

Bio

QCControl

**P0078**  
**SeraQ ARCHITECT**

**CE**  
0088

**IVD**

**REF**

**P0078**



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

P0078 SeraQ ARCHITECT is intended to be used on the Abbott ARCHITECT® platform as an external run control in combination with the assays for the detection of hepatitis B surface antigen (HBsAg), antibodies to hepatitis C virus (anti-HCV) and antibodies to human immunodeficiency virus types 1 and 2 (anti-HIV-1/2), (see Table 1) performed in diagnostic and blood screening laboratories. P0078 SeraQ ARCHITECT is a multi-marker mixture of inactivated HBsAg, anti-HCV and anti-HIV-1 standards in defibrinated plasma giving a low reactive result in the Abbott ARCHITECT® Assays. 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 for the three markers found on P0078 SeraQ ARCHITECT 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
Abbott ARCHITECT®	Hepatitis B virus Hepatitis B virus Hepatitis C virus Human immunodeficiency virus	ARCHITECT HBsAg qualitative ARCHITECT HBsAg qualitative II ARCHITECT anti-HCV ARCHITECT HIV Ag/Ab Combo

## Key to Symbols Used



Manufacturer



Lot number



Catalogue number



In vitro diagnostic  
medical device



Store below  
-20°C



Expiry date



Contents



Caution



CE mark with Notified  
Body number



Read instructions  
for use

## Principle of method

A series of SeraQ run controls for monitoring HBsAg, anti-HCV and anti-HIV-1 test performance have been designed. 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 HBsAg, anti-HCV and anti-HIV-1. The analytical sensitivity of test kits from different manufacturers varies and therefore for each combination of test kits a separate multi-marker run control has been designed. This SeraQ run control series includes the product P0078 SeraQ ARCHITECT for which the composition is optimised for use with the Abbott ARCHITECT® test system. The P0078 SeraQ ARCHITECT run control is designed to generate assay response values (i.e. S/CO ratios) positioned in the low positive range of the assays. Routine use of external run controls enables laboratories to monitor day-to-day test performance and IVD batch variation.

## Traceability of antigen and antibody concentrations

For each HBsAg, anti-HIV-1 and anti-HCV, an internal (secondary) serum standard has been established<sup>1</sup> from which reference panels and run controls are prepared by gravimetrically recorded dilution steps. The undiluted secondary standard for HBsAg is derived from the same purified heat-inactivated source material as is used for preparation of the WHO HBsAg adw2 (00/588) International Standard (IS)<sup>1-4</sup>. Studies with the later established WHO international hepatitis B virus genotype reference panel showed that the heat-inactivation of HBsAg in the International Standard had little impact on the detectability in immuno-assays<sup>4</sup>. The HBsAg concentration in the run control has been set at 0.11 IU/mL. One IU heat-inactivated HBsAg was found to be equivalent to 0.67 ng HBsAg when historically calibrated against the first WHO standard established by the Paul Ehrlich Institute<sup>1</sup>, comparable to conversion factors of 0.58 and 0.71 reported in WHO collaborative studies<sup>3,4</sup>. No unitage could be assigned to the internal standards for anti-HIV-1 and anti-HCV 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 -40°C. These reference samples are derived from the same undiluted internal (secondary) standards that are used for manufacturing of the SeraQ run controls.

## Materials Provided

Ten (10) polypropylene tubes with screw caps, each contains 5.0 mL of P0078 SeraQ ARCHITECT run control and 0.01% (w/v) Thimerosal as preservative.

## Storage Instructions

Store unopened tubes at or below -20°C. After use, the run control tubes should be stored to 2°C to 8°C (< 1 month).

## Warning and precautions

P0078 SeraQ ARCHITECT run controls are prepared from secondary serum standards, in which virus has been inactivated by in vivo validated methods applied in the plasma industry<sup>1</sup>. Infectivity and inactivation data have been analysed to demonstrate absence of residual infectivity of HBV, HCV and HIV-1 in the run controls<sup>1</sup>. The serum matrix 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<sup>5,6</sup>.
- 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 test kit.

### Test Procedure

- Allow a run control tube to adapt to room temperature.
- Mix the tubes thoroughly prior to use (any visible precipitate will then easily disappear).
- 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 platform with the assays mentioned in Table 1 according to the manufacturers instructions
- Store the opened tube immediately after use at 2-8 °C (see storage instructions).

### Expected assay response values

The expected results for the P0078 Abbott ARCHITECT run control are follows:

1. HBsAg average (range) S/CO ratio: 1.3 – 5.0
2. anti-HIV average (range) S/CO ratio: 1.3 – 5.2
3. anti-HCV average (range) S/CO ratio: 1.4 – 5.4

Each test kit batch 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 Abbott ARCHITECT batches that are in use. The observed variation in Abbott ARCHITECT batches over time is used to estimate the ranges of the markers. In future the S/CO ranges will be assessed again. P0078 SeraQ ARCHITECT run control serves as an independent secondary standard or external quality control sample for monitoring consistent analytical sensitivity of Abbott ARCHITECT batches over time.

### Interpretation of Results

#### Calculations

Subsequent test runs can be analysed by appropriate statistical approaches on the S/CO ratios and HBsAg concentrations obtained on the external control samples.

#### Assay response values

To obtain the test kit batch specific reference values for each marker, an initial collection of 10 - 30 consecutive test results is required. Upon collecting additional data the chart characteristics may be updated.

- The S/CO values for HBsAg, anti-HIV and anti-HCV are 'log normally' distributed. For the Abbott ARCHITECT assays one should use the logarithm of S/CO ratios for calculation of the geometric mean and confidence interval. The calculation should be done each Abbott Architect batch.
  - Calculate from each measurement the log S/CO value.
  - Calculate average and standard deviation on these log transformed values; log (Average) and log (Standard Deviation).
  - Calculate the (geometric) mean in S/CO ratio by taking the anti-log value of the log (Average)
  - Use Table 2 to obtain Student-t-values belonging to the 95% and 99% CI for different number of observations (n)
  - Calculate the log(95% and 99% CI) as follows:
    - Log (99% Lower limit):  $\log(\text{Average}) - (99\% \text{ Student-t-Value} \times \log(\text{Standard Deviation}))$
    - Log (95% Lower limit):  $\log(\text{Average}) - (95\% \text{ Student-t-Value} \times \log(\text{Standard Deviation}))$
    - Log (95% Upper limit):  $\log(\text{Average}) + (95\% \text{ Student-t-Value} \times \log(\text{Standard Deviation}))$
    - Log (99% Upper limit):  $\log(\text{Average}) + (99\% \text{ Student-t-Value} \times \log(\text{Standard Deviation}))$
  - Take the anti-log values for calculating the confidence 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% confidence limits at greater distance from the geometric mean S/CO value than the lower confidence limits (see example Figure 1).

**Levey-Jennings chart**

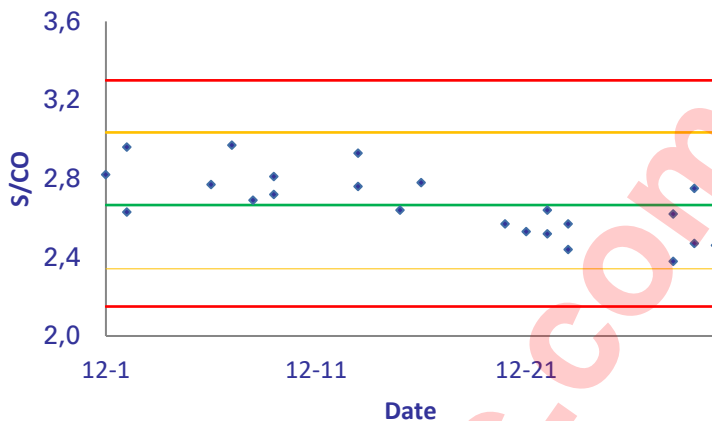
The Levey-Jennings chart is a graph in which quality control results are plotted over subsequent test runs in time to give a visual indication when a laboratory test is (not) working well. The data points for each test run in the scatter plot below (Figure 1) show the distance from the geometric mean 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% CI, respectively. The data represents individual measurements of three instruments.

**Table 2.** Relation of Student t value and numbers of runs (n) to calculate confidence intervals.

Runs (n)	t-value at 95% CI	t-value at 99% CI
10	2.306	3.355
20	2.101	2.878
30	2.048	2.763
Infinite	1.960	2.576

Infinite equals the normal distribution

Figure 1. Example of a Levey-Jennings control chart for the ARCHITECT anti-HCV assay (within a single reagent batch).



### Interpretation

Knowing the 95% and 99% CI for generating a Levey-Jennings chart one can use Westgard rules<sup>7</sup> to interpret values outside the confidence limits for identifying trends and aberrant results. One can find guidance on how to identify trends and outliers on the website [www.westgard.com](http://www.westgard.com).

- 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% CI are indicative for (incidental) random 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.

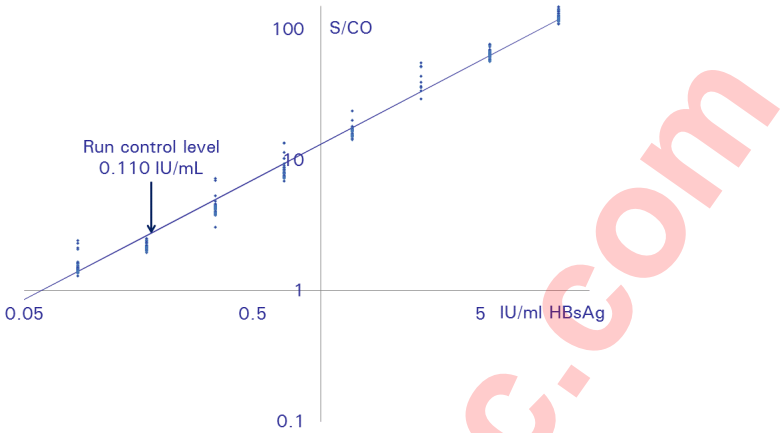
### Analytical Performance Characteristics

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.

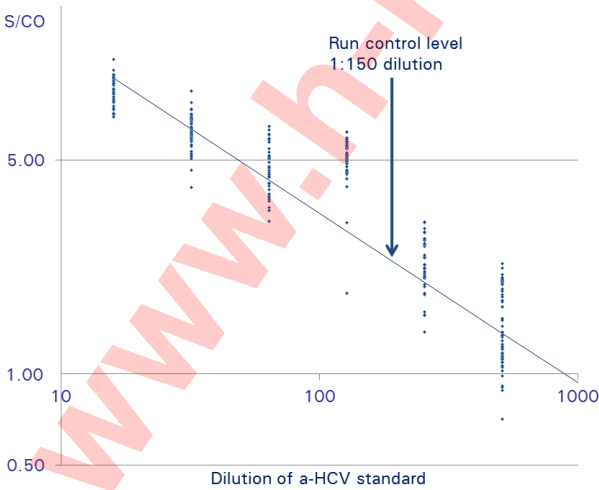
#### Dose response and analytical sensitivity

By analysing standard dilution series the relationship between S/CO values and concentration of the analyte can be established<sup>8,9</sup>. Plotting (transformed) S/CO values against (log) concentration or log (dilution analyte). Linear regression analysis enables calculation of correlation coefficients. It is recommended to use a transformation resulting in an optimal correlation. Figures 2a, b and c show dose response relations in the Abbott ARCHITECT obtained after log transformation of dilution and S/CO values.

**Figure 2a.** Dose response in Abbott ARCHITECT HBsAg assay. IU/ml input plotted against S/CO measured ( $r^2=0.996$ ).

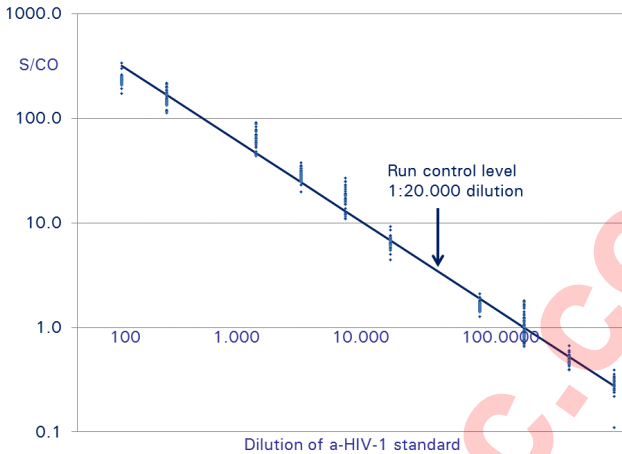


**Figure 2b.** Dose response in anti-HCV assay. Log anti-HCV S/CO values are plotted against log dilution ( $r^2 = 0.96$ ).





**Figure 2c.** Dose response in Abbott ARCHITECT HIV combo assay. Log S/CO values are plotted against log dilution ( $r^2 = 0.99$ ).



**Abbott ARCHITECT assay response values on P0078 SeraQ ARCHITECT run control**

Table 3 gives an example of results obtained within the same Abbott reagent batches. Note: Each Abbott ARCHITECT reagent batch will have its own specific values and Confidence Limits. They can differ from batch-to-batch, and do not necessarily meet the ranges shown in Table 3. In the section ‘Expected response values’ the indicated ranges have been chosen taken into account this batch-to-batch variation.

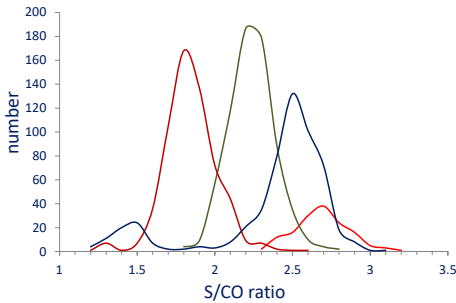
**Table 3.** Example of mean Abbott Assay response values (and 95% C.I.) on P0078 SeraQ ARCHITECT run control tested in 28 consecutive test runs in the same batches of the Abbott Architect assay

HBsAg	a-HCV	a-HIV-1
2.41 (2.06-2.83)	2.67 (2.34-3.04)	2.73 (2.40-3.11)

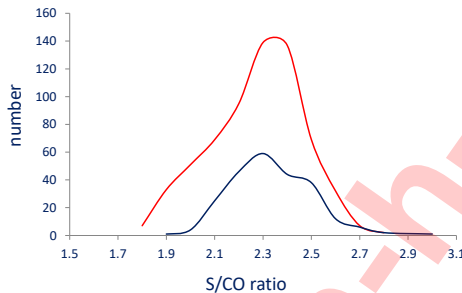
**Variation in immune-assay reagent batches**

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 3a and 3b show examples of the S/CO distribution for four different Abbott PRISM HBsAg reagent batches and two SeraQ run control batches.

**Figure 3a.** Frequency distribution of HBsAg S/CO ratios on one batch of SeraQ run control and four PRISM batches (n=1992)



**Figure 3b.** Frequency distribution of HBsAg S/CO ratios on two batches of SeraQ run control and one PRISM batch (n=879)



### Longitudinal observations for Abbott Architect batches

The SKML proficiency studies in which >50 blood bank laboratories participate were used to follow the variation in mean S/CO values in the Abbott Architect assays over time. Table 4 summarises the mean values per year expressed as a percentage and shows significant differences over time, which can only be explained by Abbott ARCHITECT batch to batch variation. Therefore laboratories should judge responses within the same Abbott ARCHITECT reagent batches. The expected response rates given above take this variation into account.

**Table 4.** Average reactivity of ARCHITECT users in SKML proficiency testing program on two-fold standard dilutions expressed to the average values found in 2011.

Agent	Relative sensitivity estimated on log(S/CO) values			
	2004	2011 (ref*)	2013	2014
HBsAg	101%	100%	170%#	N.A.
a-HCV	N.A.	100%	N.A.	169%#
HIV-Ag/Ab	N.A.	100%	N.A.	107%#

\* The 2011 data are assigned 100% to which the other data are referred to

# Significantly different from the 2011 data.

### Limitations

SeraQ run controls were designed for monitoring the analytical performance of IVD kits. They cannot be used to evaluate the diagnostic sensitivity of IVD kits. 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.

## References

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BioQControl B.V.  
Droogmakerij 31h  
1851 LX Heiloo  
The Netherlands

Tel: +31 (0)72 2020 730  
Fax: +31 (0)72 2020 731  
Internet: [www.bioQControl.com](http://www.bioQControl.com)

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