P0065
ViraQ HBV Check 125

CE
0483

IVD

REF P0065

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

P0065 ViraQ HBV Check 125 is intended to be used as external run control for detection of hepatitis B virus (HBV)-DNA by the nucleic acid amplification technology (NAT) assays on the platform defined in Table 1. P0065 ViraQ HBV Check 125 is a heat-inactivated HBV-DNA standard in plasma at a concentration of 125 copies/mL giving near 100% reactive results in the Procleix Ultrio 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 and consistent performance of the multiplex HBV/HCV/HIV transcription mediated amplification (TMA) assays. P0065 ViraQ HBV 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 P0065 ViraQ HBV Check 125 run control

Assay (manufacturer)	Platform	Test environment
Procleix® Ultrio Elite (Grifols)	Procleix® Panther®	Blood screening
Procleix® UltrioPlex E (Grifols)		

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

P0065 ViraQ HBV Check 125 control has been formulated to mimic natural plasma specimens with a low HBV-DNA 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 HBV-DNA (equivalent to 23 IU/mL) and has been designed to ensure sufficient analytical sensitivity of TMA tests in blood screening laboratories. The HBV-DNA concentration in the run control has been set

at approximately 4 times the 95% lower limit of detection (LOD) of the Ultrio, Ultrio Plus, Ultrio Elite and UltrioPlex E assays (Table 2)[1-6]. The positioning of P0065 ViraQ HBV Check 125 control ensures reactivity rates ≥ 99.5% in the NAT systems listed in Table 1. The run control enables laboratories to be alerted in case of a significant reduction of analytical sensitivity of NAT test systems. The run control is a dilution of the S0043 HBV-DNA genotype A2 standard, prepared by heat-inactivation of a pool of HBV positive plasma units from the same donor[7-9]. 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 S0043 HBV standard has been calibrated in copies/mL and IU/mL against the Viral Quality Control (VQC)-Sanquin, Eurohep and World Health Organization (WHO) International Standards (Figure 1). The low concentration of HBV genotype A in the run control is representative for HBV genotypes A to H that are prevalent in different geographical regions of the world (and that are detected with similar analytical sensitivity by the above mentioned commercial NAT assays)[1-6,10]. A positive result on the run control indicates that the NAT method has been performed with sufficient analytical sensitivity. A non-reactive 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 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 allows for comparison of analytical performance of NAT reagent lots and laboratory instruments. For this purpose, users of the Procleix assays in combination with the P0065 ViraQ HBV Check 125 Control can generate a statistical report for post-market performance follow-up[11] using the DataQ Analytics system accessible via the website www.bioqcontrol.com.

Table 2. Detection limits on native and inactivated HBV standard dilution panels in Procleix Ultrio assay versions calculated by an alternative link function instead of probit analysis for a better fit of the dose response curve.

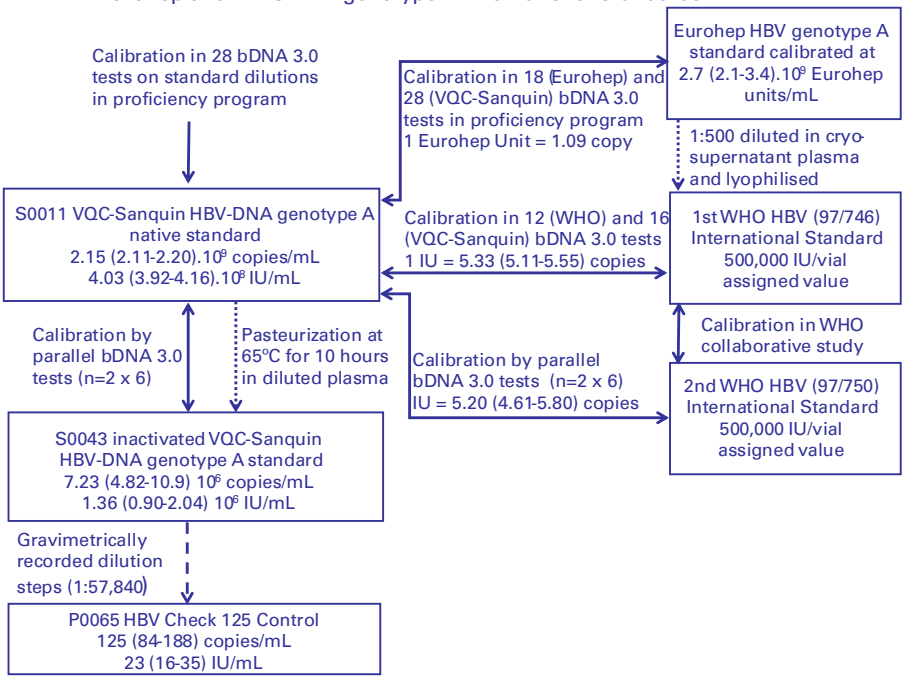
standard	BQC panel	NAT method	n	50% LOD (CI) copies/mL	95% LOD (CI) copies /mL
S0043 BioQ HBV-DNA genotype A inactivated	P0031	Ultrio Plus	24	8.4 (5.7-11.9)	38.1 (24.9-75.1)
	P0031	Ultrio Elite	25	7.2 (4.9-9.9)	30.3 (20.6-54.4)
	P0031	Ultrio Plus/Elite	49	7.8 (6.0-9.8)	33.9 (25.2-50.9)
S0011 VQC-Sanquin HBV-DNA genotype A	P0007	Ultrio Plus	48	6.1 (4.7-7.7)	25.2 (18.6-38.3)
	P0007	Ultrio Elite	74	4.4 (3.4-5.5)	28.5 (21.2-41.9)
	P0007	Ultrio Plus/Elite	122	5.0 (4.2-5.9)	27.4 (21.9-36.0)
	P0280	Ultrio Elite	48	6.6 (5.0-8.6)	38.4 (27.5-60.1)
	P0280	UltrioPlex E	98	7.4 (6.2-8.8)	36.9 (29.3-49.0)
S0010 Eurohep HBV-DNA genotype A	P0001	Ultrio Plus	96	4.7 (3.8-5.7)	28.8 (22.5-38.9)
	P0001	Ultrio Elite	24	9.6 (6.4-13.3)	38.9 (26.1-75.7)
WHO HBV-DNA 97/750#	P0023	Ultrio Plus	303	4.4 (3.3-5.9)	28.4 (18.0-57.7)
	P0023	Ultrio Elite	252	4.4 (3.6-5.4)	30.9 (22.4-47.4)

1 IU = 5.33 copies

Traceability to HBV-DNA copies and International Units

Figure 1 shows the traceability chain between the ViraQ run control, the inactivated and native VQC-Sanquin standard, the Eurohep standard and the 1st and 2nd WHO 97/746 and 97/750 International Standards for HBV-DNA. The inactivated S0043 HBV-DNA standard (used for preparation of the P0065 ViraQ run control) is derived from the S0011 VQC-Sanquin HBV-DNA genotype A standard and has been calibrated in copies/mL by replicate testing in the Siemens Versant bDNA 3.0 assay[12] against this primary standard[13]. The VQC-Sanquin HBV-DNA genotype A standard has been calibrated at 5.33 (5.11-5.55) and 5.20 (4.61-5.80) copies per IU against the first and second WHO HBV-DNA (97/746 and 97/750) standards respectively in two experiments[13]. It must be emphasized that this conversion factor from copies to IU values has not been confirmed for the later 3rd WHO 10/264 replacement standard. The copy number assigned to the VQC-Sanquin standard was found to be comparable to that of the Eurohep standard[14] used for preparation of the WHO standards[15]. The accurate calibration of the native and inactivated VQC-Sanquin standards against the WHO and Eurohep standards in IU/mL and in copies/mL has been confirmed in analytical sensitivity studies of the Grifols Procleix TMA and Roche cobas MPX assays[1-5,13]. The manufacturing and quality control procedures of BioQControl guarantee consistent virus concentrations in consecutive ViraQ HBV Check 125 batches[11,16]. The inactivated VQC-Sanquin HBV genotype 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 run control, inactivated and native VQC-Sanquin, Eurohep and WHO HBV genotype A International Standards



Stability of HBV standards and run control

The long-term stability of the liquid frozen native S0011 and inactivated S0043 HBV standard stored at ≤−65 °C has been firmly established[17]; hence the stock solution from which the run control is prepared has shown to be stable in the BioQControl storage facilities. Real time stability experiments using quantitative NAT assays showed no degradation of HBV-DNA in P0065 ViraQ HBV Check 125 control when stored at −30 °C[17]. Hence, it can be guaranteed that the run control is still functional and should generate a reactivity rate greater than 99.5% when stored at −30 °C and used before the expiration date (two years after preparation of the run control batch)[6,11,16].

Kit contents (materials provided)

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

Table 3. Description of P0065 ViraQ HBV Check 125# kit formats and contents.

Cat. Code	GTIN/UDI-DI code^	Quantity	Tube size	Sample volume	Secondary packing
P0065/01	8718719832790	60 tubes	10 mL	1.4 mL (+overfill)	Rack in box
P0065/02	8718719832028	10 tubes	10 mL	1.4 mL (+overfill)	Plastic zip bag

^ Global Trade Item Number = Unique Device Identification - Device Identifier (UDI-DI) code,
# Global Model Number (GMN) = Basic UDI-DI code for P0065 is 871871983P0065EP

P0065/01 and P0065/02 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. In addition, the label includes a barcode identifying the product, sequential batch number, and marker: HBV. The barcode of each run control tube can be read by the automated NAT systems.

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 controls 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[17]. 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[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 P0065 ViraQ HBV Check 125 contains inactivated HBV particles[7,8] the plasma may still be potentially biohazardous. 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-HBs, 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[18,19]. 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 Procleix Ultrio assays are expressed as a sample to cut-off ratio (S/CO). P0065 ViraQ HBV Check 125 Control should be reactive in more than 99.5% of TMA test runs.

The positioning of P0065 ViraQ HBV Check 125 control is near the Poisson detection endpoint range of the Procleix Ultrio assay versions but at enough distance to guarantee sufficient reproducibility of S/CO ratios. This has been demonstrated by testing dilution panels of the native S0011 HBV genotype A standard (Figure 2) and of the inactivated S0043 HBV genotype A standard used for preparation of the run control (Figure 3). At the concentration of 125 copies/mL S/CO ratios follow a non-parametric distribution.

Figure 2. Distributions of S/CO ratios on dilutions of native S0011 HBV standard dilutions in reference panel P0280 tested in 48 replicates by the UltrioPlex E assay with a 95% LOD (CI) of 36.9 (29.3-49.0) copies/mL.

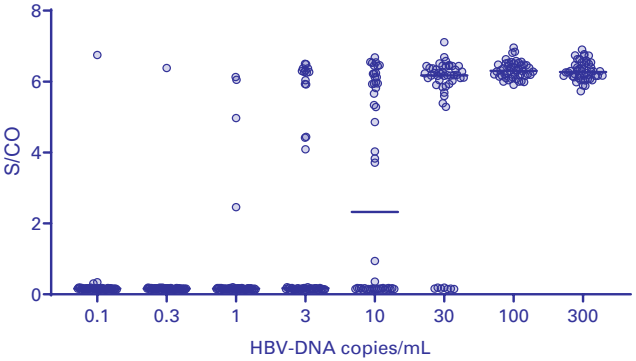
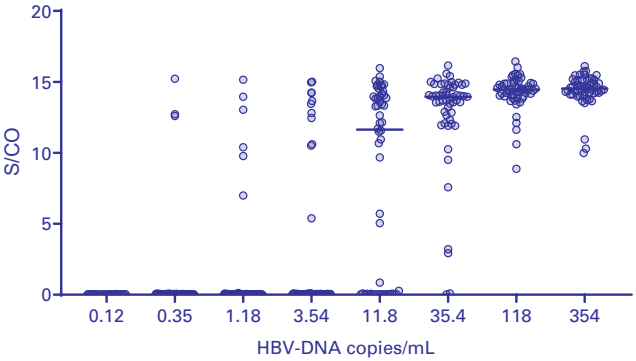


Figure 3. Distributions of S/CO ratios on dilutions of inactivated S0043 HBV standard dilutions in P0031 reference panel tested by the Ultrio Plus and Ultrio Elite assays with a 95% LOD (CI) of 33.9 (25.2-50.9) copies/mL being ~4-fold lower than the run control concentration of 125 (84-188) copies/mL.



Expected assay response values on run control

The expected results for the P0065 ViraQ HBV Check 125 Control are as follows:

Procleix Ultrio Elite assay
HBV-DNA S/CO ratios range: 9.6 – 15.7

Procleix UltrioPlex E assay
HBV-DNA S/CO ratios range: 5.5 – 8.1

Each TMA assay and reagent lot has its own distribution of response values on HBV standard dilutions and on P0065 ViraQ HBV 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. P0065 ViraQ HBV Check 125 run control serves as an independent standard for monitoring the reproducibility and the analytical sensitivity of Procleix Ultrio Elite and UltrioPlex E test runs and reagent lots in detecting HBV-DNA 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.

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 (Figures 5 and 6) 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[20] to identify deviations in the Levey-Jennings trend analysis.

The Procleix Ultrio Elite and UltrioPlex E test results on P0065 ViraQ HBV Check 125 control are expected to be reactive in 99.5-100% of cases according to alternative link analysis on the inactivated S0043 HBV genotype A standard dilutions in the P0031 reference panel. 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 HBV-DNA can be plotted in a Levey-Jennings chart using the statistical report function of the DataQ Analytics system available on www.bioqcontrol.com as shown in the charts of Figure 5 and Figure 6.

Table 8 summarizes the Levey-Jennings chart parameters in Figure 5, which were deduced from the Ultrio Elite S/CO ratios reported on six P0065 ViraQ HBV Check Control batches by five laboratories over a period of 14 months.

Table 8. Median S/CO ratios with 95% and 99% ranges as found on six batches of P0065 ViraQ HBV Check 125 Control in 5314 Ultrio Elite test runs in the period from 1-09-2023 to 6-11-2024 (data in Figure 5).

Assay	n	Median S/CO	95% range S/CO	99% range S/CO
Ultrio Elite	5314	13.61	11.81 – 14.93	9.38 – 15.54

Table 9 summarizes the Levey-Jennings chart parameters in Figure 6, which were calculated from the UltrioPlex E S/CO ratios reported on three P0065 ViraQ HBV Check Control batches by three laboratories over a period of 14 months.

Table 9. Median S/CO ratios with 95% and 99% ranges as found on three batches of P0065 ViraQ HBV Check 125 Control in 1369 UltrioPlex E test runs in the period from 5-09-2023 to 5-11-2024 (data in Figure 6).

Assay	n	Median S/CO	95% range S/CO	99% range S/CO
UltrioPlex E	1369	7.11	6.14 – 7.86	5.49 – 8.05

Figure 5. Levey-Jennings QC chart of Ultrio Elite assay S/CO ratios for HBV-DNA on six batches of P0065 ViraQ HBV Check Control.

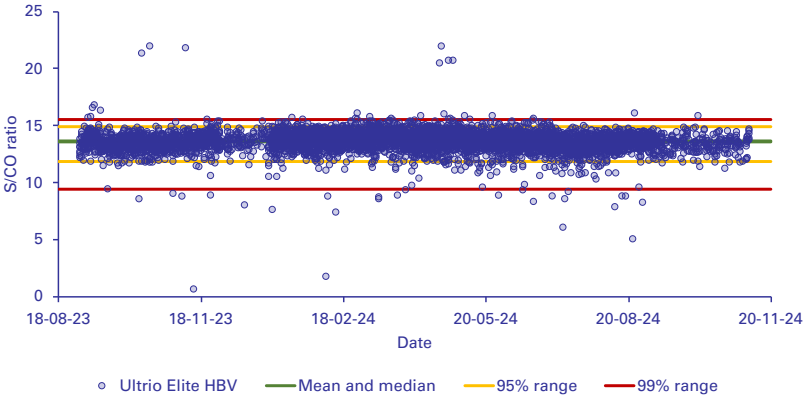
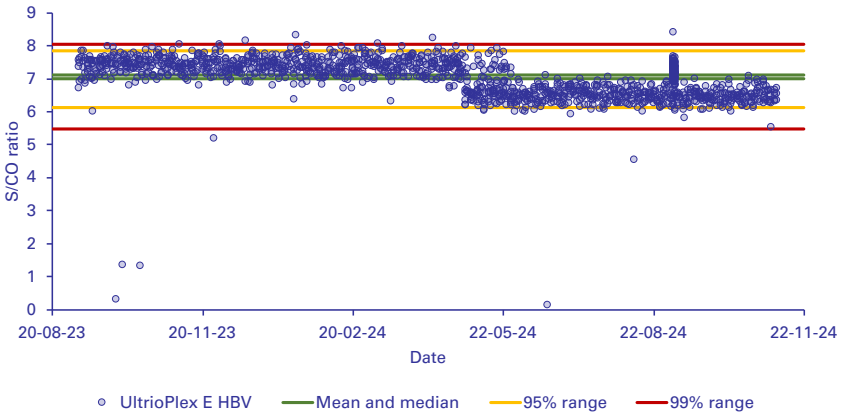


Figure 6. Levey-Jennings QC chart of UltrioPlex E assay S/CO ratios for HBV-DNA on three batches of P0065 ViraQ HBV Check Control.



Post-market performance follow-up of run control batches

One can use P0065 ViraQ HBV 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 10 and Figure 7 (Ultrio Elite), and Table 11 and Figure 8 (UltrioPlex E) compare the median S/CO ratios on P0065 ViraQ HBV batches and Procleix Ultrio reagent lots for HBV-DNA, showing no indications for changes in analytical sensitivity. The shift to lower S/CO values in Figure 6 coincided with introduction of a new UltrioPlex E reagent lot but does not have any predictive value for the analytical sensitivity of the assay.

Table 10. Comparison of Ultrio Elite S/CO on P0065 ViraQ HBV Check 125 Control batches and between consecutive Procleix Ultrio Elite reagent lots.

P0065 ViraQ batch	Ultrio Elite reagent lot	n	Median S/CO (range)	Avg. S/CO	$\Delta S/CO_{M-A}$	S/CO values < 5
B4060-009	154471	639	14.36 (8.39 - 16.63)	14.21	0.15	0 (0.00%)
	All	**639**	**14.36 (8.39 - 16.63)**	**14.21**	**0.15**	**0 (0.00%)**
B4060-010	154471	95	14.27 (11.43 - 15.75)	14.03	0.24	0 (0.00%)
	159260	598	13.42 (8.74 - 15.02)	13.23	0.19	0 (0.00%)
	171962	394	13.39 (7.62 - 17.89)	13.19	0.19	0 (0.00%)
	All	**1087**	**13.44 (7.62 - 17.89)**	**13.28**	**0.16**	**0 (0.00%)**
B4060-011	171962	238	13.49 (9.51 - 23.42)	13.53	-0.04	0 (0.00%)
	180939	670	13.93 (8.09 - 22.87)	13.89	0.04	0 (0.00%)
	186731	270	13.41 (9.46 - 15.68)	13.39	0.01	0 (0.00%)
	All	**1178**	**13.73 (8.09 - 23.42)**	**13.71**	**0.02**	**0 (0.00%)**
B4060-017	(blank)	1536	13.98 (1.61 - 21.38)	13.89	0.09	2 (0.13%)
	706108	*1*	*0.60 (0.60 - 0.60)*	*0.60*	*0.00*	*1 (100.00%)*
	All	**1537**	**13.98 (0.60 - 21.38)**	**13.89**	**0.09**	**3 (0.20%)**
B4060-018	(blank)	2851	13.85 (2.69 - 19.48)	13.77	0.08	2 (0.07%)
	All	**2851**	**13.85 (2.69 - 19.48)**	**13.77**	**0.08**	**2 (0.07%)**
B4060-020	*(blank)*	*8*	*13.95 (13.16 - 14.60)*	*13.86*	*0.08*	*0 (0.00%)*
	706348	25	13.77 (11.83 - 14.77)	13.78	-0.01	0 (0.00%)
	706570	177	13.23 (8.58 - 15.04)	13.19	0.04	0 (0.00%)
	706741	337	13.61 (8.00 - 15.37)	13.56	0.05	0 (0.00%)
	707145	156	13.65 (7.37 - 15.40)	13.56	0.09	0 (0.00%)
	707276	177	13.13 (11.04 - 14.54)	13.08	0.05	0 (0.00%)
	707306	49	13.66 (12.12 - 14.57)	13.51	0.15	0 (0.00%)
	707932	26	13.44 (12.13 - 14.47)	13.32	0.12	0 (0.00%)
	708054	108	13.30 (11.20 - 15.82)	13.24	0.06	0 (0.00%)
	708074	29	13.29 (11.79 - 14.43)	13.25	0.04	0 (0.00%)
	(blank)	676	13.48 (9.05 - 21.97)	13.51	-0.03	0 (0.00%)
	All	**1768**	**13.44 (7.37 - 21.97)**	**13.43**	**0.01**	**0 (0.00%)**
B4060-021	*(blank)*	*1*	*12.05 (12.05 - 12.05)*	*12.05*	*0.00*	*0 (0.00%)*
	707145	18	12.20 (10.96 - 13.35)	12.31	-0.11	0 (0.00%)
	707276	55	12.22 (10.62 - 14.35)	12.25	-0.03	0 (0.00%)
	(blank)	2814	13.81 (1.71 - 21.99)	13.73	0.08	1 (0.04%)
	All	**2888**	**13.79 (1.71 - 21.99)**	**13.69**	**0.10**	**1 (0.03%)**

(continued)

Table 10 *(continued)*

P0065 ViraQ batch	Ultrio Elite reagent lot	n	Median S/CO (range)	Avg. S/CO	$\Delta S/CO_{M-A}$	S/CO values < 5
B4060-022	707306	72	13.69 (11.99 - 15.29)	13.62	0.07	0 (0.00%)
	707355	52	13.55 (10.61 - 15.06)	13.32	0.22	0 (0.00%)
	707932	184	13.22 (5.01 - 14.67)	13.10	0.12	0 (0.00%)
	708054	84	13.16 (10.56 - 14.62)	13.13	0.03	0 (0.00%)
	708074	*5*	*13.53 (12.72 - 14.67)*	*13.74*	*-0.21*	*0 (0.00%)*
	(blank)	236	13.50 (7.84 - 14.57)	13.38	0.12	0 (0.00%)
	All	**633**	**13.41 (5.01 - 15.29)**	**13.29**	**0.12**	**0 (0.00%)**
B4060-023	*(blank)*	*2*	*14.49 (14.30 - 14.67)*	*14.49*	*0.00*	*0 (0.00%)*
	708054	13	13.31 (11.74 - 14.51)	13.20	0.11	0 (0.00%)
	708074	*8*	*13.67 (12.77 - 14.54)*	*13.65*	*0.01*	*0 (0.00%)*
	All	**23**	**13.41 (11.74 - 14.67)**	**13.47**	**-0.06**	**0 (0.00%)**
All	**All**	**12604**	**13.73 (0.60 - 23.42)**	**13.67**	**0.06**	**6 (0.05%)**

Figure 7. Median S/CO (and min – max range) ratios for HBV-DNA in Procleix Ultrio Elite assay reagent lots on P0065 ViraQ HBV Check 125 run control batches (data in Table 10).

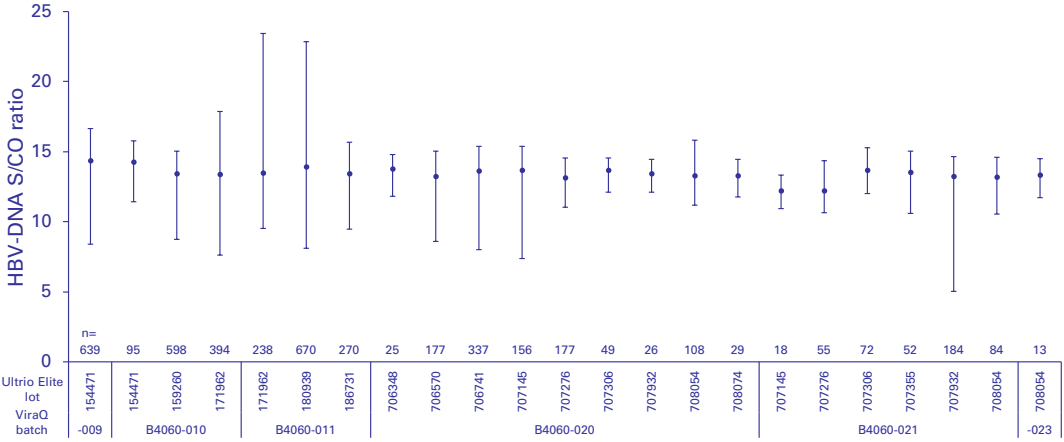


Table 11. Comparison of UltrioPlex E S/CO on P0065 ViraQ HBV Check 125 Control batches and between consecutive Procleix UltrioPlex E reagent lots.

P0065 ViraQ batch	UPxE reagent lot	n	Median S/CO (range)	Avg. S/CO	$\Delta S/CO_{M-A}$	S/CO values < 3
B4060-015	704385	21	6.85 (5.78 - 7.56)	6.84	0.01	0 (0.00%)
	All	**21**	**6.85 (5.78 - 7.56)**	**6.84**	**0.01**	**0 (0.00%)**
B4060-020	705949	635	7.43 (0.32 - 8.34)	7.38	0.05	3 (0.47%)
	707795	*1*	*6.72 (6.72 - 6.72)*	*6.72*	*0.00*	*0 (0.00%)*
	All	**636**	**7.43 (0.32 - 8.34)**	**7.38**	**0.05**	**3 (0.47%)**

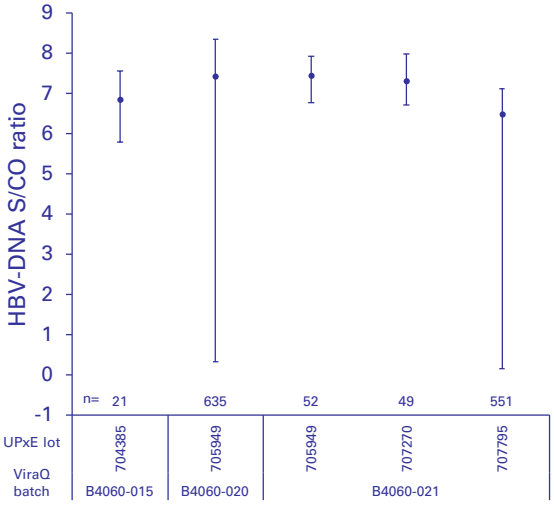
(continued)

Table 11 *(continued)*

P0065 ViraQ batch	UPxE reagent lot	n	Median S/CO (range)	Avg. S/CO	$\Delta S/CO_{M-A}$	S/CO values < 3
B4060-021	705949	52	7.45 (6.78 - 7.93)	7.42	0.03	0 (0.00%)
	707270	49	7.30 (6.71 - 7.98)	7.33	-0.03	0 (0.00%)
	707795	551	6.49 (0.15 - 7.12)	6.48	0.01	1 (0.18%)
	All	**652**	**6.54 (0.15 - 7.98)**	**6.62**	**-0.08**	**1 (0.15%)**
B4060-022	*707795*	*1*	*6.50 (6.50 - 6.50)*	*6.50*	*0.00*	0 (0.00%)
	(blank)	80	7.19 (6.41 - 8.42)	7.20	-0.02	0 (0.00%)
	All	**81**	**7.18 (6.41 - 8.42)**	**7.19**	**-0.01**	**0 (0.00%)**
All	**All**	**1390**	**7.10 (0.15 - 8.42)**	**7.00**	**0.10**	**4 (0.29%)**

The S/CO responses on P0065 ViraQ HBV Check 125 in the Procleix Ultrio Elite and UltrioPlex E assays are not normally distributed, since >98% of S/CO ratios are in the saturation range of the assays. Therefore, an increase in the number of S/CO ratios below the saturation range will increase the difference between the median and the average of S/CO values ($\Delta S/CO_{M-A}$). Hence, $\Delta S/CO_{M-A}$ is expected to become higher with lower analytical sensitivity of the NAT system and may be used for trend analysis[11,17].

Figure 8. Median S/CO (and min – max range) ratios for HBV-DNA in Procleix UltrioPlex E assay reagent lots on P0065 ViraQ HBV Check 125 run control batches (data in Table 11).



Limitations

- P0065 ViraQ HBV 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).

- P0065 ViraQ HBV 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 HBV-DNA concentrations cannot guarantee that 100% reactive results will always be found on P0065 ViraQ HBV 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 Procleix Ultrio Elite and UltrioPlex E assays on P0065 ViraQ HBV Check 125 Control that are presented in this package insert were based on performance evaluation studies involving a limited number of run control batches and NAT reagent lots. It cannot be guaranteed that slightly different results will not be found on other run control batches, assay reagent lots or laboratory instruments.
- The parameter $\Delta(S/CO_{M-A})$ is an indicator of the skewness of the distribution curve of S/CO values and may be a performance indicator for the analytical sensitivity of Ultrio assay versions and reagent lots. However, a threshold value for $\Delta(S/CO_{M-A})$ above which a deterioration of the test system is predicted cannot be given.
- It cannot be excluded that some variation exists between the performance of consecutive batches of the P0065 ViraQ HBV Check 125 control due to matrix effects or other manufacturing variables.

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Revision history

Date	Version	Description of change
December 2024	V8.0	Performance evaluation data and expected results added.
January 2026	V8.1	Figure 1 updated to align with production optimization.
July 2026	V8.2	Contact information added for reporting serious incidents in chapter “Warning and precautions”. Revision history table added. Symbol for positive control added.

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