Bio QControl

# P0318
# ViraQ HIV-2 Check 125

**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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## Table of contents


Intended Use....3
Key to Symbols Used....3
Principle of method....3
Traceability of HIV-2-RNA concentration in copies/ml....4
Kit Contents....4
Storage Instructions....4
Warning and precautions....4
Test Procedure....5
Intepretation of results....5
Performance characteristics....5
Limitations....7
References....8


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## Intended Use

P0318 ViraQ HIV-2 Check 125 is intended to be used as external run control for monitoring consistent performance and analytical sensitivity of multiplex nucleic acid test (NAT) blood screening assays for detection of HIV-2-RNA (see Table 1). P0318 ViraQ HIV-2 Check 125 must not be used to replace the internal kit controls or calibrators required for the release of test results. The product is intended for performance evaluation only.

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

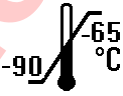
| Equipment | Agent | Test kits |
|---|---|---|
| PANTHER®<br>COBAS s 201 system | Human immunodeficiency virus type 2 | Procleix ULTRIO Elite®<br>TaqScreen MPX 1.0<br>TaqScreen MPX 2.0 |

## Key to Symbols Used

Manufacturer


Lot number


Catalogue number




Store between -65°C and -90°C


Biological substance Category B

Device for performance evaluation

Expiry date


Contents

Caution

Read instructions for use

## Principle of method

P0318 ViraQ HIV-2 Check 125 enables blood screening laboratories to monitor the performance of transcription mediated amplification (TMA) or polymerase chain reaction (PCR) assays for the qualitative detection of human immunodeficiency virus type 2 (HIV-2)-RNA in plasma or serum samples. The external run control is designed to mimic naturally occurring plasma specimens with a low concentration of HIV-2-RNA. The concentration of HCV-RNA in P0318 ViraQ HIV-2 Check 125 control samples is set at 125 copies/mL. The concentration is determined by parallel testing in replicate Murex HIV Antigen Mab (p24) against the Sanquin secondary HIV-RNA group M subtype B standard dilutions. This level is chosen at 4 to 5 times the 95 % lower limit of detection (LOD) of the Ultrio Elite and TaqScreen MPX 1.0, 2.0 assays[1-4]. The external run control generates Ct values in the lower dynamic range of the TaqScreen assays and sample to cut-off (S/CO) ratios in the saturation range of the Ultrio Elite assay. Occasionally lower S/CO values will be found in the dynamic assay response range of the Ultrio Elite assay. In rare cases a nonreactive result can be expected (see below). Repeatedly low or nonreactive results on the run control may indicate systematic or random errors in execution of the assay on the automated NAT screening systems. The external run control tubes are barcoded and comparable in size to donor blood collection tubes. After thawing the tubes are ready for use and can be placed at random positions in sample racks of the laboratory instruments.

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## Traceability of HIV-2-RNA concentration in copies/ml

The BQC HIV-2-RNA genotype A standard comprises of a field isolate, typed as genotype A by sequence analysis in the env V3 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. The homogenised viral standard was stored in aliquots at -70°C.

Two-fold dilutions of the secondary Sanquin HIV-RNA group M subtype B standard and the HIV-2-RNA genotype A standard were tested in the Murex HIV antigen Mab ELISA (Ortho) that detects p24 antigen. The estimate concentrations of p24 core antigen (pg/mL) present in the HIV-RNA standards were used to quantify the HIV-2-RNA standard in copies/mL.

The concentration was verified by testing HIV-RNA group M subtype B and HIV-2-RNA genotype A dilution series in the Grifols Ultrio Elite and Roche MPX 1.0 assay. Using parallel probit analysis for Grifols Ultrio Elite and comparison of Ct values from Roche MPX 1.0 the concentration in the HIV-2-RNA standard was confirmed. Standard dilution series of the WHO HIV-2-RNA standard (08/150) were also tested in Grifols Ultrio Elite[3]. Using probit analysis on dilution series revealed one copy equals 1.29 (0.6-2.8) IU. This figure is indicative, as the results were obtained from different studies using only one assay. The production and quality control methods guarantee a consistent virus concentration in consecutive ViraQ Check Control batches.

## Kit Contents

10 Tubes, each containing 1.5 ml P0318 ViraQ HIV-2 Check 125 in polypropylene tubes with screw caps and comparable in size to Vacutainer tubes used for donor sample collection. The run control contains HIV-2-RNA genotype A standard diluted in human plasma without preservatives.

## Storage Instructions

The run controls can be stored at or below -65°C during one year to ensure minimal degradation of HIV-2-RNA. It is recommended that P0318 ViraQ HIV-2 Check 125 is stored at or below 70°C to ensure long term stability for several years. Once thawed the run control samples should be used immediately. Do not refreeze the controls after thawing. Any control sample that appears cloudy or contains precipitates after thawing and mixing should be discarded.

## Warning and precautions

P0318 ViraQ HIV-2 Check 125 contains inactivated HIV-2 particles[4]. The matrix is prepared from human blood plasma that tested negative for blood borne viruses (HBV-DNA, HCV-RNA, HIV-RNA, HBsAg, anti-HIV, anti-HCV and anti-*Treponema pallidum*). No test method can offer complete assurance that products derived from human blood cannot transmit (unknown) infectious agents. Observe the universal precautions for prevention of transmission of infectious agents when handling these materials[15,16].

- 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 HIV-2 run controls are 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.

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- 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.

## Test Procedure

- Thaw the run control quickly in a water bath at 37°C.
- Mix gently during thawing until contents are just thawed.
- Immediately after thawing remove the run control tube from the water bath.
- Vortex the run control.
- Give a short spin in a centrifuge before releasing screw cap from vial.
- Minimise the time period from thawing until usage of the control samples.
- The controls should be handled and tested in a manner identical to that of clinical specimens in the test procedure being evaluated.

## Intepretation of results

P0318 ViraQ HIV-2 Check 125 Control should react positive in more than 99.5% of NAT blood screening test runs.

*Ultrio Elite*

In the Ultrio assay versions a S/CO ratio above 7 is expected on the run control samples. Lower S/CO ratio's may occur in frequencies less than 5 %. The Westgard[11] rules provide guidance for the interpretation on frequency of lower S/CO results.

*TaqScreen MPX 1.0 and 2.0*

In TaqScreen MPX 1.0 and 2.0 assays Ct values between 29 and 32 are expected on the run control samples. An increased frequency of test runs with high Ct values should be investigated. The warning level is a Ct value>32. The Westgard[11] rules provide guidance for the interpretation on frequency of high Ct values.

There is a small probability of nonreactive results, but these can also be related to incidental or systematic errors in the test system. Thus a nonreactive result should be investigated when it occurs. Repeatedly nonreactive results on the run control should trigger a root cause analysis.

## Performance characteristics

**Analytical sensitivity Ultrio Elite**

The analytical sensitivity of the Ultrio Elite is evaluated in validation studies[1-4]. Table 1 compares the 50% and 95% LODs in these studies showing consistent analytical sensitivity on the different HIV-2 standards.

**Table 2**. Analytical sensitivity of Procleix Ultrio Elite versions on BQC HIV-2-RNA standard and WHO HIV-2 standards

| HIV-2-RNA standard | n | 50 % LOD (CI) | 95 % LOD (CI) | Ref |
|---|---|---|---|---|
| BQC tertiary HIV-2 genotype A [a] | 42 | 2.1 (1.0-4.4) | 16.8 (8.0-40.4) | 1 |
| WHO HIV-2 08/150[b] | 52 | 3.6 (2.8-4.7) | 28.1 (19.5-45.3) | 3 |

a) Expressed in copies/mL b) expressed in IU/ml

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**Predicted response on P0318 ViraQ HIV-2 Check 125 run control in Ultrio Elite**

Table 3 presents the predicted test results on P0318 ViraQ HIV-2 Check 125 run control in the Ultrio Elite.

**Table 3.** Predicted number of non-reactive results on P0318 ViraQ HIV-2 Check 125 based on probit analysis of percentage Ultrio Elite reactive results on HIV-2 standard dilutions.

| HIV-2 run control level | Cps/mL | Predicted number of nonreactive results per 1000 |
|---|---|---|
| 1 x 95 % LOD | 17 (8-40) | 50 |
| 3 x 95 % LOD | 51 (24-120) | 6 |
| 5 x 95 % LOD | 85 (40-200) | 1.7 |
| Run control | 125 | 0.6 |

**Analytical sensitivity TaqScreen MPX 1.0 and 2.0 assays**

The analytical sensitivity of the TaqScreen 1.0 assay has been established in different validation studies[2,12,13]. Table 4 compares the 50% and 95% LODs in these studies showing consistent analytical sensitivity on the Sanquin and WHO HIV-2 standards. Although no data are available on the inactivated HCV genotype 3a standard used for preparation of P0318 ViraQ HIV-2 Check 125 control, the analytical sensitivity studies on the other HIV standards indicate that the HIV-2 RNA concentration of 125 cps/mL in the run control is chosen at 3 to 5 times the 95 % LOD of the TaqScreen 1.0 assay.

**Table 4.** Analytical sensitivity of TaqScreenMPX 1.0 and 2.0 assays on BioQControl, Roche, CBER and WHO HIV-2 genotype A standards

| HIV-2-RNA standard | n | 50 % LOD (CI) | 95 % LOD (CI) | Unit | Ref |
|---|---|---|---|---|---|
| BioQControl HIV-2 genotype A[a] | 12 | 3.1 (1.8-5.6) | 29.1 (13.6-125.2) | Cps/mL | 2 |
| CBER HIV-2 standard[a] | 120 | 12.5 (3.1-20.0) | 48.9 (40.2-60.3) | Cps/mL | 12 |
| WHO HIV-2 standard 08/150[b] | | | 7.9 (5.6-13.8) | IU/mL | 13 |
| Roche primary standard[a] | 194 | 13.9 (12.0-15.6) | 59.4 (51.8-69.7) | Cps/mL | 12 |
| Roche primary standard[b] | | | 57.4 (49.7-68.1) | Cps/mL | 13 |

a) MPX 1.0, b) MPX 2.0

Using probit analysis on HIV-2 standard dilutions it is expected TaqScreen 1.0 reacts positive on P0318 ViraQ HIV-2 Check 125 in >99.5 % of test runs. The Ct values are normally distributed, which allows Levey-Jennings graph data analysis.

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**Predicted response on P0318 ViraQ HIV-2 Check 125 run control in Roche MPX 1.0 and 2.0**
Table 5 presents the predicted test results on P0318 ViraQ HIV-2 Check 125 run control in the Ultrio Elite.

**Table 5.** Predicted number of non-reactive results on P0318 ViraQ HIV-2 Check 125 based on probit analysis of percentage Ultrio Elite reactive results on HIV-2 standard dilutions.

| HIV-2 run control level | Cps/mL | Predicted number of nonreactive results per 1000 |
|---|---|---|
| 1 x 95 % LOD | 29(14-125) | 50 |
| 3 x 95 % LOD | 87(52-375) | 7.2 |
| 5 x 95 % LOD | 145(70-625) | 2.3 |
| Run control | 125 | 3.3 |

## Limitations

- P0318 ViraQ HIV-2 Check 125 Control cannot be used to evaluate the analytical or diagnostic sensitivity of NAT blood screening assays.
- P0318 ViraQ HIV-2 Check 125 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 Poisson distribution in samples with low HCV concentrations cannot guarantee that 100% reactive results will 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 distributions of assay response values on P0318 ViraQ HIV-2 Check 125 Control that presented in this package insert were based on evaluation studies involving a limited number of assays and reagent batches. Therefore it cannot be guaranteed that slightly different results will be found on other assay versions or reagent batches.

www.mabo.com

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