P0312 SeraQ Elecsys Syphilis

CE
0483

IVD

REF P0312

The kit insert contains a detailed protocol and should be read carefully before testing the run control to ensure optimal performance.

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Intended Use

P0312 SeraQ Elecsys Syphilis is intended to be used on the Roche cobas® platform in diagnostic and blood screening laboratories as an external run control in combination with the assay for the detection of antibodies to *Treponema pallidum* (see Table 1). P0312 SeraQ Elecsys Syphilis is a single-marker dilution of an anti-*Treponema pallidum* standard in defibrinated plasma giving a low reactive result in the Roche Elecsys® Syphilis assay. The run control is intended for repeated testing in consecutive runs of the immunoassay over time by trained laboratory workers. By comparison of the sample to cut off (S/CO) values found on P0312 SeraQ Elecsys Syphilis one can monitor whether the analytical sensitivity of test runs is consistent. The run control should not be used to replace internal controls or calibrators in the test kits. The test result on the run control should not be used to reject the run or delay the release of test results on donor or patient samples.

Table 1. Test kit and platform covered by this run control

Equipment	Agent	Assay
cobas e immunoassay analyzers	Anti-*Treponema pallidum*	Elecsys Syphilis

Key to Symbols Used

Manufacturer

Lot number

Catalogue number

In vitro diagnostic medical device

Country of origin

Contains human blood derivatives

Store below −20 °C

Expiry date

Number of controls

Caution

CE mark with Notified Body number

Unique device identification

Read instructions for use

Positive control

Principle of method

A series of SeraQ run controls has been designed for monitoring anti-*Treponema pallidum* test performance. The run control tubes are barcoded and can be placed at random positions in sample racks of the blood screening device. The tubes are comparable in size to donor blood collection tubes. The run controls are designed to mimic naturally occurring serum specimens with low reactivity for anti-*Treponema pallidum*. The analytical sensitivity of test kits from different manufacturers varies and therefore for each test kit a separate single-marker run control has been designed. This SeraQ run control family includes the product P0312 SeraQ Elecsys Syphilis for which the composition is optimised for use with the Roche cobas® test system. The P0312 SeraQ Elecsys Syphilis run control is designed to generate assay response values (i.e. S/CO ratios) positioned in the low positive range of the assay. Routine use of external run controls enables laboratories to monitor day-to-day test performance and *in-vitro* medical diagnostic device (IVD) reagent lot variation.

Traceability of antibody concentrations

BioQControl has established an internal serum standard for anti-*Treponema pallidum* from which reference panels and run controls are prepared by gravimetrically recorded dilution steps. A WHO standard for anti-*Treponema pallidum* does exist; however, our internal standard has not been calibrated to this WHO standard, since quantification in SI units or IUs has no meaning for the reactivity in antibody tests. The traceability of SeraQ run controls for anti-*Treponema pallidum* is based on the dilutional titres in the Elecsys assay and potency of the BioQControl antibody standard used for preparation of the run controls. The consistent concentration of the analyte in consecutive SeraQ run control batches is guaranteed by batch release control testing against suitable reference samples kept frozen at −30 °C. These reference samples are derived from the same undiluted internal standard that is used for manufacturing of the SeraQ run controls. The BioQControl anti-*Treponema pallidum* standard has been in use since 2015 and is known to be stable when stored at ≤ −30 °C.

Materials Provided

The run control contains human serum and 0.01% (w/v) Thimerosal as preservative and is provided in two formats as detailed in Table 2.

Table 2. Description of P0312 SeraQ Elecsys Syphilis kit formats and contents

Cat. Code	GTIN/UDI-DI code^	Quantity run control	Tube size	Claimed sample volume	Secondary packaging
P0312/01	8718719831502	60 x 2.0 mL	10 mL	1.9 mL (+overfill)	60 tube rack in box
P0312/02	8718719833834	10 x 2.0 mL	10 mL	1.9 mL (+overfill)	10 tubes in bag

^ Global Trade Item Number = Unique Device Identification - Device Identifier (UDI-DI) code

The basic UDI-DI code (or Global Model Number (GMN)) of the P0312 SeraQ Elecsys Syphilis run control is 871871983P0312EH.

To facilitate automation the run control is presented in a polypropylene tube with screw cap comparable in size to vacutainer tubes used for donor sample collection. In addition, the label includes a barcode identifying the product, sequential batch number and marker: SYP. The barcode of each run control tube can be read by the Roche cobas instruments.

Materials not provided

Pipetting devices in IVD test systems, a vortex instrument for thorough mixing of samples prior to use and a water bath of 37 °C for quickly thawing of run control are not provided.

Storage Instructions

Store unopened tubes at or below −20 °C. For each cobas instrument thaw one run control tube in a water bath of 37 °C until ice clot has disappeared. After thawing, the run control tubes should be stored at 2 °C to 8 °C for no longer than four weeks.

Warning and precautions

P0312 SeraQ Elecsys Syphilis run control is prepared from a serum standard, which is considered to be non-infectious since *Treponema pallidum* is only transmitted by fresh blood products and is not resistant to cooling or freezing[1]. The serum matrix in the run controls has been tested for infectious disease markers by serologic and molecular

screening methods. However, no screening strategy can offer complete assurance that products derived from human blood cannot transmit undetected infectious agents. The run control should only be used by trained laboratory workers who are aware of the potential risk of infectious agents in human serum samples and take the necessary precautions. In case of a serious incident related to the use of the run control, report it immediately to BioQControl's technical support group (tel: +31 (0)72 2020 730; e-mail: info@bioqcontrol.com) and to the competent authority of the country/EU Member State where the incident occurred.

- SeraQ run controls should be handled with the normal preventive measures in a serology laboratory[2,3].
- This product contains human plasma and traces of biological source material of non-human origin (bovine thrombin).
- The use of the run control in other assay configurations should be avoided and is not supported by the manufacturer.
- Wear disposable gloves when handling samples.
- Do not eat drink, smoke or apply cosmetics in areas where specimens are handled.
- Do not pipette by mouth.
- If skin or mucous membrane exposure occurs, immediately wash the area with copious amounts of water.
- Disinfect spills using a 0.5% hypochlorite solution (1:10 v/v household bleach) or equivalent disinfectant.
- Dispose unused or spilled materials according to the normal practices for biological waste disposal in your institution.
- If precipitates are visible, mix the run controls for 2 minutes thoroughly using a vortex instrument.
- Do not use run controls beyond four-week storage at 2-8 °C.
- Store run controls in an upright position.
- Validation of the diagnostic test results must be based on the specifications set by the manufacturer of the test kit and not be influenced by the test result on the run control.
- Matrix effects may reduce S/CO values in assays with a relatively high input volume when residual volumes in the run control tubes become low, even within the 4-week storage period. Use fresh tubes when volumes are low and monitor results carefully toward the end of the usage period.
- Do not pool residual volumes from different tubes or usage periods. Pooling may combine materials with different evaporation levels and matrix effects that compromise assay performance. These matrix effects increase as residual volumes decrease.
- Cap tubes immediately after use and return to storage at 2-8 °C to minimize evaporation.

Reagent preparation

- For first use of the run control thaw the tube quickly in a water bath at 37 °C.
- Mix gently during thawing until contents are just thawed.
- Immediately after ice clot has disappeared remove the run control tube from the water bath.
- Before testing allow the run control tube to adapt to room temperature.
- Mix the run control tube thoroughly prior to use with a vortex instrument.
- Place the run control tube at the specified positions in the sample racks of the cobas system for regular donor or patient samples.

- Test on the Roche cobas platform with the assays mentioned in Table 1 according to the manufacturer's instructions.
- Recap and store the opened tube immediately after use at 2-8 °C (see storage instructions).

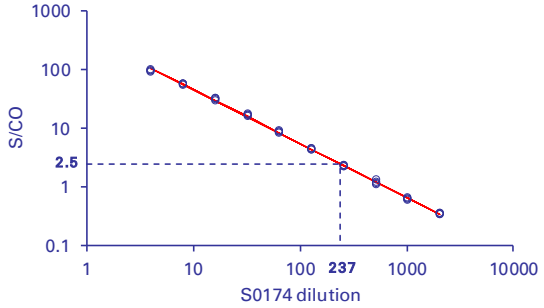
Performance Characteristics

SeraQ run controls have been designed by examination of the response curves on dilutions of the internal standards and as such relate to the analytical sensitivity of immunoassays. In the following paragraphs the essential performance characteristics of SeraQ run controls are presented.

Dose response and analytical sensitivity

By analysing standard dilution series, the relationship between S/CO values and concentration of the analyte can be established[4,5]. Plotting Log transformed Elecsys Syphilis S/CO values against Log dilution of anti-*Treponema pallidum* using linear regression analysis enables calculation of a correlation coefficient. Figure 1 shows a linear dose response relation in the Roche Elecsys Syphilis assay on logarithmic scales of dilution factor and S/CO values.

Figure 1. S0174 anti-*Treponema pallidum* standard dilution against S/CO in the Elecsys Syphilis assay and regression line on logarithmic scales. The S0174 dilution for the target S/CO = 2.5 is indicated.



Expected assay response values on run control

The expected results on the P0312 SeraQ Elecsys Syphilis run control are as follows:

Anti-*Treponema pallidum* range S/CO ratio: 2.1 – 3.2

Each Elecsys reagent lot appears to have its own dose response curve and distribution of S/CO values on SeraQ run controls. This depends on the analytical sensitivity of the Roche Elecsys Syphilis reagent lots that are in use. Thus, it cannot be guaranteed that the assay response values will always fall within these ranges. P0312 SeraQ Elecsys Syphilis run control serves as an independent standard for monitoring consistent analytical sensitivity of Roche Elecsys Syphilis reagent lots over time.

Interpretation of Results

Calculations

Subsequent test runs can be analysed by appropriate statistical approaches on the S/CO ratios obtained on the external control samples. A software system (DataQ Analytics) is available via the website www.bioqcontrol.com for entering S/CO values and generating a statistical report with the following calculations for preparing a Levey-Jennings Chart:

Transforming assay response values

To obtain the test kit batch specific reference values, an initial collection of at least 30 consecutive test results is required. Upon collecting additional data, the chart characteristics may be updated.

- The S/CO values for anti-*Treponema pallidum* are 'log normally' distributed. For the Roche Elecsys Syphilis assay one should use the logarithm of S/CO ratios for calculation of the geometric mean and predictive interval (pred. int.) as follows:
  - Calculate from each measurement the log S/CO value.
  - Calculate average and standard deviation (SD) on these log transformed values; Average (log) and Standard Deviation (log).
  - Calculate the (geometric) mean in S/CO ratio by taking the anti-log value of the Average (log).
  - Calculate Student-t-values belonging to the 95% and 99% pred. int. for different number of observations (n) (Table 3).
  - Calculate the 95% and 99% pred. int. (log) as follows:

    99% Lower limit (log): Average (log) – (99%) Student-t-Value x SD (log) x $\sqrt{(1 + 1/n)}$
    95% Lower limit (log): Average (log) – (95%) Student-t-Value x SD (log) x $\sqrt{(1 + 1/n)}$
    95% Upper limit (log): Average (log) + (95%) Student-t-Value x SD (log) x $\sqrt{(1 + 1/n)}$
    99% Upper limit (log): Average (log) + (99%) Student-t-Value x SD (log) x $\sqrt{(1 + 1/n)}$
  - Take the anti-log values for calculating the predictive limits in S/CO ratio. To visualize the individual S/CO values make a Levey-Jennings control chart on a linear scale. S/CO ratios plotted on a linear scale depict the upper 95% and 99% predictive limits at greater distance from the geometric mean S/CO value than the lower predictive limits (see Figure 2).

Table 3. Relation of Student t value and numbers of runs (n) to calculate predictive intervals.

Runs (n)	t-value at 95% pred. int.	t-value at 99% pred. int.
10	2.262	3.250
20	2.093	2.861
30	2.045	2.756
Infinite	1.960	2.576

Infinite equals the normal distribution

Levey-Jennings Chart

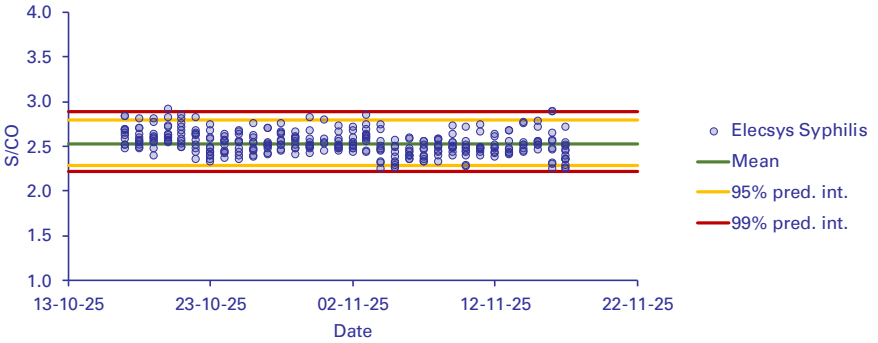
Table 4 summarizes the Levey-Jennings chart parameters in Figure 2, which are based on the S/CO values reported on one P0312 SeraQ Elecsys Syphilis batch by one laboratory. The Levey-Jennings chart is a graph in which quality control results are plotted over subsequent test runs in time to give a visual indication when a laboratory test is or is not working well. The data points for each test run in the scatter plot in Figure 2 show the distance from the geometric mean S/CO ratio (green line in graph) which is the expected response level for the run control. The yellow and red lines represent the 95% and 99%

predictive intervals, respectively. The data represents individual measurements of different instruments (of one laboratory in this example).

Table 4. Geometric mean S/CO value with 95% and 99% predictive intervals as found on one batch (B4304-003) of P0312 SeraQ Elecsys Syphilis run control in 315 test runs by one laboratory.

Assay	n	Geomean	95% pred. int.	99% pred. int.
Elecsys Syphilis	315	2.53	2.29 – 2.80	2.21 – 2.89

Figure 2. Levey-Jennings chart of P0312 SeraQ Elecsys Syphilis run control results in the Roche Elecsys Syphilis assay from one laboratory. The average (green line) and 95% and 99% predictive intervals (yellow and red lines) are based on log transformed S/CO values as explained in the text.



Interpretation

Knowing the 95% and 99% predictive intervals for generating a Levey-Jennings chart one can use Nelson rules[6] to interpret values outside the predictive limits and for identifying trends and aberrant results. The statistical report generated by the DataQ Analytics system (on the website www.bioqcontrol.com) identifies these trends and outliers for the laboratory requesting the report.

- Negative or positive trends resulting from gradual changes in test performance and not reported by the internal kit controls and/or alert systems in the test robot, are indicative for a lack of maintenance, the need for recalibration of equipment, or degradation of reagents. These are systematic errors. In case a trend is recognised, the laboratory is encouraged to identify the root cause of the deviation.
- Aberrant results like a negative response on the run control or a result outside the 99% predictive interval are indicative for incidental errors that need further investigation to identify the root cause. The identification of the root cause of aberrant results is beyond the scope of the intended use of the run controls.
- Differences between S/CO values of laboratories could be attributed to different reagent lots or run control batches that are in use. The statistical report that can be obtained from the DataQ Analytics system (available on www.bioqcontrol.com) compares the assay response values on different lab instruments, test reagent lots and run control batches.

Variation in immunoassay reagent lots and run control batches

Variation in S/CO ratios on run controls reflects differences in analytical sensitivity between assay runs and reagent lots. Different batches of SeraQ run controls are prepared from the same standards. Therefore, the composition of the SeraQ run controls is consistent from batch to batch. Variance component analyses of results obtained with other SeraQ run controls have previously shown that test reagent lots are a larger source of variation in S/CO values than run control batches.

Limitations

- SeraQ run controls were designed for monitoring the analytical performance of serologic test systems. They cannot be used to evaluate the diagnostic sensitivity of the assays.
- The run control must not be substituted for the mandatory controls or calibrators provided with IVD test kits for calculating the cut off and/or criteria for releasing test results.
- The response values on the run controls should not be used to release or reject the test run but can be used as an aid in the assessment of analytical performance.
- The expected S/CO values and 99% predictive intervals have been established with a limited number of Elecsys reagent lots. It cannot be guaranteed that S/CO values obtained with new reagent lots will always fall within these limits.
- Although the batch-to batch composition of SeraQ run controls is consistent, some variation in the measurable potency of the serum standards in the run control batches cannot be avoided due to matrix effects and other manufacturing variables.

References

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4. Plikaytis BD, Turner SH, Gheesling LL, Carlone GM. Comparisons of standard curve-fitting methods to quantitate Neisseria meningitidis group A polysaccharide antibody levels by enzyme-linked immunosorbent assay. J Clin Microbiol. 1991;29(7):1439-46
5. Bank HL. A quantitative enzyme-linked immunosorbent assay for rat insulin J Immunoassay. 1988; 9(2):135-58.
6. Nelson LS, "The Shewhart Control Chart—Tests for Special Causes". Journal of Quality Technology 1984;16, no. 4: 238-239

Revision history

Date	Version	Description of change
March 2026	V3.0	Error in formula for calculations changed in chapter “Interpretation of results”. Performance data added. Contact information added for reporting serious incidents in chapter “Warnings and precautions”. Symbol for positive control added.

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