P0318
ViraQ HIV-2 Check 125

CE
0483

IVD

REF P0318

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

P0318 ViraQ HIV-2 Check 125 is intended to be used as external run control for detection of human immunodeficiency virus type 2 (HIV-2) RNA by the nucleic acid amplification technology (NAT) assays on the platforms defined in Table 1. P0318 ViraQ HIV-2 Check 125 is a heat-inactivated HIV-2-RNA standard in plasma at a concentration of 125 copies/mL giving 100% reactive results in the Procleix Ultrio and cobas MPX assay versions. The run control is intended for repeated testing in consecutive test runs of these NAT assays over time by trained laboratory workers. The run control helps laboratories to ensure sufficient analytical sensitivity of the multiplex HBV/HCV/HIV transcription mediated amplification (TMA) and real-time PCR assays for detection of HIV-2 RNA. P0318 ViraQ HIV-2 Check 125 should not be used to replace the 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 samples.

Table 1. Assays and platform covered by P0318 ViraQ HIV-2 Check 125 run control

Assay (manufacturer)	Platform	Test environment
Procleix® Ultrio Elite (Grifols)	Procleix® Panther®	Blood screening
Procleix® UltrioPlex E (Grifols)		
cobas® MPX (Roche)	cobas 5800/6800/8800	

Key to Symbols Used

Manufacturer

Lot number

Catalogue number

In vitro diagnostic medical device

Country of origin

Expiry date

Number of controls

Caution

CE mark with Notified Body number

Unique device identification

Biological substance Category B

Store below –30 °C

Positive control

Contains human blood derivatives

Read instructions for use

Principle of method

P0318 ViraQ HIV-2 Check 125 control has been formulated to mimic natural plasma specimens with a low HIV-2-RNA concentration. After thawing the run control tubes are ready for use and can be placed at random positions in sample racks on the NAT platform. The run control contains 125 copies/mL of heat-inactivated HIV-2 RNA (equivalent to 158

IU/mL) and has been designed to ensure sufficient analytical sensitivity of NAT tests in blood screening laboratories. The HIV-2-RNA concentration in the run control has been set at 13 - 24 times the 95% lower limit of detection (LOD) of the cobas MPX, Ultrio Elite and UltrioPlex E assays (Table 2)[1-5]. The positioning of P0318 ViraQ HIV-2 Check 125 control ensures reactivity rates ≥ 99.9% in the NAT assays listed in Table 1. The run control enables laboratories to be alerted in case of a significant reduction in analytical sensitivity of these NAT test systems. The run control is a dilution of the S0185 HIV-2-RNA subtype A standard, prepared by heat-inactivation of tissue culture derived virus spiked in plasma. The plasma matrix in which the run control is diluted is manufactured from plasma units that tested negative for all relevant markers of blood borne viruses. The S0185 HIV-2 standard has been calibrated in copies/mL and IU/mL against the Viral Quality Control (VQC)-Sanquin and World Health Organization (WHO) International Standards (Figure 1)[5]. The low concentration of HIV-2 subtype A in the run control is representative for HIV-2 subtype B as well[5]. A reactive result on the run control indicates that the NAT method has been performed with sufficient analytical sensitivity. A nonreactive result is indicative of reduced analytical sensitivity of the NAT system and should trigger investigation of the technical performance of the assay. The run control generates Ct values in the cobas MPX assay and sample to cut-off (S/CO) ratios in the Procleix Ultrio Elite and UltrioPlex E assays. Statistical analysis of these assay response values generated over a certain period allows for comparison of analytical performance of NAT reagent lots and laboratory instruments. For this purpose, users of the cobas MPX, Procleix Ultrio Elite and UltrioPlex E assays in combination with the P0318 ViraQ HIV-2 Check 125 Control can generate a statistical report for post-market performance follow-up using the DataQ Analytics system accessible via the website www.bioqcontrol.com.

Table 2. Detection limits on native and inactivated HIV-2 standard dilution panels

standard	panel	NAT method	n	50% LOD (CI) copies/mL	95% LOD (CI) copies/mL
S0185 BioQ HIV-2 RNA subtype A inactivated				no data	no data
S0024 VQC-Sanquin HIV-2 RNA subtype A native	S2403	TaqScreen 1.0	12	3.2 (1.8-5.6)	29.1 (13.5-125)
	P0034	cobas MPX	10	1.3 (1.0-1.6)	5.2 (3.7-8.8)
	P0034	Ultrio Elite	42	2.2 (1.7-2.8)	9.3 (6.7-14.4)
	P0298	Ultrio Elite	24	1.3 (0.9-1.8)	9.4 (5.5-22.4)
	P0298	UltrioPlex E	48	1.1 (0.9-1.4)	9.0 (6.0-15.9)
1st WHO HIV-2 RNA 08/150^	P0207	Ultrio Elite	278	2.2 (1.3-3.5)	18.3 (9.3-64.0)

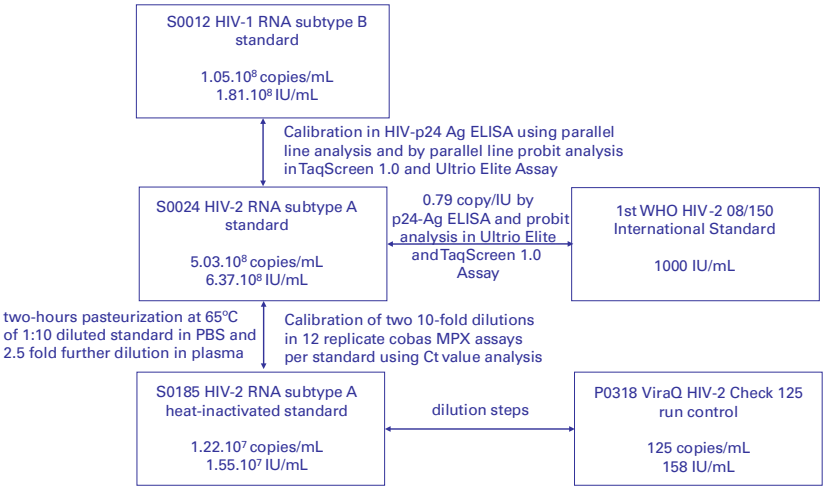
^1 IU is equivalent to 0.79 copies

Traceability to HIV-2 RNA copies and International Units

The HIV-2-RNA genotype A standard is a field isolate, typed as genotype A by sequence analysis in the env region, diluted in a pool of clarified citrated plasma that was negative for all relevant blood screening markers. The field isolate was propagated on MT2 cells for 8 weeks until an infectivity titre of $10^{4.5}$ $TCID_{50}$/mL was reached and used to prepare the standard in human plasma. The homogenised S0024 viral standard was stored in aliquots at ≤–70 °C. This S0024 HIV-2 RNA standard was pasteurized for 2 hours at 65 °C in a 1:10 dilution in PBS and further diluted 2.5-fold in plasma to obtain the inactivated S0185 HIV-2 RNA standard. Figure 1 shows the traceability chain between the P0318 ViraQ HIV-2 Check

125 run control, the heat-inactivated S0185 and native S0024 HIV-2 standard and the 1st WHO 08/150 International Standard for HIV-2 RNA. The heat-inactivated S0185 HIV-2 RNA standard (used for preparation of the P0318 ViraQ HIV-2 Check 125 run control) has been calibrated against the native S0024 standard by replicate testing of 10-fold standard dilutions in the cobas MPX assay. The original quantification of the native S0024 HIV-2 subtype A standard in copies/mL was based on comparison with the S0012 HIV-1 subtype B standard by p24 HIV-Ag testing using the Murex ELISA in a parallel line assay. Later the concentration was adjusted based on parallel line probit analysis in the TaqScreen 1.0 and Ultrio Elite assay[1,4]. Using these assays, we estimated a conversion factor of 0.79 copies/IU against the 1st WHO HIV-2 08/150 standard. This conversion factor was confirmed for the heat-inactivated S0185 HIV-2 standard in a parallel line assay against the heat-inactivated 2nd WHO HIV-2 16/296 standard by testing dilutions of the two standards in the cobas MPX assay. The manufacturing and quality control procedures of BioQControl guarantee consistent virus concentrations in consecutive ViraQ HIV-2 Check 125 batches. The inactivated S0185 HIV-2 subtype A standard is available in sufficient supply to ensure batch-to-batch consistency of ViraQ run controls for a prolonged period.

Figure 1. Traceability chain between P0318 ViraQ HIV-2 Check 125 run control and inactivated S0185 and native S0024 standards and the first WHO International Standard



Stability of HIV-2 standards and run control

For the long-term stability of the liquid frozen S0024 and S0185 HIV-2 standards stored below –70 °C, we refer to the stability data of the S0012 and S0041 HIV-1 standards[6]. Real time stability experiments using quantitative NAT assays showed less than 10% degradation of HIV-1 RNA per year in standard dilutions stored at –30 °C[6] and a similar decay per year was observed with batches of the P0318 ViraQ HIV-2 Check 125 control. Hence, it can be guaranteed that the P0318 ViraQ HIV-2 Check 125 control is still functional

and should generate a reactivity rate greater than 99.9% when stored at ≤–30 °C during the two-year shelf-life of the product.

Kit Contents (materials provided)

The run control contains human plasma without preservatives and is provided in four formats as detailed in Table 3.

Table 3. Description of P0318 ViraQ HIV-2 Check 125# kit formats and contents.

Cat. Code	GTIN/UDI-DI code^	Quantity No tubes (size 10 mL)	Sample volume	Secondary packing	Tube labels suitable for assay:
P0318/01	8718719831557	60 tubes	1.5 mL (+overfill)	Rack in box	cobas MPX
P0318/02	8718719830307	10 tubes	1.5 mL (+overfill)	Plastic zip bag	cobas MPX
P0318/03	8718719830581	60 tubes	1.4 mL (+overfill)	Rack in box	Ultrio versions
P0318/04	8718719830635	10 tubes	1.4 mL (+overfill)	Plastic zip bag	Ultrio versions

^ Global Trade Item Number = Unique Device Identification - Device Identifier (UDI-DI) code,
# Global Model Number (GMN) = Basic UDI-DI code for P0318 is 871871983P0318EV

P0318/01 and P0318/02 are intended to accommodate blood screening laboratories using the Roche cobas MPX assay and P0318/03 and P0318/04 are suitable for laboratories using the Ultrio Elite and UltrioPlex E assays. 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. The barcode of each run control tube can be read by the automated NAT systems but the tube labels of the P0318/03 and P0318/04 products are not suitable for the Roche cobas MPX assays, whereas those of the P0318/01 and P0318/02 products are not optimal for the Ultrio Elite and UltrioPlex E assays (Table 3).

Materials required but not supplied

The test kits and liquid handling devices by the NAT manufacturer as specified in Table 1, a water bath of 37 °C for quickly thawing of run control and a vortex instrument for thorough mixing of samples are not provided.

Storage instructions

The run control should be stored at or below –30 °C for a maximum of two years after preparation of the run control batch and not be used after the expiry date. Once thawed the run control samples should be used within 8 hours. During this period, when the run control is not in use, store sample at 2-8 °C. Do not refreeze the controls after thawing to prevent formation of cryoprecipitates. Any control sample that appears cloudy or contains precipitates after thawing and mixing should be discarded.

Warning and precautions

Although P0318 ViraQ HIV-2 Check 125 contains inactivated HIV-2 particles[5,7] the plasma may still be potentially bio-hazardous. The matrix is prepared from human blood plasma

that tested negative for blood borne viruses (HBV-DNA, HCV-RNA, HIV-RNA, HBsAg, anti-HBc, anti-HIV, anti-HCV, anti-HTLV and anti-*Treponema pallidum*). No test method can offer complete assurance that products derived from human blood cannot transmit (unknown) 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 plasma samples and take the necessary precautions. Observe the universal precautions for prevention of transmission of infectious agents when handling these materials[8,9]. 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.

- Do not pipette by mouth.
- Use personal protective equipment, including lab coats, gloves and safety glasses.
- Do not eat, drink or smoke in areas where the run control is handled.
- 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.
- Once thawed, do not re-freeze and thaw the run control samples to avoid formation of cryoprecipitates that could alter reactivity or cause pipetting errors in the automated sampling systems.
- Store run controls in an upright position.

Reagent preparation

- Thaw the run control quickly in a water bath at 37 °C.
- Mix gently during thawing until contents are just thawed.
- Immediately after the 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.
- Give a short spin in a centrifuge to remove liquid before releasing screw cap from vial.
- Minimise the time from thawing until testing of the control samples.
- Test run control sample within 8 hours after thawing.
- After thawing when not in use, store run control tube at 2-8 °C.

Performance characteristics

The results of the cobas MPX assays are Ct values and those of the Procleix Ultrio assays are expressed as a sample to cut-off ratio (S/CO). P0318 ViraQ HIV-2 Check 125 Control should be reactive in more than 99.9% of test runs with these NAT blood screening assays.

The positioning of P0318 ViraQ HIV-2 Check 125 control is near the Poisson detection endpoint range of the Procleix Ultrio assays but at enough distance to guarantee sufficient reproducibility of S/CO ratios. This has been demonstrated by testing dilution panels of the S0024 HIV-2 subtype A standard in the cobas MPX, Ultrio Elite and UltrioPlex E Assay (data not shown). At the concentration of 125 copies/mL, the cobas MPX assay Ct values are normally distributed, and the Ultrio Elite and UltrioPlex E assay S/CO ratios follow a non-parametric distribution.

Expected assay response values on run control

The expected results for the P0318 ViraQ HIV-2 Check 125 Control are as follows:

Cobas MPX assay
HIV-2-RNA Ct value range: 32.5 – 36.0

Procleix Ultrio Elite assay
HIV-2 RNA S/CO ratios range: 7.0 – 15.0

Procleix UltrioPlex E assay
HIV-2 RNA S/CO ratios range: 4.0 – 7.0

Each TMA assay and reagent lot has its own distribution of response values on HIV-2 standard dilutions and on P0318 ViraQ HIV-2 Check 125 Control. This depends on the design of the assay and the analytical sensitivity of the reagent lots that are in use. Thus, it cannot be guaranteed that the assay response values will always fall within these ranges. P0318 ViraQ HIV-2 Check 125 run control serves as an independent standard for monitoring the reproducibility and the analytical sensitivity of the cobas MPX, the Procleix Ultrio Elite and UltrioPlex E test runs and reagent lots in detecting HIV-2 RNA over time.

Interpretation of results

The run control should be tested in a manner identical to that of clinical specimens and the result be calculated according to the instructions for use of the NAT procedure. Subsequent test runs can be analysed by appropriate statistical approaches on the response values obtained on the external control samples. A software system (DataQ Analytics) is available via the website www.bioqcontrol.com for entering response values and generating a statistical report with assay-specific calculations for preparing a Levey-Jennings Chart.

cobas MPX Assay
Calculations
Use Student-t-values belonging to the 95% and 99% predictive intervals (Table 4). Calculate the 95% and 99% predictive limits as follows:

- 99% Lower limit: Average – 99% Student-t-Value x SD x $\sqrt{(1 + 1/n)}$
- 95% Lower limit: Average – 95% Student-t-Value x SD x $\sqrt{(1 + 1/n)}$
- 99% Upper limit: Average + 99% Student-t-Value x SD x $\sqrt{(1 + 1/n)}$
- 95% Upper limit: Average + 95% Student-t-Value x SD x $\sqrt{(1 + 1/n)}$

Table 4. Student t value to calculate predictive interval for 30 test runs.

Runs (n)	t-value at 95% int.	t-value at 99% int.
30	2.045	2.750
∞	1.960	2.576

Test the run control at least 30 times during the reference period. Since Ct values are used no log transformation is required and predictive intervals can be calculated from the arithmetic mean and standard deviation (SD). The Levey-Jennings chart is designed to identify individual aberrant values outside the 95% and 99% predictive intervals. By collecting additional data, the chart characteristics may be updated.

Use Nelson rules[10] to identify deviations in the Levey-Jennings trend analysis.

The cobas MPX results on P0318 ViraQ HIV-2 Check 125 control are expected to be reactive in more than 99.9% of test runs. Repeatedly non-reactive results (no Ct value) are indicative of a significantly reduced analytical sensitivity of the NAT system. A single event of a non-reactive result is however possible without deterioration of the test system and can be explained by Poisson distribution.

Levey-Jennings Chart

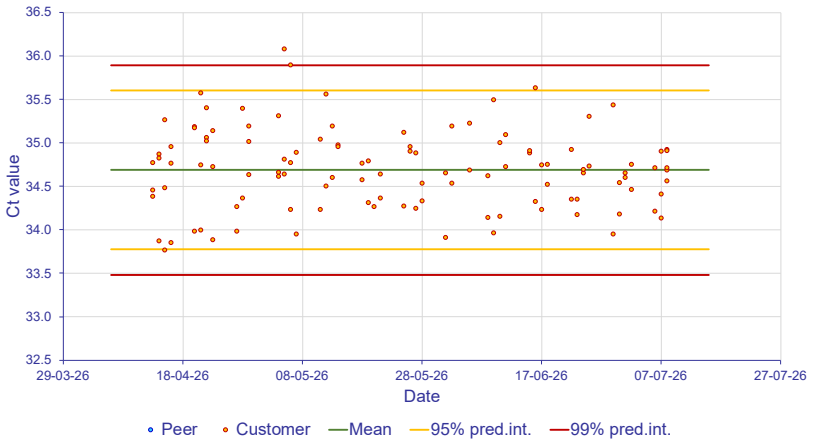
The Ct values in consecutive cobas MPX test runs for HIV-2 RNA can be plotted in a Levey-Jennings chart using the statistical report function of the DataQ Analytics system available on www.bioqcontrol.com.

Table 5 summarizes the Levey-Jennings chart parameters in Figure 2, which were deduced from the cobas MPX Ct values reported by one laboratory testing one batch of the P0318 ViraQ HIV-2 Check Control for three months.

Table 5. Mean Ct values with 95% and 99% predictive intervals as found on one batch of P0318 ViraQ HIV-2 Check 125 Control in 113 cobas MPX test runs in the period from 13-4-2026 to 8-7-2026 (data in Figure 2).

Assay	n	Average Ct value	95% predictive interval of Ct values	99% predictive interval of Ct values
cobas MPX	113	34.69	33.78 – 35.60	33.48 – 35.90

Figure 2. Levey-Jennings QC chart of cobas MPX Ct values for HIV-2-RNA obtained by one laboratory testing one batch of P0318 ViraQ HIV-2 Check 125 Control for three months.



Post-market performance follow-up of run control batches

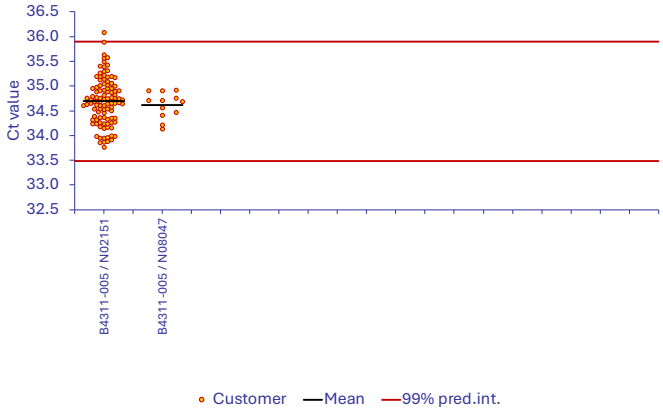
One can use P0318 ViraQ HIV-2 Check 125 in combination with the DataQ Analytics system on www.bioqcontrol.com to compare the Ct values on different run control batches, cobas

MPX reagent lots or cobas instruments. Figure 3 compares Ct values of two cobas MPX reagent lots on one run control batch tested by one laboratory.

Table 6 Comparison of mean cobas MPX Ct values on one P0318 ViraQ HIV-2 Check 125 Control batch and two consecutive cobas MPX reagent lots (data in Figure 3).

P0318 ViraQ batch	Cobas MPX reagent lot	n	Average Ct value
B4311-005	N02151	101	34.70
	N08047	12	34.61

Figure 3. Scatter plot of Ct values by P0318 run control batch – cobas MPX reagent lot combination



Ultrio Elite and UltrioPlex E Assay

Calculations

Since the Procleix Ultrio Elite and UltrioPlex E assays return non-parametrically distributed S/CO ratios, predictive ranges are based on the percentiles of the data range. Calculate the 95% and 99% predictive limits as follows:

- 99% Lower limit: (interpolated) 0.005th percentile
- 95% Lower limit: (interpolated) 0.025th percentile
- 99% Upper limit: (interpolated) 0.995th percentile
- 95% Upper limit: (interpolated) 0.975th percentile

Test the run control at least 30 times during the reference period. The Levey-Jennings chart is designed to identify individual aberrant values outside the 95% and 99% ranges. By collecting additional data, the chart characteristics may be updated. Use Nelson rules[9] to identify deviations in the Levey-Jennings trend analysis.

The Procleix Ultrio Elite and UltrioPlex E test results on P0318 ViraQ HIV-2 Check 125 control are expected to be reactive in more than 99.9% of test runs. Repeatedly non-reactive results (S/CO ratios <1) are indicative of a significantly reduced analytical

sensitivity of the NAT system. A single event of a non-reactive result is however possible without deterioration of the test system and can be explained by Poisson distribution.

Levey-Jennings Chart

The S/CO ratios obtained in consecutive Procleix Ultrio Elite and UltrioPlex E test runs for HIV-2 RNA can be plotted in a Levey-Jennings chart using the statistical report function of the DataQ Analytics system available on www.bioqcontrol.com.

Table 7 summarizes the Levey-Jennings chart parameters in Figure 4, which were deduced from the UltrioPlex E S/CO ratios reported by one laboratory testing one batch of P0318 ViraQ HIV-2 Check Control for more than one month.

Table 7. Median S/CO ratios with 95% and 99% ranges as found by one laboratory testing one batch of P0318 ViraQ HIV-2 Check 125 Control in 116 UltrioPlex E test runs in the period from 13-4-2026 to 26-5-2026 (data in Figure 4).

Assay	n	Median S/CO	95% range S/CO	99% range S/CO
UltrioPlex E	116	5.69	5.11 – 6.31	<5.10 – >6.45

Figure 4. Levey-Jennings QC chart of UltrioPlex E S/CO ratios for HIV-2-RNA on one batch of P0318 ViraQ HIV-2 Check Control.

So far, a performance evaluation study of the P0318 ViraQ HIV-2 run control in the Ultrio Elite assay has not been conducted.

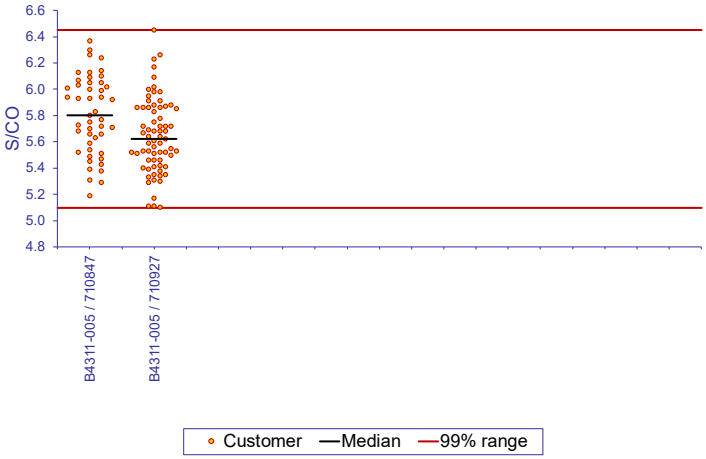
Post-market performance follow-up of run control batches

One can use P0318 ViraQ HIV-2 Check 125 in combination with the DataQ Analytics system on www.bioqcontrol.com to compare the S/CO ratios on different run control batches, Procleix Ultrio Elite and UltrioPlex E reagent lots or Procleix Panther instruments. Table 8 and Figure 5 compare S/CO ratios of two Procleix UltrioPlex E reagent lots on one run control batch.

Table 8. Comparison of UltrioPlex E S/CO on P0318 ViraQ HIV-2 Check 125 Control batches and between consecutive Procleix UltrioPlex E reagent lots.

P0318 ViraQ batch	UltrioPlex E reagent lot	n	Median S/CO	S/CO values < 5
B4311-005	710847	47	5.80	0 (0.00%)
	710927	69	5.62	0 (0.00%)
	All	**116**	**5.69**	**0 (0.00%)**

Figure 5. Scatter plot of S/CO ratios by P0318 run control batch – UltrioPlex E reagent lot combination



Limitations

- P0318 ViraQ HIV-2 Check 125 Control cannot be used to evaluate the analytical or diagnostic sensitivity of NAT blood screening assays (although a significant reduction of analytical sensitivity of the NAT system can become apparent with repeated occurrence of non-reactive results and a higher frequency of weak reactive results).
- P0318 ViraQ HIV-2 Check 125 Control must not be substituted for the mandatory controls or calibrators provided with NAT test kits for calculating the cut-off and/or criteria for releasing test results.
- The Poisson distribution in samples with low HIV-2 RNA concentrations cannot guarantee that 100% reactive results will always be found on P0318 ViraQ HIV-2 Check 125 Control in NAT blood screening assays. Therefore, the response values on the run controls should not be used for a decision to accept or reject the test run.
- The expected ranges of results in the cobas MPX, Procleix Ultrio Elite and UltrioPlex E assays on P0318 ViraQ HIV-2 Check 125 Control that are presented in this package insert were based on a very limited amount of data. It cannot be guaranteed that slightly different results will not be found on other run control batches, assay reagent lots or laboratory instruments.
- It cannot be excluded that some variation exists between the performance of consecutive batches of the P0318 ViraQ HIV-2 Check 125 control due to matrix effects or other manufacturing variables.

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Revision history

Date	Version	Description of change
July 2026	V2.0	Contact information added for reporting serious incidents in chapter “Warning and precautions”. Revision history table added. Symbol for positive control added. UltrioPlex E performance evaluation data added

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