analysis.

Accelerated shelf-life tests are used to obtain provisional data on the stability of the product by storing it at higher temperatures (e.g. finished pharmaceutical products in final packaging at 40°C and 75% rel. humidity). In the early stages of pharmaceutical development, kinetic studies can provide information about the stability over time to be expected of the product. With isothermal tests, for example, the pharmaceutical product is stored at 35, 45 and 55°C and the decomposition of the active agent is determined by analysing the decrease in the content of the relevant substance. LABSGraphic can then be used to translate the measurement results to room temperature using the Arrhenius equation.
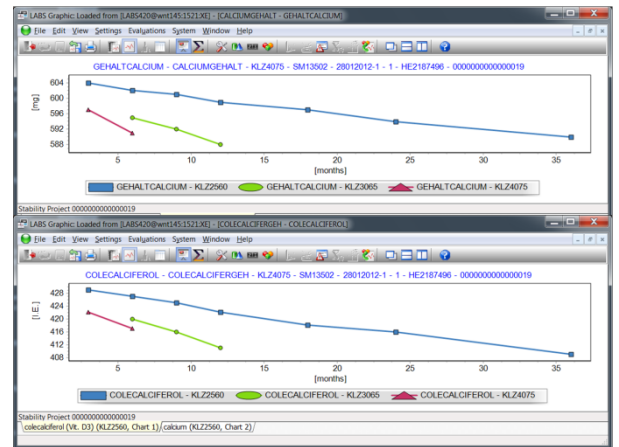
The results of a stability study such as this can be individually selected and compared with each other based on the material, batch, packaging or storage conditions (climate zone).

There is also the option of projecting and presenting the further course of an observed trend based on a number of different regression models.
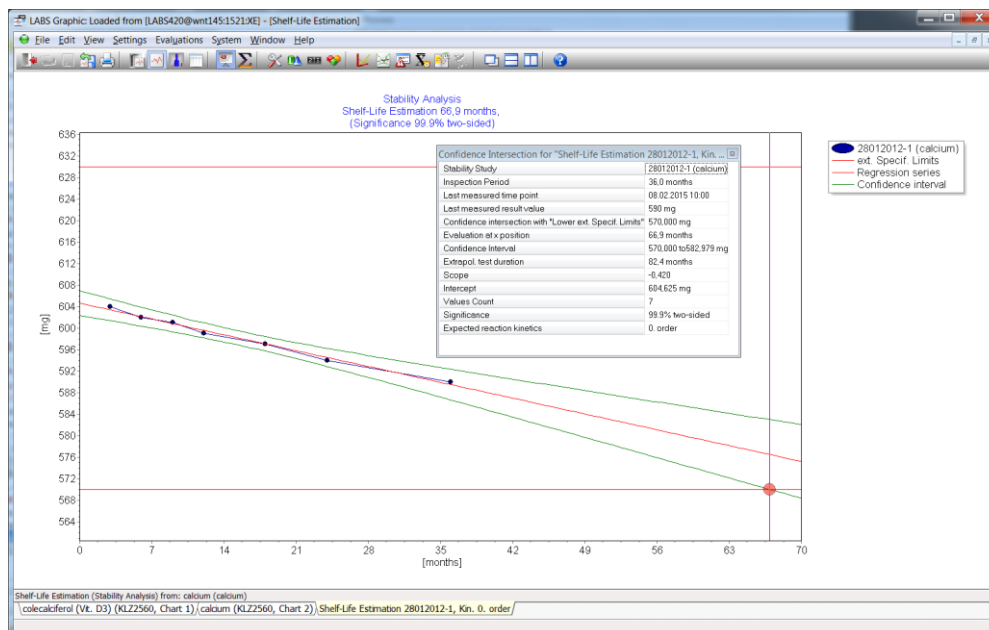
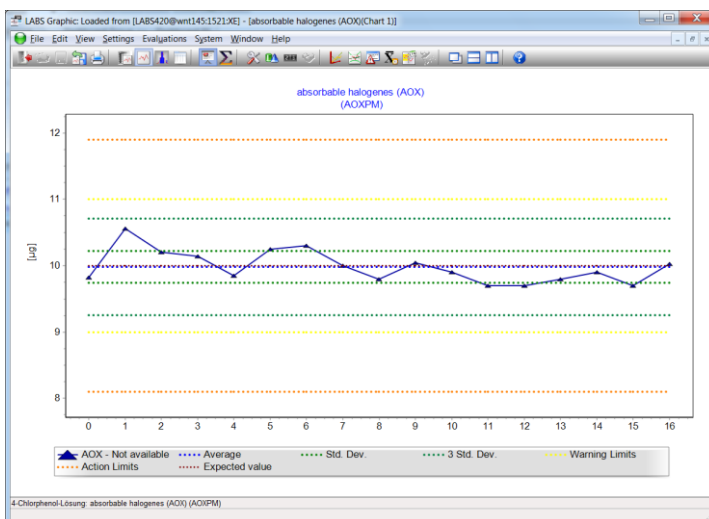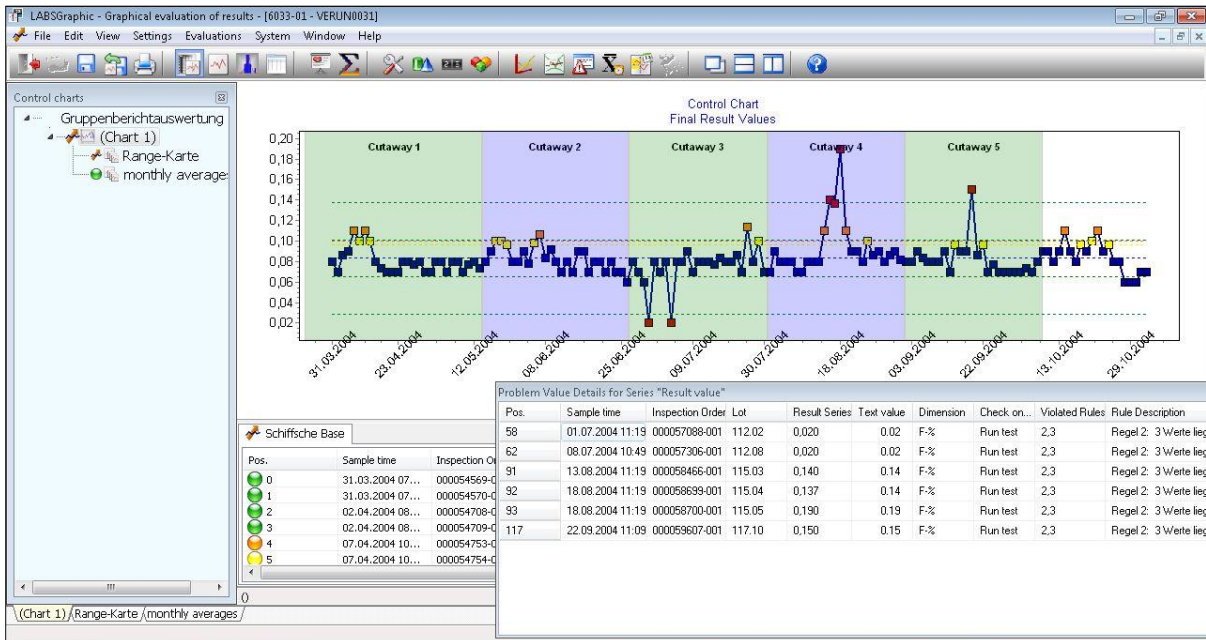The evaluation here shows that the specifications could cease to be met after around 67 months.

04 Evaluation options for monitoring testing and measuring equipment

Statistical and graphical evaluations for monitoring testing and measuring equipment

A large number of measurement results are also generated in the process of monitoring testing and measuring equipment. In this case too, it also makes sense to identify trends, such as the drift of a measuring device or a change in a calibration solution, in good time.

In conjunction with LABS/Q® a tool for evaluating the results of testing and measuring equipment monitoring is offered to help with just this task. The results from a particular item of testing equipment and calibration tool batch across a user-defined time period can be selected, statistically evaluated and graphically displayed. By means of an evaluation not dependant on testing equipment, the user can quickly identify whether there has been a change in an item of testing or measuring equipment.

The results can be displayed in an easy-to-view format both graphically and in a data list. Cutaways from a series can be exported for further analysis with a click of the right mouse button and rows of results can be grouped by dragging and dropping them.

05 Statistical methods with LABSGraphic

The following statistical methods are provided for all the applications described above:

Key statistical data

The selected results can be evaluated in a number of different ways. The following key data are provided as standard for every list of measurement readings:

- Average
- Standard deviation
- Relative standard deviation
- Process capability key figures Cp and Cpk values
- Measuring equipment capability key figures Cg and Cgk values
- David test for normal distribution
- Grubbs' test for outliers (recommended in accordance with DIN 53 804)
- Neumann trend test

Grubbs' test for outliers

Outliers within the result series can be determined using Grubbs' method. Outliers can be highlighted graphically or removed from the result series.

Neumann trend test

The Neumann method can be used to identify trends within a result series. Values for which a trend may apply can be highlighted graphically or removed from the result series.

David test for normal distribution

A result series can be tested for normal distribution using the David test. This test provides information on whether normal distribution can be assumed for a given result series.

Trend rules (situations outside control)

The option is available of saving user-defined trend rules in order to be able to detect trends and outliers in the measurement values. The results are then checked against these trend rules and any violations are logged and displayed in the control charts. The following trend rules come pre-installed:

- 1 value is outside 2x sigma
- 7 consecutive values are above the average
- 7 consecutive values are below the average
- 7 consecutive values display a downwards trend
- 7 consecutive values display an upwards trend
- 2 out of 3 consecutive values are outside a warning limit

Regression analysis

A number of different regression methods can be applied to the data for the purposes of evaluation. This capability is particularly important, for example, in the case of stability testing if there is a requirement for forecasts to be made about the further course of the stability study. The following methods are used and supported:

- Linear regression, including with confidence intervals
- Non-linear regression for various model functions (e.g. square, exponential)
- Direct comparison between linear trend and selected model function
- Calculation of extrapolated x-values based on the regression

06 Regression analysis and options for graphical evaluation

The following key statistical data (among other information) is provided with every regression to enable the quality of the regression change to be evaluated and compared:

- Linear/non-linear correlation coefficient
- Degree of freedom of the regression
- Square of the correlation coefficient, including corrected for degree of freedom
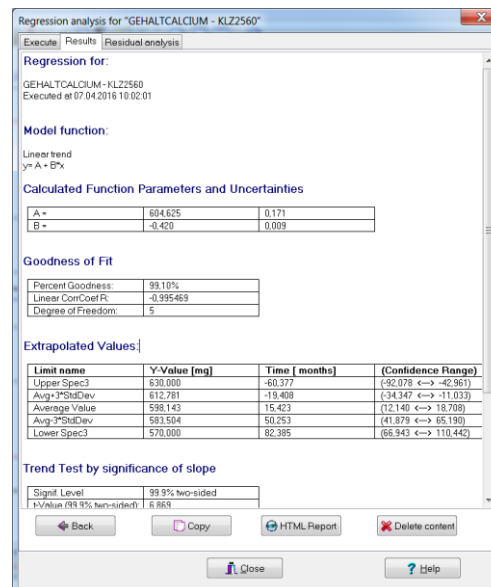- Residual standard deviation
- Residual chart

Confidence intervals (confidence bands) for linear regression

For the linear regression of the measurement data, the branches of the curves for the upper and lower confidence intervals can be calculated and plotted.

Graphical evaluation

The results, including limit values, statistical evaluations (regression) and trend rule violations, are displayed in the control chart. The following individual graphical displays and evaluation options are available:

- Average control chart (with configurable statistics for previous periods), CUSUM control chart
- Raw data chart (plotting of the smallest/largest raw data from the measurement result)
- Percentage setpoint deviation as bar chart
- Histogram
- Shelf-life forecasts based on stability data in accordance with ICH recommendation
- Thermal stress tests based on Arrhenius equation (accelerated testing)
- Results for interval features (display of interval bars for each result value)
- Result curve with user-defined statistical lines (e.g. average +/- 3x std. dev., trend line, etc.)
- Series grouping (group multiple result series in the same graphic for the purpose of comparison)
- Freely configurable grouping of result series by dragging and dropping
- Extraction and analysis of cutaways of series by clicking the right mouse button
- Confidence intervals and intersections with limit lines
- Statistical group evaluations
- Calculation and visualisation of daily, monthly and annual averages
- F-test with covariance analysis
- Wide range of options for exporting all information and evaluations to other applications
- Saving and loading of project and all associated data, including graphic, as a file
- Updating of data from database or project file without opening LABS/Q®
- One-click report: all evaluation data + chart graphic as HTML overview in browser

The benefits of using LABSGraphic

- LABSGraphic is easy to use and enables quick graphical and statistical evaluation of the final results of your tests
- The plethora of options for statistical and graphical evaluation with LABSGraphic can be employed, for example, for quality control and in-process control, for evaluating stability studies and for monitoring testing and measuring equipment
- LABSGraphic also offers the option of transferring the evaluations and information to other applications
- LABSGraphic helps in the decision-making process by enabling you to prepare and evaluate the array of different results in a simple, straightforward way.

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