P0068
ViraQ HIV-1 Trend 25

CE
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IVD

REF P0068

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

P0068 ViraQ HIV-1 Trend 25 is intended to be used as external trend control for human immunodeficiency virus type 1 (HIV-1) RNA detection by the multiplex transcription mediated amplification (TMA) assays on the automated nucleic acid amplification technology (NAT) platforms defined in Table 1. The trend control helps laboratories to ensure that HIV-1 is detected with sufficient analytical sensitivity by consecutive reagent lots of the Procleix Ultrio assay versions and by each of the Tigris or Panther instruments in use. The trend control can be used in daily test runs to continuously monitor NAT performance over time or tested occasionally in multiple replicates in one test run for:

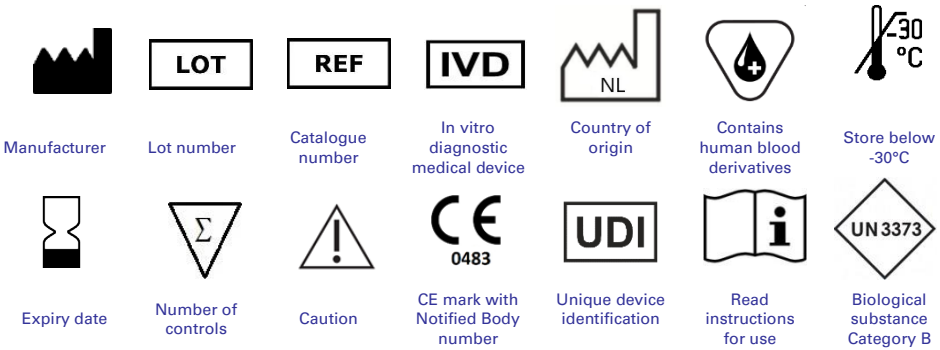
- acceptance (transport integrity) testing of TMA reagent lots
- installation qualification of instruments
- training of technicians

Table 1. Assays and platforms covered by P0068 ViraQ HIV-1 Trend 25 control

Assays (manufacturer)	Platform	Test environment
Procleix Ultrio® (Grifols)	Procleix Tigris®	Blood screening
Procleix Ultrio Plus® (Grifols)		
Procleix Ultrio Elite® (Grifols)	Procleix Panther®	

P0068 ViraQ HIV-1 Trend 25 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.

Key to Symbols Used



Principle of method

P0068 ViraQ HIV-1 Trend 25 control has been formulated to mimic natural plasma specimens with a low HIV-RNA concentration. After thawing the trend control tubes are ready for use and can be placed at random positions in sample racks on the NAT platforms. The trend control contains 25 copies/mL of HIV-1 RNA (equivalent to 43 International Units (IU)/mL) and has been designed to ensure sufficient analytical sensitivity of transcription mediated amplification (TMA) tests in blood screening laboratories. The HIV-1 RNA concentration in the run control has been set near the 95% lower limit of detection (LOD) of the Ultrio (Plus and Elite) assays (table 2)[1-5]. P0068 ViraQ HIV-1 Trend 25 Control enables laboratories to be alerted in case of a reduction of analytical sensitivity of NAT instruments or reagent batches and to identify changes in TMA performance over time. The run control is a dilution of the S0041 HIV-1-RNA subtype B standard, prepared by heat-inactivation of tissue culture derived virus spiked in plasma[6-

[8]. 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 S0041 HIV-1 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). The low concentration of HIV-1 subtype B in the run control is meant to be representative for HIV-1 genotypes A-K and circulating recombinant forms that are prevalent in different geographical regions of the world (although not all genetic variants are detected with comparable analytical sensitivity by the commercial NAT assays)[4,9-11]. A positive result on the trend control indicates that the NAT method has been performed with sufficient analytical sensitivity. A higher than expected proportion of non-reactive or weakly reactive results 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 sample to cut-off (S/CO) ratios in the Procleix Ultrio assay versions. Statistical analysis of these assay response values generated over a certain period of time allows for comparison of analytical performance of NAT reagent lots and laboratory instruments. The trend control can also be used in multiple replicates in the same test run to ensure that TMA reagents or instruments fulfil the minimum requirements for analytical sensitivity before they are accepted for routine blood screening.

Table 2. Detection limits on native and inactivated HIV-1 standard dilution panels in Procleix Ultrio assay versions

standard	panel	NAT method	n	50% LOD (CI) cp/mL	95% LOD (CI) cp/mL
S0041 BioQ HIV-1 RNA subype B inact.	P0026	Ultrio	52	3.1 (2.4-3.9)	20.2 (13.9-33.3)
S0012 VQC-Sanquin HIV-1 RNA subtype B	P0025	Ultrio	60	1.5 (1.0-2.2)	11.2 (6.3-29.8)
	P0025	Ultrio Plus	48	1.7 (1.3-2.2)	15.1 (9.9-26.9)
	P0025	Ultrio Elite	24	2.1 (1.5-2.9)	9.0 (5.8-19.5)
WHO HIV-1 RNA 97/650#	P0022	Ultrio	40	2.6 (2.1-3.3)	11.8 (8.2-20.7)
	P0022	Ultrio Plus	288	2.4 (2.2-2.6)	13.4 (11.4-16.3)
	P0022	Ultrio Elite	229	2.2 (1.4-3.2)	17.2 (10.3-40.1)

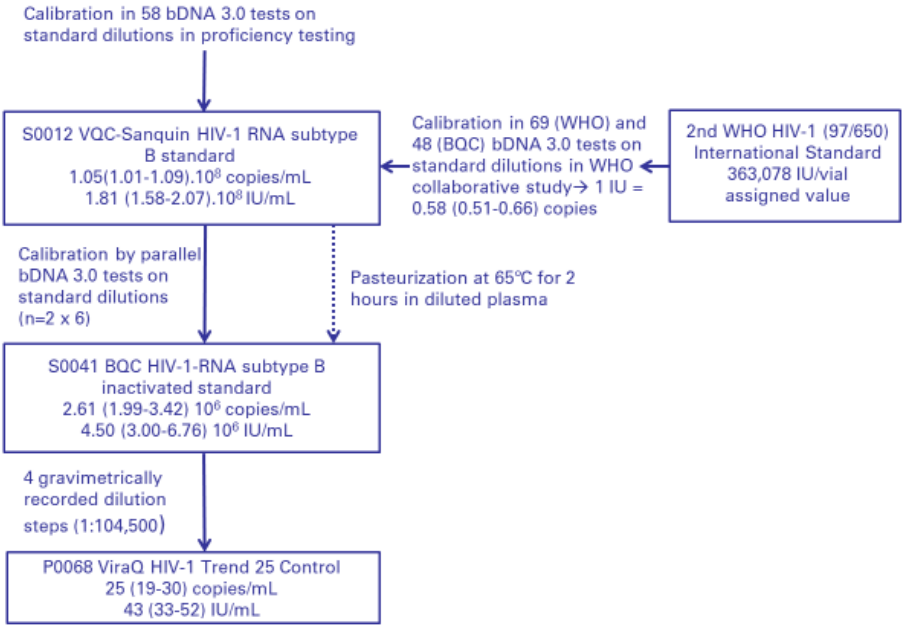
1 IU = 0.58 copy

Traceability to HIV-1 RNA copies and International Units

Figure 1 shows the traceability chain between the ViraQ trend control, the Bio Quality Control (BQC) standard, VQC-Sanquin standard and the 2nd WHO 97/650 International Standard for HIV-1 RNA. The inactivated S0041 HIV-1 RNA standard (used for preparation of the P0068 ViraQ trend control) has been calibrated in copies/mL by replicate testing in the Siemens Versant bDNA 3.0 assay[12] against the historically established S0012 VQC-Sanquin HIV-1 RNA subtype B standard[13]. The VQC-Sanquin HIV-1 RNA subtype B standard has been calibrated at 0.58 (0.51-0.66) copies per IU against the second WHO HIV-1 RNA 97/650 standard in multiple replicate bDNA 3.0 assays[14-16]. It must be emphasized that this conversion factor from copies to IU values was 0.39 (0.34-0.44) for the 1st WHO HIV-1 97/656 standard and has not been determined for the 3rd WHO 10/152 and 4th WHO16/149 replacement standards[14]. The accurate calibration of the native VQC-Sanquin and inactivated BQC HIV-1 subtype B standards in copies/mL and IU/mL has been confirmed in analytical sensitivity studies of the Grifols Procleix TMA and Roche cobas MPX assays[4,14]. The BioQControl manufacturing and quality control procedures guarantee consistent virus concentrations in consecutive ViraQ HIV-1 Trend 25 Control batches[17]. The

inactivated BQC HIV-1 subtype B standard is available in sufficient supply to ensure batch to batch consistency of ViraQ trend controls for a prolonged period of time.

Figure 1. Traceability chain between run control, BQC and VQC-Sanquin standards and WHO International Standard



Stability of HIV-1 standards and run control

The long term stability of the liquid frozen S0041 HIV-1 standard stored below -65˚C has been firmly established[18]; hence the stock solution from which the trend control is prepared has shown to be stable in the BioQControl storage facilities. Real time stability experiments using quantitative NAT assays showed less than 10% degradation of HIV-1 RNA per year in the ViraQ Check 125 and Trend 25 controls (and in standard dilutions of higher concentration) when stored at -30˚C[18]. Hence, it can be guaranteed that the trend control is still functional and should generate a reactivity rate near 95% when stored at -30˚C and used before the expiration date (two years after preparation of the run control batch)[17,18].

Kit contents (materials provided)

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

P0068/01 and P0068/02 are intended to accommodate blood screening laboratories. 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. The tube label has a barcode identifying the product, sequential batch number and marker. The barcode can be read by the automated NAT systems.

Table 3. Description of kit formats and contents

Cat. Code	UDI code	Quantity run control	Size vials	packing
P0068/01	8718719830684	60 x 1.5 mL	10 mL	60 vials in rack/box
P0068/02	8718719830288	10 x 1.5 mL	10 mL	Plastic zip bag

Materials required but not supplied

The test kits and liquid handling devices provided by the NAT manufacturer as specified in Table 1.

Storage instructions

The trend controls should be stored at or below -30°C for a maximum of two years[17]. Once thawed the run control samples should be used within 8 hours. During this period, when not in use, store sample at 2-8°C[17]. 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 P0068 ViraQ HIV-1 Trend 25 contains inactivated HIV-1 particles[6-9] 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 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[19,20].

- 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 controls 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 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 thawing remove the run control tube from the water bath.
- Vortex the run control.
- Give a short spin in a centrifuge to remove liquid before releasing screw cap from vial.
- Minimise the time period from thawing until usage of the control samples.
- Use within 8 hours after thawing
- After thawing when not in use: store at 2-8°C

Test procedure and calculations

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.

The following sections in this package insert provide guidance on interpretation and analysis of test results on P0068 ViraQ HIV-1 Trend 25. The statistical evaluation methods were developed by BioQControl and were not reviewed nor approved by the manufacturer of the Ultrio assay versions.

Qualitative detection of HIV-1 RNA in Procleix Ultrio versions

The results of the Procleix Ultrio, Ultrio Plus and Ultrio Elite assays are expressed as a sample to cut-off ratio (S/CO). P0068 ViraQ HIV-1 Trend 25 Control is expected to react positive in approximately 95% of TMA test runs or more.

Approximately 80% or more of test results on the run control are expected in the (near) saturated range of the TMA assay with S/CO values equal to or above 8.0 (range 8.0-15.0). Approximately 15% of results or less are expected in the lower dynamic range of the TMA assay with S/CO rations between 8.0 and 1.0, whereas approximately 5% or less of S/CO rations are expected to be nonreactive (see interpretation of test results below)[17]. A Levey-Jennings QC chart can be used to monitor the performance of the Ultrio assay versions on the run control.

Levey-Jennings QC chart.

The S/CO responses on ViraQ HIV-1 Trend 25 in the Ultrio Plus and Elite assay versions are not normally distributed, also not after transformation of the S/CO ratios. For developing a Levey-Jennings QC chart a distribution-free approach can be taken whereby the ranges containing 95% and 99% of the data are calculated. For this purpose the 0.5% and 99.5% percentiles are calculated for the 99% predictive interval, and the 2.5% and 97.5% percentiles for the 95% predictive interval. In case the total dataset does not contain sufficient data, values just outside the observed range can be presented in order to allow for a graphical presentation. For this non-defined distribution of S/CO ratios the median is a relevant measure, in addition to the mean. The difference between the median and the average of S/CO values is an indicator of the skewness of the distribution curve. The value of this parameter $\Delta(S/CO_{M-A})$ is expected to become higher with lower analytical sensitivity of the NAT system or lower virus concentration in the run control. It is recommended to use the Nelson rules[21] to identify deviations in the Levey Jennings trend analysis.

Interpretation of test results on trend control in Procleix Ultrio assay versions

The expected frequency of S/CO values on P0068 ViraQ HIV Trend 25 control in the below cut-off, the lower dynamic and the (near) saturated range of the TMA assay as well as the interpretation of these categories of test result are shown in table 4. The majority of S/CO values on the run control reach (near) saturated TMA response levels and are found between 8.0 and 15.0 (figure 2). Approximately 15% or less of TMA reactions on the trend control are not yet complete and have S/CO values in the lower dynamic range of the assay (between 1.0 and 8.0). In a four year observation period of 2689 Ultrio (Plus and Elite) test runs the overall proportion of reactive results was 96.0%, but the reactivity rate varied between TMA reagent lots and trend control batch combinations (table 5)[17].

Table 4. Interpretation of a single TMA test result on P0068 ViraQ HIV-1 Trend 25 in Procleix Ultrio assay versions and expected frequency of S/CO values in three ranges

Result	S/CO	Expected frequency per 1000[#]	Interpretation
Reactive (near) saturated	>8.0	795 – 867	The test signal on the trend control reaches values in the (near) saturated range of the TMA assay. This is an expected result.
Reactive lower dynamic	1.0–8.0	120 – 149	The test signal on the run control is in the lower dynamic range of the assay because the TMA reaction is not yet complete. This is an expected result.
Non-reactive	<1.0	28-42	The test signal on the run control is below the cut-off. This is an expected result

[#]95% confidence limits found in 2689 Ultrio (Plus and Elite) test runs

Table 5. Proportion of reactive results observed in daily test runs on P0068 ViraQ HIV-1 Trend 25 Control (TC) batches in consecutive Ultrio (U), Ultrio Plus (UP) and Ultrio Elite (UE) reagent lots.

TMA reagent lot	Trend Control batch	reactive/n	% reactive	delta (95%CI) % to overall %
U	TC1	180/200	90.0%	-5.5 (-6.9,-4.1)%
UP1	TC1	70/73	95.9%	0.4 (-0.6, 1.3)%
	TC1 All	250/273	91.6%	-4.0 (-2.9, -5.0)%
UP1	TC2	99/100	99.0%	3.5 (3.2,3.7)%
UP1 All		169/173	97.7%	2.2 (1.8, 2.5) %
UP2	TC3	67/67	100.0%	4,5 (4.3,4.6)%
UP3	TC3	172/179	96.1%	0.6 (0.0,1.2)%
UP4	TC3	202/204	99.0%	3.5 (3.3,3.7)%
UP5	TC3	219/228	96.1%	0.5 (0.0,1,1)%
UP6	TC3	89/89	100.0%	4.5 (4.3,4.6)%
UP7	TC3	90/91	98.9%	3.4 (3.1,3.7)%
	TC3 All	839/858	97.8%	2.3 (2.0,2.5)%
UP All		1293/1330	97.2%	1.7 (1.5,1.9)%
UE1	TC4	120/139	86.3%	-9.2 (-6.9, -11.5)%
UE2	TC4	338/355	95.2%	-0.3 (-0.8,0.2)%
UE3	TC4	67/73	91.8%	-3.8 (-5.7,-1.8)%
	TC4 All	525/567	92.6%	-2.9 (-2.6, -2.6)%
UE3	TC5	445/452	98.5%	2.9 (2.7,3.1)%
UE4	TC5	139/140	99.3%	3.8 (3.5,4.0)%
	TC5 All	584/592	98.6%	3.1 (2.9,3.3)%
UE All		1109/1159	95.7%	0.2(-0.1, 0.5)%
U, UP, UE All		2582/2689	96.0%	reference

Monitoring performance of Procleix Ultrio assay versions on trend control

Figure 2 shows Ultrio Elite performance data on P0068 ViraQ HIV-1 Trend 25 obtained during six months of testing by one national blood service in a Levey-Jennings QC Chart.

Figure 2. Levey-Jennings chart of P0068 ViraQ HIV-1 Trend 25 Control results in Grifols Ultrio Elite assay reported by one national blood organisation using four Panther instruments. The average and median (green lines) and 95% and 99% predictive intervals (orange and red lines) are calculated as described in the text.

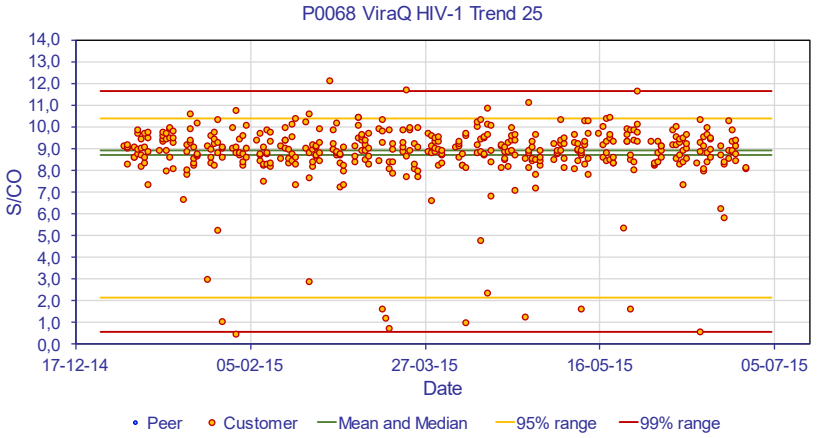


Table 6 presents the same Ultrio Elite data as presented in Figure 2 as well as a larger set of earlier obtained Ultrio Plus and Elite data presented in table 5.

Table 6. Reproducibility of Ultrio Plus and Elite S/CO values on P0068 ViraQ HIV-1 Trend 25 control

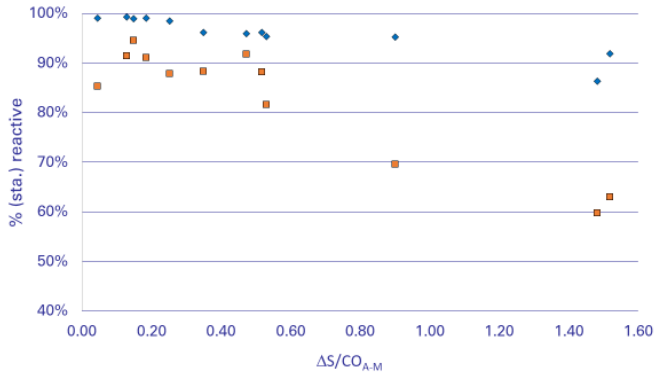
n test runs	Median S/CO	Average S/CO	$\Delta(S/CO_{M-A})$	S/CO Predictive interval	
				95%	99%
429#	8.91	8.72	0.19	2.13 – 10.40	0.57 – 11.64
2689^	8.79	8.32	0.47	0.69 – 10.59	0.11 – 12.58

#Ultrio Elite data if figure 2 ^Ultrio Plus and Elite data of table 5

The difference between the median and the average of S/CO values can be used as an indicator of the skewness of the distribution curve and analytical sensitivity of the NAT system (table 6). Based on the available results one may conclude that when $\Delta(S/CO_{M-A})$ is below 0.80 the system is properly functioning[17]. The presence of a higher proportion of non-reactive results coincides with higher values of $\Delta(S/CO_{M-A})$, thereby confirming its ability to be a trend indicator for analytical performance of the TMA assay (figure 3). An alert threshold value for this parameter that is indicative for poor NAT performance cannot be given with the available data.

The parameter $\Delta(S/CO_{M-A})$ can also be applied to compare other experimental conditions such as the TMA reagent lot, the ViraQ Trend Control batch or the testing robot (Tigris or Panther). An example using $\Delta(S/CO_{M-A})$ as performance indicator is shown in figure 3 comparing different TMA/trend control batch combinations[17]. The result shows that the values of $\Delta(S/CO_{M-A})$ for TMA/trend control reagent batch combinations correlate with the reactivity rates. Hence, if the reagent batch performance indicator $\Delta(S/CO_{M-A})$ has an outlier value it could be used as an alert signal for checking technical performance of that particular TMA reagent lot or trend control batch.

Figure 3. Correlation between $\Delta(S/CO_{M-A})$ and proportion reactive (diamonds, S/CO≥1.0) and saturated (squares, S/CO≥8.0) response levels observed with different Ultrio, Ultrio Plus and Ultrio Elite reagent batches on P0068 ViraQ HIV-1 Trend 25 control. Each point represents a TMA reagent lot/trend control batch combination.



Acceptance testing of NAT system component using trend control

P0068 ViraQ HIV-1 Trend 25 can also be used for acceptance testing of a new TMA reagent lot, a new trend control batch, a reagent transport integrity check, a (re)-installation qualification of a Panther or Tigris instrument or training of an operator. For these applications it is recommended to test 20 vials of the trend control in one Ultrio (Plus or Elite) test run. The reagent lot, instrument or operator performance is approved when at least 17/20 (85%) of tests are reactive and the median S/CO value is above 8.1 If either one of these criteria is not fulfilled it is recommended to repeat the acceptance test procedure in another test run. If in the repeat test either one of these criteria is again not fulfilled further investigation of the performance of the reagent batch or instrument is required. These acceptance criteria were established by a simulation study with sliding sets of 20 sequential results out of a data base of 2689 Ultrio Plus and Elite test runs[17]. The decision algorithm for accepting the NAT system component is summarized in table 7.

Table 7. Decision algorithm and criteria for acceptance of reagents, instruments or operators by replicate testing of 20 vials of P0068 ViraQ HIV-1 Trend 25 control in one Procleix Ultrio (Plus or Elite) assay run

Acceptance criteria		Expected frequency	Decision
reactivity rate ≥17/20 (85%)	Median S/CO ≥8.1		
OK	OK	>95%	Accept
either one of criteria not fulfilled on initial test		<5%	Repeat acceptance test protocol
either one of criteria not fulfilled on repeat test		<0.25%	Initiate root cause analysis

Limitations

- P0068 ViraQ HIV-1 Trend 25 Control cannot be used to determine the analytical or diagnostic sensitivity of NAT blood screening assays (although changes in analytical sensitivity of the NAT system can become apparent with the trend control).
- P0068 ViraQ HIV-1 Trend 25 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.
- A single nonreactive test result on P0068 ViraQ HIV-1 Trend 25 Control cannot be used to invalidate a test run. The Poisson distribution in samples with low HIV-1 concentrations cannot guarantee that the response values are reproducible. Therefore the trend control cannot be used for a decision to accept or reject a test run.
- The expected distributions of assay response values on P0068 ViraQ HIV-1 Trend 25 Control that are presented in this package insert were based on evaluation studies involving a limited number of tests and NAT reagent lots. Therefore it cannot be guaranteed that slightly different results will be found on other TMA assay versions or reagent lots.
- The parameter $\Delta(S/CO_{M\text{-}A})$ as performance indicator of Ultrio (Plus and Elite) assays and the proposed threshold value of 0.80 above which a deterioration of the test system may be possible needs to be further evaluated and confirmed in post-market performance follow up studies.
- The decision algorithm for acceptance testing of NAT system components was based on testing of a limited number of Ultrio Plus and Elite reagent lots. The validity of the acceptance criteria need to be confirmed by testing more Ultrio Plus and Elite reagent lots on the P0068 HIV-1 trend control in multiple replicates.

References

1. Grabarczyk P, van Drimmelen H, Kopacz A, Gdowska J, Liszewski G, Piotrowski D, Górska J, Kuśmierczyk J, Candotti D, Lętowska M, Lelie N, Brojer E. Head-to-head comparison of two transcription-mediated amplification assay versions for detection of hepatitis B virus, hepatitis C virus, and human immunodeficiency virus Type 1 in blood donors. Transfusion. 2013; 53:2512-2524.
2. Assal A, Barlet V, Deschaseaux M, Dupont I, Gallian P, Guitton C, Morel P, David B, and De Micco P. Comparison of the analytical and operational performance of two viral nucleic acid test blood screening systems: Procleix Tigris and cobas s 201. Transfusion 2009; 49:289-300.
3. Koppelman M, Assal A, Chudy M, Torres P, de Villaescusa RG, Reesink HW, Lelie PN, Cuypers HT. Multi-center performance evaluation of a transcription-mediated amplification assay for screening of human immunodeficiency virus-1 RNA, hepatitis C virus RNA, and hepatitis B virus DNA in blood donations. Transfusion 2005; 45:1258-66.
4. Grabarczyk P, Koppelman M, Boland F, Sauleda S, Fabra C, Cambie G, O'Riordan K, Van Drimmelen H, Vermeulen M, O'Riordan J, Lelie N. Inclusion of human immunodeficiency virus Type 2 (HIV-2) in a multiplex transcription-mediated amplification assay does not affect detection of HIV-1 and hepatitis B and C virus genotypes: a multicenter performance evaluation study. Transfusion 2015; 55:2246-55.
5. Lelie PN, Van Drimmelen AAJ. Positioning of ViraQ Check and Trend Controls compatible with analytical sensitivity of NAT assays. VR4059. www.bioqcontrol.com
6. Lelie PN. Van Drimmelen AAJ. Preparation of inactivated secondary viral standards: Safety assessment of quality control samples for viral serology and NAT assays in blood screening laboratories.CE4006. www.bioqcontrol.com
7. Lelie PN, Reesink HW, Lucas CJ. Inactivation of 12 viruses by heating steps applied during manufacture of a hepatitis B vaccine. J Med Virol. 1987;23:297-301.
8. Tersmette M, de Goede RE, Over J, de Jonge E, Radema H, Lucas CJ, Huisman HG, Miedema F. Thermal inactivation of human immunodeficiency virus in lyophilised blood products evaluated by ID50 titrations. Vox Sang. 1986;51:239-43
9. Bruzzone B, Bisio F, Caligiuri P, Mboungou FA, Nigro N, Sticchi L, Ventura A, Saladini F, Zazzi M, Icardi G, Viscoli C.Discordances with HIV-1 RNA quantitative determinations by three commercial assays in Pointe Noire, Republic of Congo. J Virol Methods. 2014;203:102-6
10. Sauné K, Delaugerre C, Raymond S, Nicot F, Boineau J, Pasquier C, Izopet J. Analytical sensitivity of three real-time PCR assays for measuring subtype B HIV-1 RNA. J Clin Virol. 2013;57:80-3.
11. Pyne MT, Wilson A, Hillyard DR. Large-scale comparison of Roche Cobas AmpliPrep/Cobas TaqMan and Abbott RealTime HIV assays. J Virol Methods. 2012 ;184:106-8.
12. Collins ML, Zayati C, Detmer JJ, Daly B, Kolberg JA, Cha TA, Irvine BD, Tucker J, Urdea MS. Preparation and characterization of RNA standards for use in quantitative branched DNA hybridization assays. Anal Biochem. 1995 20; 226:120-9.
13. Lelie PN, Van Drimmelen AAJ, Cuypers HTM, Best SJ, Stramer Hyland SL C, J.- Allain P, Moncharmont P, Defer C, Nubling CM, Glauser A, da Silva Cardoso M, -F. Viret J, Lankinen M, Grillner L, Wirthmuller U, Coste J, Schottstedt V, Masecar B. and E.M. Dax. Sensitivity of HCV-RNA and HIV-RNA blood screening assays. Transfusion. 2002,42:527-36.

14. Lelie PN, Van Drimmelen AAJ. Calibration of native and inactivated viral standards and traceability to viral nucleic acid copies and International Units. VR4060, www.bioqcontrol.com
15. Holmes H, Davis C, Heath A, Hewlett I and Lelie PN. An international collaborative study to establish the 1st International Standard for HIV-1-RNA for use in Nucleic Acid-Based Techniques. J. Virol. Methods 2001, 92: 141-150
16. C. Davis, A. Heath, S. Best, I. Hewlett, N. Lelie, R. Schuurman, H. Holmes Calibration of HIV-1 working reagents for nucleic acid amplification techniques against the 1st international standard for HIV-1 RNA. J of Virol Methods 2003;107:37-44.
17. Van Drimmelen AAJ, Lelie PN. Performance evaluation of ViraQ run controls for HBV, HCV and HIV-1 detection in different NAT assays. VR4061. www.bioqcontrol.com
18. Van Drimmelen AAJ, Lelie PN. Stability of ViraQ run controls for NAT. VR4058. www.bioqcontrol.com
19. Centers for Disease Control (CDC). Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other blood borne pathogens in health-care settings. MMWR 1988; 37:377-388.
20. Centers for Disease Control (CDC). Guidelines for prevention of transmission of human immunodeficiency virus and hepatitis B virus to health-care and public-safety workers. MMWR 1989; 38(S-6): 1-36.
21. Nelson LS, "The Shewhart Control Chart—Tests for Special Causes". Journal of Quality Technology 1984;16, no. 4: 238-239 https://doi.org/10.1080/00224065.1984.11978921

Biologicals Quality Control B.V.
De Droogmakerij 31h
1851 LX, Heiloo
The Netherlands

Tel : +31 72 2020 730
E-mail: info@bioQControl.com
Internet: www.bioQControl.com

KI4064
V6.1 May 2022