Evaluation of external NAT controls from two manufacturers

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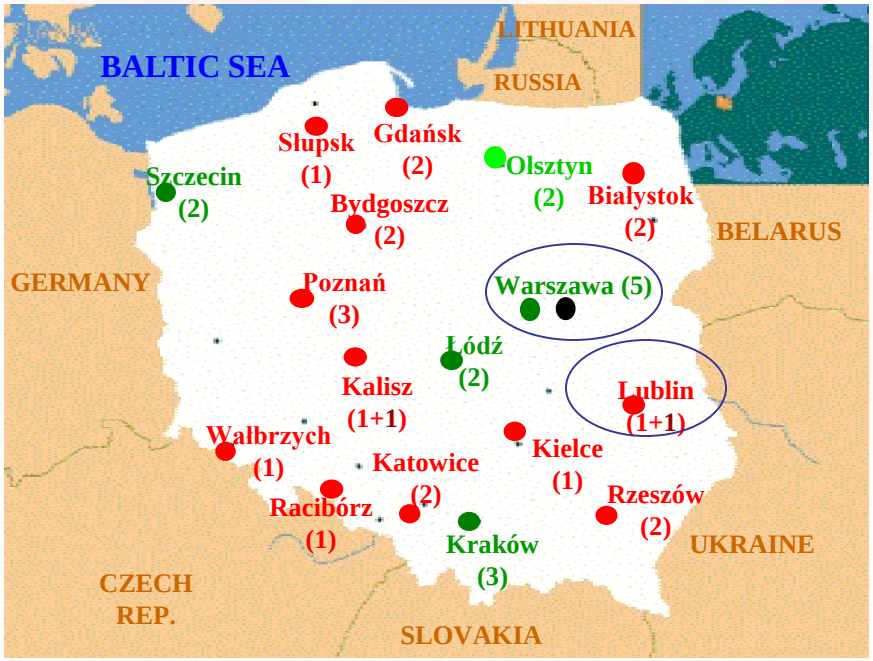
NAT and External QC in Poland (2018)

SCREENING

Regional Blood Transfusion Centers (RBTC)



Mini-pool (MP) testing

- MP 6 - cobas s201 MPX v2 (12-19)
  - cobas 6800 MPX (2-2)
- MP 4 - Ultrio Elite (1-1 Panthers)

Individual Donation Testing (IDT)

- Ultrio Elite (4-12 Panthers)

External Quality Control in each RBTC

- EDCNet : Every instrument's working-day from 2005- till now
- QC Program: 2/year

- February 2018: Evaluation of ViraQ vs QConnect Controls

Characteristics run controls#

Item	QConnect Controls	ViraQ Controls
Inactivated viral stock/standard	HBV, HCV, HIV-1 heat treated	HBV 10h 65˚C, HIV 2h 65˚C at low protein conc. HCV beta-propiolactone
Infectivity		Viral reduction assessed
Matrix	Citrate plasma (HBV-DNA, HCV RNA, HIV-1-RNA, HBsAg, a-HCV, a-HIV-1/2 nonreactive)	EDTA plasma (HBV-DNA, HCV-RNA, HIV-1/2 RNA, HBsAg, a-HBc, a-HBs, a-HCV, a-HIV-1/2 nonreactive)
Storage temp (shelf life)	-20°C (18 months)	-30°C (24 months)
Thawing	At room temperature (4 freeze-thaw cycles permitted)	At 37°C in water bath to prevent formation of cryoprecipitate
Intended use	Generic	Assay specific
Traceability to higher order standards	3rd and 4th WHO IS	1st and 2nd WHO IS for IUs$ bDNA 3.0 assay calibrators for copies$
Viral concentration	not reported	Check Controls 125 and 75 copies/mL$ Trend Controls 25 copies/mL$
Positioning to LOD of target NAT assay	not established	Check Controls at 3-6 times 95%LOD Trend Controls near 95% LOD
Expected results	not reported	Described in package insert
Statistical evaluation	Internet data exchange (EDC-net), real time analysis, reports: Levey-Jennings, Mean/Scatter (graphical or tabular)	Described in package insert. e-system not yet available

 # review package inserts, CE files

$ 1IU = 5.33 HBV, 2.73 HCV and 0.58 HIV-1 copies

QConnect and BioQControls testing in parallel

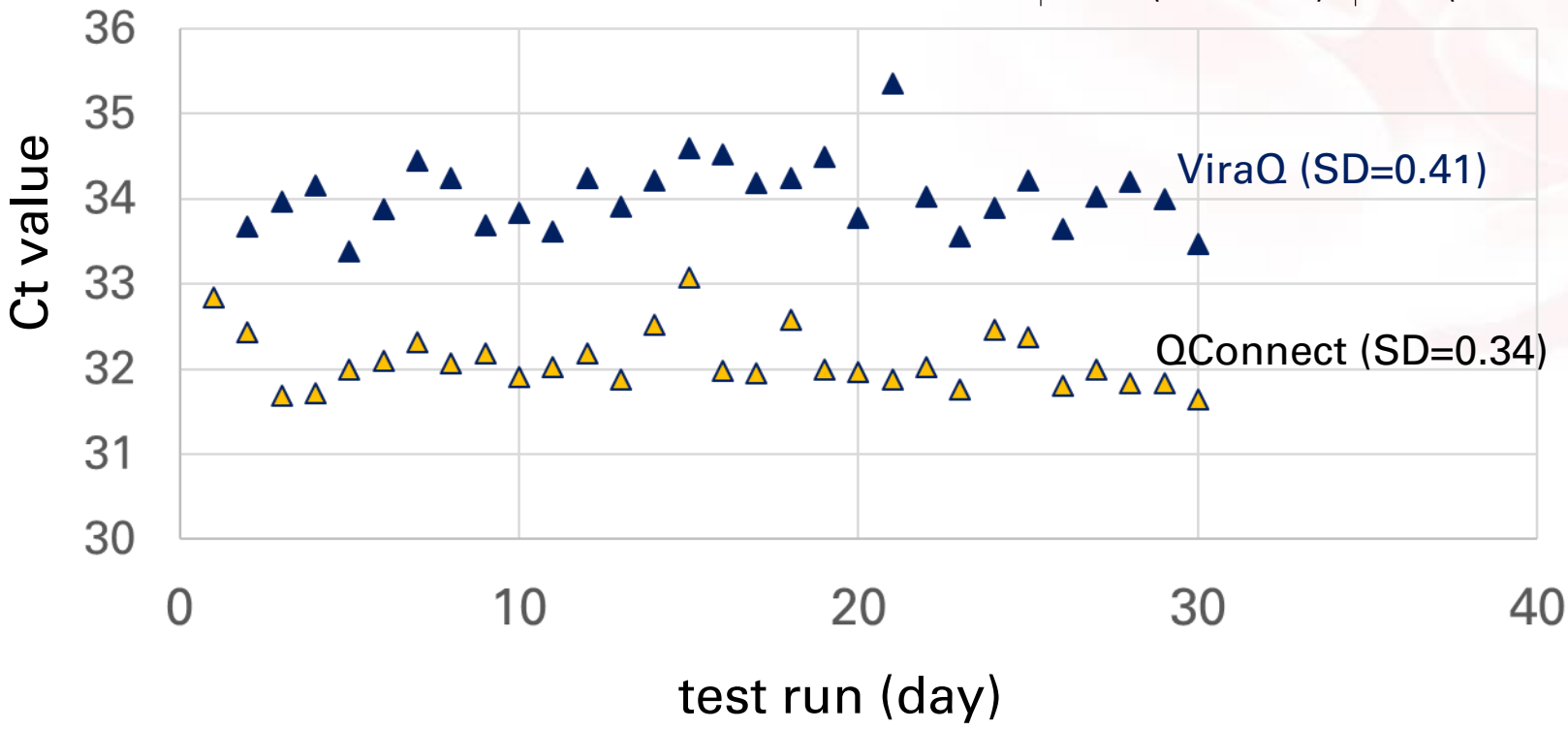
NAT Assay	Platform	Markers	Test runs	QConnect Controls	ViraQ Controls
Ultrio Elite	Panther	HBV	20	HBV DNA Low (NT 10701) HCV RNA Low (NT 10801) HIV RNA Low (NT 11001)	P0065 HBV Check 125
		HCV			P0063 HCV Check 125
		HIV			P0064 HIV-1 Check 125
		HBV			P0069 HBV Trend 25
		HCV			P0067 HCV Trend 25
		HIV			P0068 HIV-1 Trend 25
cobas MPX	cobas 6800	HBV/ HCV/ HIV	30	TriScreen (NT 10101)	P0273 Multi-Marker Check 75

Reactivity rates on run controls

NAT assay	Marker	QConnect	ViraQ Check 125 cp/mL	ViraQ Check 75 cp/mL	ViraQ Trend 25 cp/mL
cobas MPX	HBV-DNA	30/30 (100%)		30/30 (100%)	
	HCV-RNA	30/30 (100%)		30/30 (100%)	
	HIV-1 RNA	30/30 (100%)		30/30 (100%)	
Ultrio Elite	HBV-DNA	20/20 (100%)	20/20 (100%)		19/20 (95%)
	HCV-RNA	20/20 (100%)	20/20 (100%)		20/20 (100%)
	HIV-1 RNA	20/20 (100%)	20/20 (100%)		20/20 (100%)

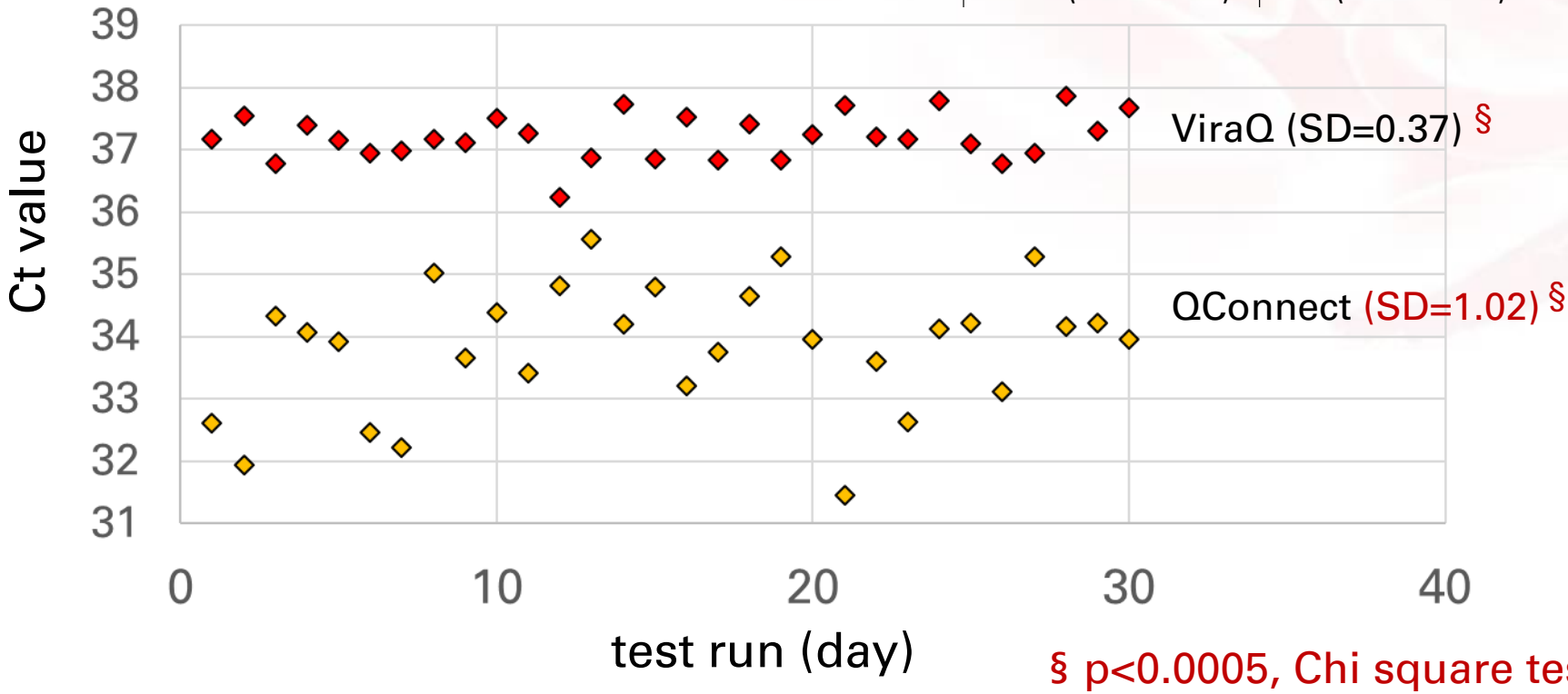
Ct values on QConnect and ViraQ Check Controls in cobas MPX for HBV-DNA

	Ct (95% CI)	cp/mL (95% CI)
QConnect Triscreen	32.1 (31.3 - 32.9)	290 (138-606)
ViraQ Multi-Marker	34.1 (33.1-34.9)	75 (reference)



Ct values on QConnect and ViraQ Check Controls in cobas MPX for HCV-RNA

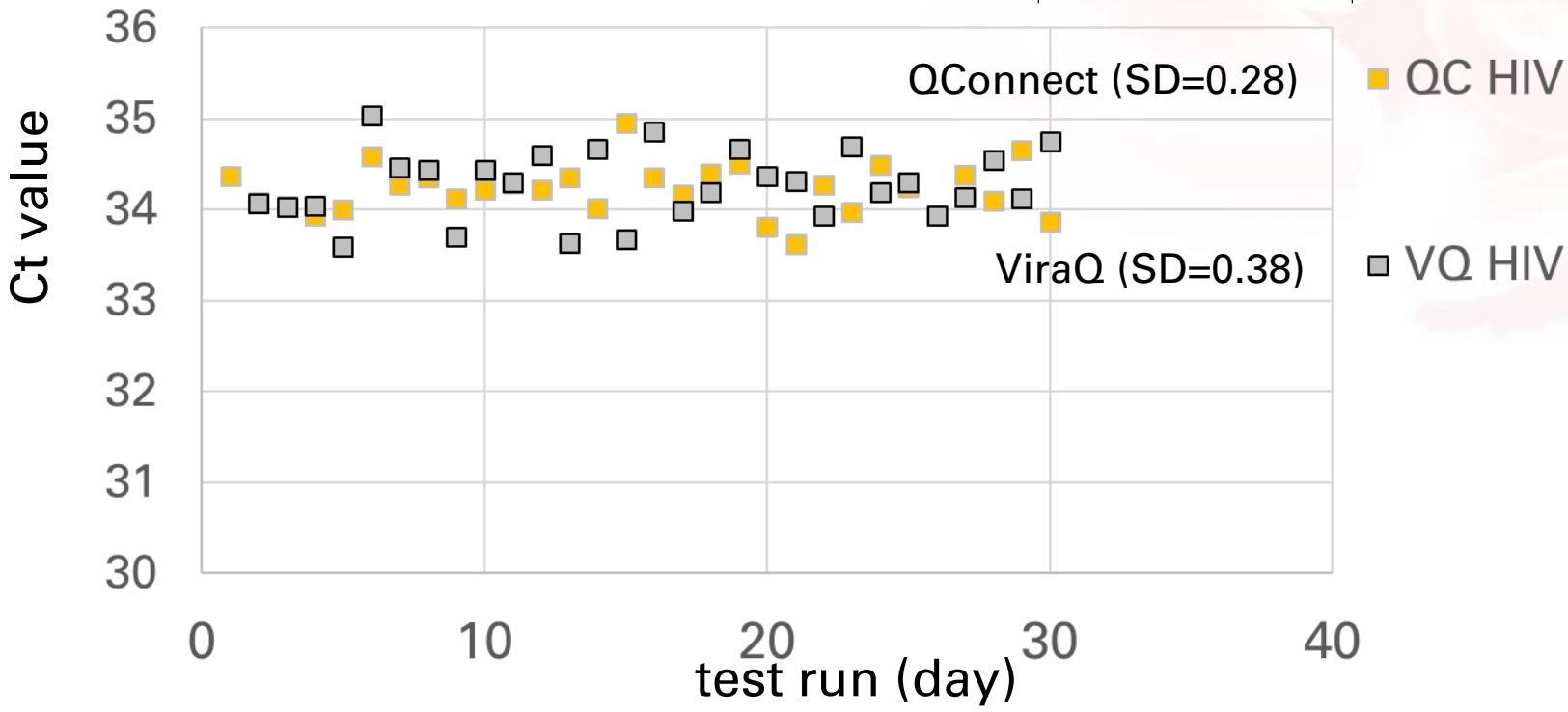
	Ct (95% CI)	cp/mL (95% CI)
QConnect Triscreen	33.8 (31.4 - 34.6)	776 (172 -3512)
ViraQ Multi-Marker	37.2 (36.3-38.0)	75 (reference)#



§ p<0.0005, Chi square test

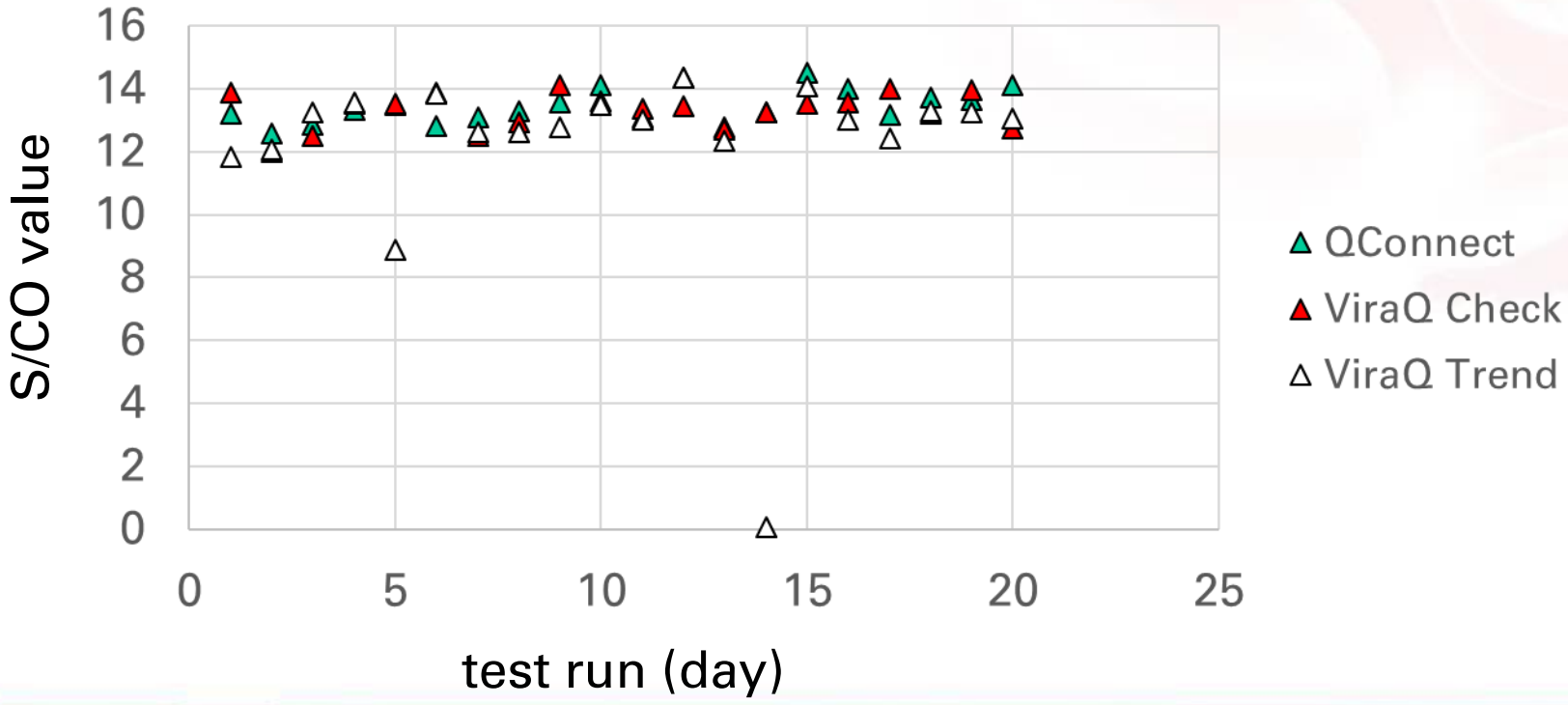
Ct values on QConnect and ViraQ Check Controls in cobas MPX for HIV-1 RNA

	Ct (95% CI)	cp/mL (95% CI)
QConnect Triscreen	34.2 (33.6 - 35.0)	77 (40 - 148)
ViraQ Multi-Marker	34.3 (33.4 - 35.1)	75 (reference)



S/CO values on QConnect and ViraQ Controls in Ultrio Elite for HBV-DNA

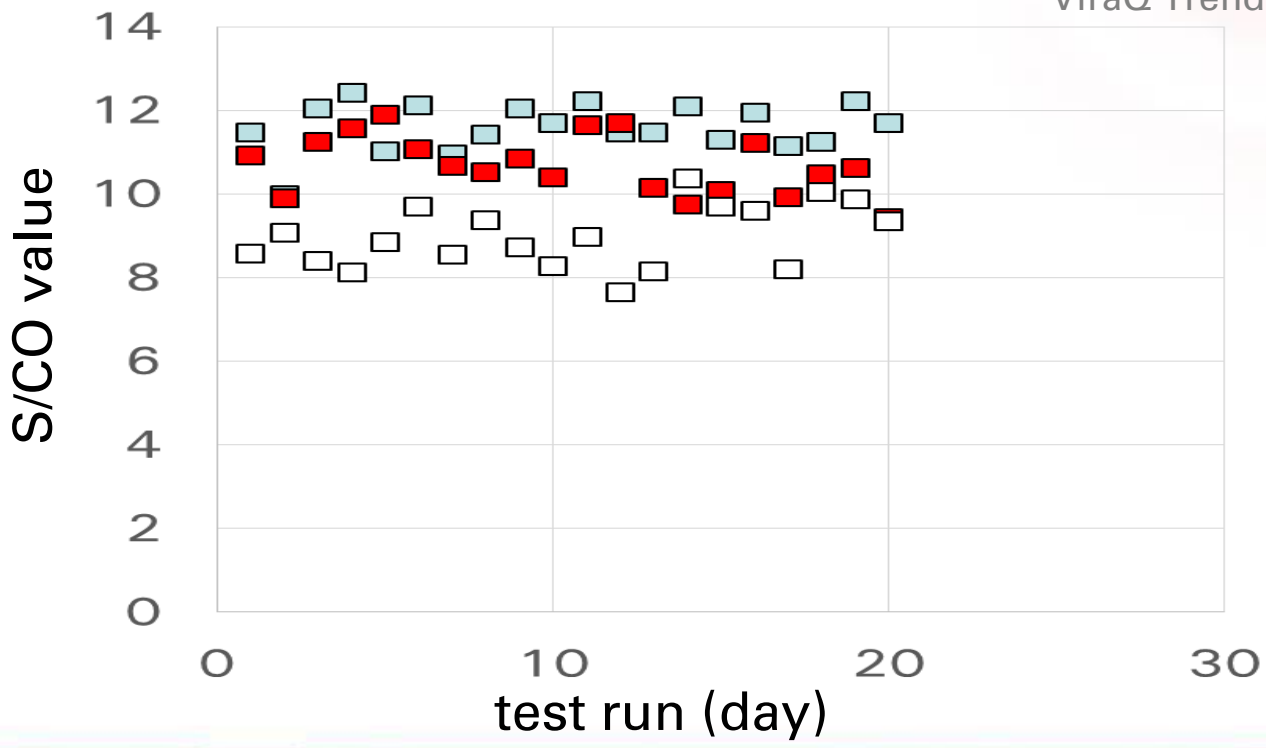
	median	average	delta
QConnect	13.31	13.45	-0.15
ViraQ Check	13.49	13.32	0.17
ViraQ Trend	13.03	12.15	0.88



S/CO values on QConnect and ViraQ Controls in Ultrio Elite for HIV-1 RNA

	median	average	delta
QConnect	11.60	11.61§	-0.01
ViraQ Check	10.66	10.71§	-0.06
ViraQ Trend	8.93	8.99	-0.06

§ p<0.00001, t-test



Conclusions

- HBV and HCV concentration in QConnect TriScreen Control is 3.9 and 10.3 fold higher ($p<0.05$) than in ViraQ Multi-Marker Control according to Ct quantification in cobas MPX assay, while HIV concentrations were comparable.
- Standard deviation of HCV Ct values in cobas MPX assay on QConnect TriScreen Control is 3-fold higher ($p<0,0005$) than on ViraQ Multi-Marker Control
- Viral concentration in single marker QConnect Controls seems higher than in ViraQ Check Controls in Ultrio Elite according to:
  - higher average S/CO values for HIV and HCV ($p<0,0005$)
  - higher value of Δ $S/CO_{(median - average)}$ for HBV
- ViraQ Check and Trend Controls have viral concentrations at a known distance to the 95% LOD of the target NAT methods whereas this is unknown for QConnect Controls

Discussion

- According to the manufacurer's instructions the positioning of ViraQ Controls and the statistical parameters allow for being alerted when a significant reduction in analytical sensitivity of the NAT systems occurs.
- The Qconnect Controls are used in conjunction with internet based software for real time analysis and statistical reports, but this is not yet available for ViraQ Controls..
- QConnect Controls are CE marked while ViraQ Controls are not.

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