# P0218 SeraQ ARCHITECT Syphilis

REF **P0218**

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

P0218 SeraQ ARCHITECT Syphilis is intended to be used on the Abbott ARCHITECT SYPHILIS TP® platform as an external run control in combination with the assay for the detection of antibodies to *Treponema pallidum* (see Table 1) performed in diagnostic and blood screening laboratories. P0218 SeraQ ARCHITECT Syphilis is a single-marker dilution of an internal anti-*Treponema pallidum* standard in defibrinated plasma giving a low reactive result in the Abbott ARCHITECT SYPHILIS TP® assay. The run control is intended to be tested in consecutive runs of the immunoassays over time. By comparison of the sample to cut off (S/CO) values found on P0218 SeraQ ARCHITECT Syphilis one can monitor the consistent analytical sensitivity of test runs. The run control should not be used to replace internal controls or calibrators in the test kits.

**Table 1.** Test kits covered by this run control

| Equipment | Agent | Tests |
|---|---|---|
| ARCHITECT | *Treponema pallidum* | Abbott ARCHITECT SYPHILIS TP® |

## Key to Symbols Used

Manufacturer

Lot number

Catalogue number

Store below -20°C

Country of origin

Contains human blood derivatives

Expiry date

Number of controls

Caution

For IVD performance evaluation only

Unique device identification

Read instructions for use

## Principle of method

A number of SeraQ run controls have been designed for monitoring the performance of different anti-*Treponema pallidum* assays. 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. The SeraQ run control series includes the product P0218 SeraQ ARCHITECT Syphilis for which the composition is optimised for use with the Abbott ARCHITECT SYPHILIS TP® test system. The P0218 SeraQ ARCHITECT 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 IVD batch variation.

## Traceability of antibody concentrations

For anti-*Treponema pallidum*, an internal serum standard has been established[1] from which reference panels and run controls are prepared by gravimetrically recorded dilution steps. No unitage could be assigned to the internal standard for anti-*Treponema pallidum* since international reference preparations are not available. The consistent concentration of the analytes 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 standards that are used for manufacturing of the SeraQ run controls.

## Kit contents (materials provided)

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

**Table 2.** Description of kit formats and contents

| Cat. Code | GTIN/UDI-DI code^ | Quantity run control | Tube size | Claimed sample volume | Secondary packaging |
|---|---|---|---|---|---|
| P0218/01 | 8718719833698 | 60 x 2.0 mL | 10 mL | 1.9 mL (+overfill) | 60 tube rack in box |
| P0218/02 | 8718719833704 | 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 P02018 SeraQ ARCHITECT Syphilis run control is 871871983P0218EQ.

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 with sequential batch number and marker: SYPH. The barcode of each run control tube can be read by the ARCHITECT 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 ARCHITECT 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 a month.

## Warning and precautions

P0218 SeraQ ARCHITECT Syphilis run controls are prepared from an internal serum standard, in which the bacterium has been inactivated by refrigerated storage[1]. The serum matrix in in the run controls has been tested for infectious disease markers by serologic and molecular screening methods. However, no screening procedure can offer complete assurance that products derived from human blood cannot transmit undetected infectious agents.

- 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.
- Do not use run controls beyond one month 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 IVD test kit and not be influenced by the test result on the run control.

## 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 using a vortex instrument.
- For automated test systems, place the run control tube at the specified positions in the sample racks for regular donor or patient samples. Otherwise, pipet run controls manually as with regular test specimens at the target position in test plates.
- Test on the Abbott ARCHITECT Syphilis TP platform with the assay mentioned in Table 1 according to the manufacturer's instructions.
- Store the opened tube immediately after use at 2-8°C (see storage instructions).

## Analytical Performance Characteristics

SeraQ run controls have been designed by examination of the response curves on dilutions of the internal (secondary) standards and as such relate to the analytical sensitivity of immunoassays. In the following paragraphs the essential analytical 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[5,6]. Plotting (transformed) S/CO values against (log) concentration analyte using linear regression analysis enables calculation of correlation coefficients. It is recommended to use a transformation resulting in an optimal correlation. Figure 1 show linear dose response relations in the Abbott ARCHITECT SYPHILIS TP assay obtained after log transformation of dilution and S/CO values.

**Figure 1.** Dose response in ARCHITECT SYPHILIS TP assay. Log ARCHITECT Syphilis TP S/CO values are plotted against log dilution ($r^2 = 0.996$).

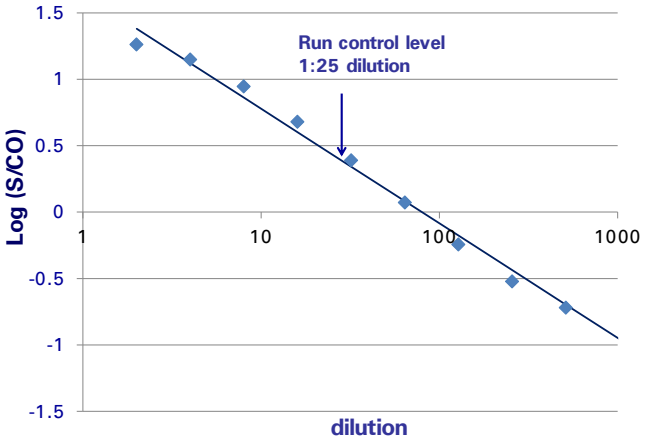



Table 3 shows the results obtained on four Abbott Architect reagent batches. These data confirm that when a new reagent batch is introduced the 95% and 99% predictive interval in the Levey-Jennings chart need to be reassessed (see Interpretation of Results).

**Table 3.** Response values on 4 Abbott Architect Syphilis TP batches on P0218 SeraQ ARCHITECT Syphilis run control

| Abbott batch | n | Geomean | 95% pred. int.* | 99% pred. int.* |
|---|---|---|---|---|
| 1 | 71 | 3.5 | 3.0 - 4.1 | 2.9 - 4.3 |
| 2 | 91 | 5.3 | 4.2 - 6.7 | 3.9 - 7.2 |
| 3 | 66 | 3.2 | 2.6 - 4.0 | 2.4 - 4.3 |
| 4 | 5 | 5.6 | 4.8 - 6.5 | 4.2 - 7.4 |

*for calculation see instructions below

**Variation in immune-assay reagent batches**

Variation in S/CO ratio on run controls reflects the difference in analytical sensitivity of assay runs and reagent batches. Different batches of SeraQ run controls are prepared from the same secondary standards. As a consequence the composition of the multi-marker run controls is consistent from batch to batch. This is confirmed by multi-variance analysis on large data sets showing that immuno-assay reagent batches are the major source of variation in analytical sensitivity. Figure 2a and 2b show examples of the S/CO distribution for four different Abbott PRISM HBsAg reagent batches and two SeraQ run control batches. Similar results were observed for other serologic assays.

**Figure 2a.** Frequency distribution of HBsAg S/CO ratios on one batch of SeraQ run control and four PRISM batches (n=1992)

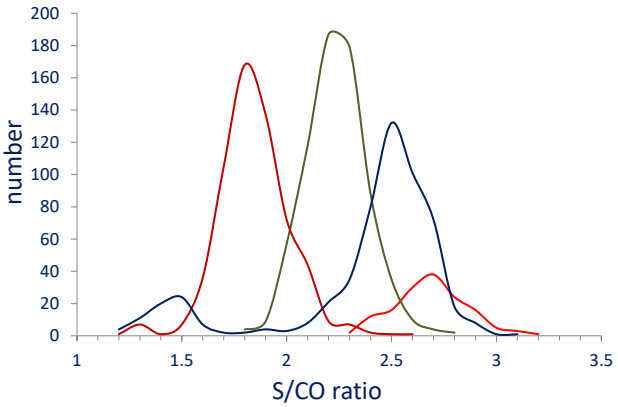
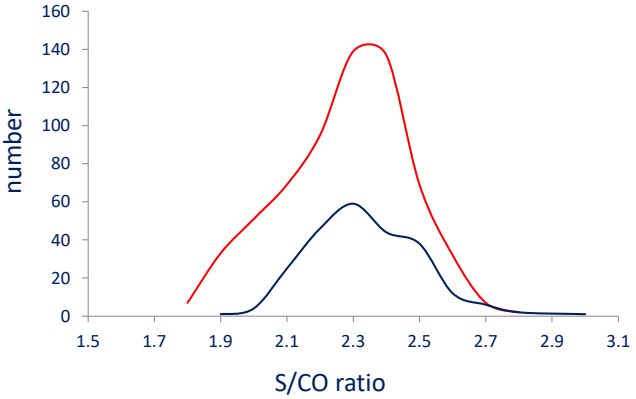



**Figure 2b.** Frequency distribution of HBsAg S/CO ratios on two batches of SeraQ run control and one PRISM batch (n=879)




Thus, the variability in results is mainly caused by differences in test batches.

## Expected assay response values

The expected results for the P0218 SeraQ ARCHITECT Syphilis run control is as follows:

1. *Treponema pallidum* range S/CO ratio: 1.5 – 7.0

Each batch of Abbott Architect SYPHILIS TP® has its own dose response curve and distribution of S/CO values on SeraQ run controls. This depends on the analytical sensitivity of the Abbott reagent batches that are in use. Thus, one can expect that batch to batch variability (Table 3). P0218 SeraQ ARCHITECT Syphilis serves as an independent

external run control for monitoring consistent analytical sensitivity of Abbott reagent batches 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 Abbott Architect SYPHILIS TP® batch specific reference values for each marker, an initial collection of 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 ABBOTT ARCHITECT SYPHILIS TP assay, one should use the logarithm of S/CO ratios for calculation of the geometric mean and predictive interval (pre. int.).

- Calculate from each measurement the log S/CO value.
- Calculate average and standard deviation on these logs 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 4).
- Calculate the 95% and 99% pred. int. (log) as follows:

  99% Lower limit (log): Average (log) – (99%) Student-t-Value x Standard Deviation (log)
  95% Lower limit (log): Average (log) – (95%) Student-t-Value x Standard Deviation (log)
  95% Upper limit (log): Average (log) + (95%) Student-t-Value x Standard Deviation (log)
  99% Upper limit (log): Average (log) + (99%) Student-t-Value x Standard Deviation (log)
- 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 example Figure 3).

### Levey-Jennings chart

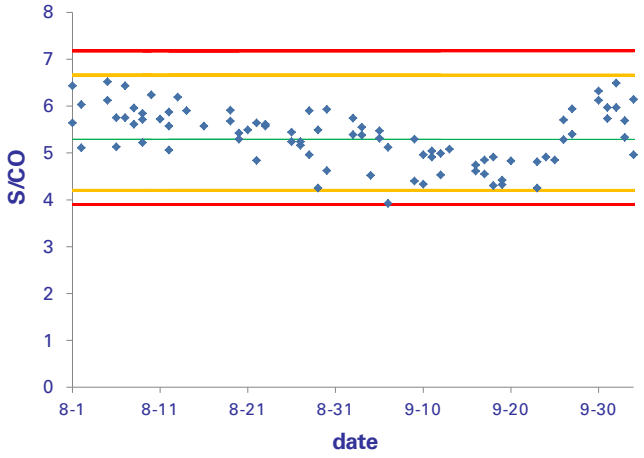
Figure 3 shows examples of Levey-Jennings charts for ARCHITECT assay on the P0218 SeraQ ARCHITECT Syphilis run control as can be obtained from the statistical reports by the DataQ Analytics software system. The Levey-Jennings chart is a graph in which quality control results are plotted over subsequent test runs in time to give a visual indication when a laboratory test is (not) working well. The data points for each test run in the scatter plots in Figure 3 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 orange and red lines represent the 95% and 99% predictive intervals respectively. The data represents individual measurements of different laboratories and instruments.

**Table 4.** 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

**Figure 3.** Example of a Levey-Jennings control chart for one Abbott ARCHITECT SYPHILIS TP batch. The predictive limits for the S/CO ratio are log transformed as explained in the text.



**Interpretation**
Knowing the 95% and 99% predictive for generating a Levey-Jennings chart one can use Nelson rules[7] to interpret values outside the predictive limits 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 range of 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.

## 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 ARCHITECT 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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