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A comparison of Sigma metrics for three IVD manufacturers

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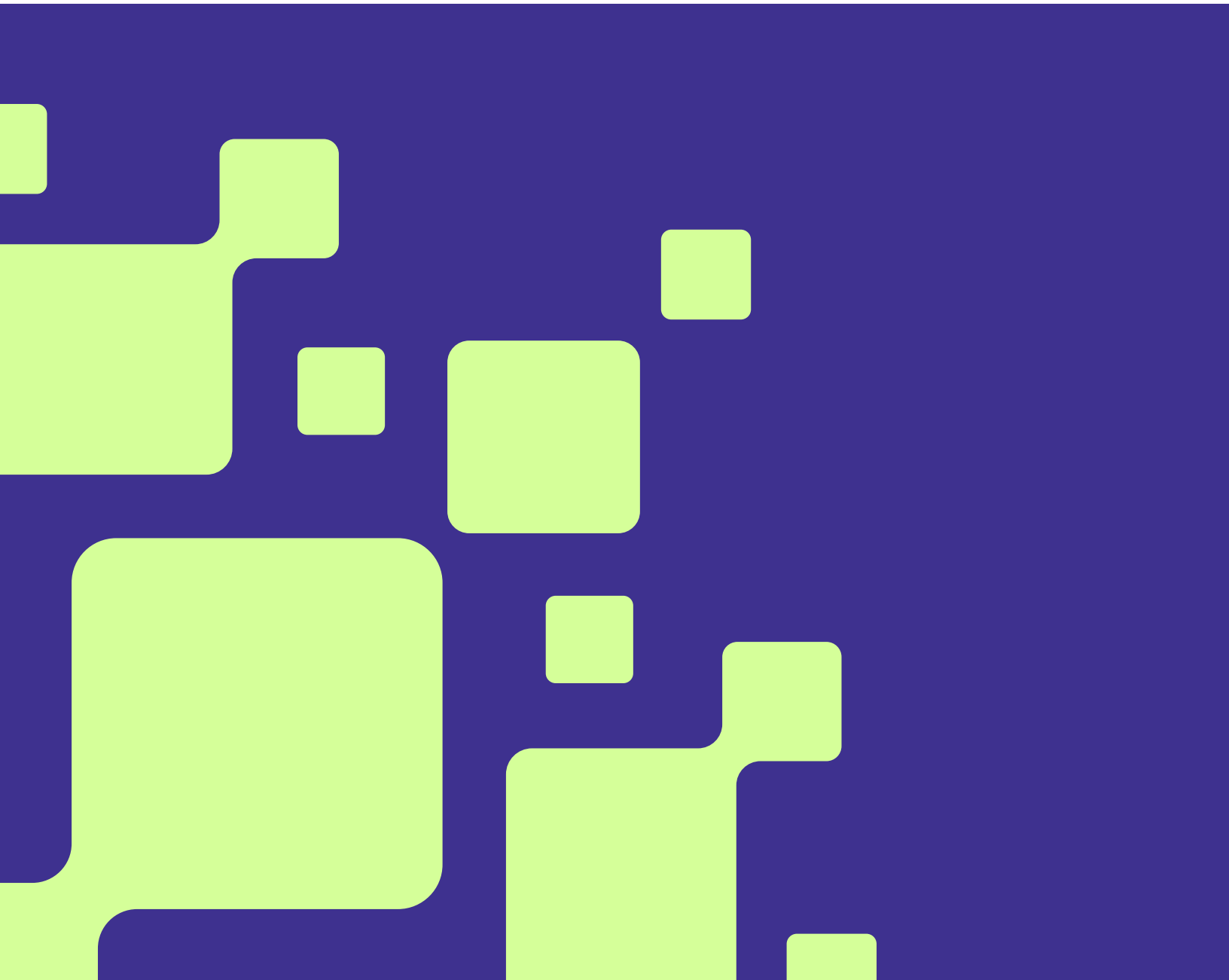

A comparison of Sigma metrics for three IVD manufacturers

Introduction

Sigma metrics are a useful way to measure quality and they have been adapted for the clinical laboratory to incorporate observed accuracy, precision, and total error allowed (TEa) into a single metric.[1] Sigma metrics typically run from 0 to 6. The higher the Sigma level for a process, the better performance that process has. "World-class quality" products have a level of performance of Six Sigma.[2]

The Sigma performance observed in a laboratory is a combination of many factors: the inherent performance of the reagent, the state of the analyzer, and the state of the laboratory. The state of the laboratory can include environmental conditions, along with processes such as operator interactions and material handling. Sigma metric performance can also vary across an assay's measuring range.[3]

Sigma metrics can be used for process improvement and for comparing performance across manufacturers. To assist laboratories around the world in understanding the current state of Sigma metrics across in vitro diagnostic manufacturers (IVD), a competitive comparison is demonstrated in this white paper.

Methods

The QuidelOrtho E-Connectivity® Technology system connects Vitros® systems to a secure hub where results are collated without any patient information. This rich detail led to the hypothesis that it could be possible to calculate Sigma metrics across the population of Vitros systems. Quality control (QC) data was extracted from Vitros systems around the world for each assay in the study time range (January to August 2022).

The data set included the Vitros XT 7600, Vitros XT 3400, Vitros 4600, Vitros 3600, Vitros 5600, and the Vitros 5,1 systems. A peer median was derived for each assay and QC fluid and used as the reference value for the Sigma calculation. Sigma metrics were then derived for each set of QC data from all systems, reagent lots, and calibration curves (referred to as "QC set") across the field using the following equation:

$$\%\ Bias_i = 100\% \times \left| \frac{mean_i - peer\ median}{peer\ median} \right|$$

$$\%CV_i = 100\% \times \left| \frac{SD_i}{mean_i} \right|$$

$$Sigma\ metric_i = \left| \frac{TEa - \%\ Bias_i}{\%CV_i} \right|$$

Where $mean_i$ is the average concentration for a QC set, SD_i is the standard deviation for points within a QC set, *peer median* is the median concentration across the means of all QC sets, and *TEa* is the "total error allowed" expressed as a percentage. Then, the reported Sigma metric for an assay is the median value across all systems, reagent lots and calibrations.

New CLIA TEa limits[4] are slated to be adopted in 2024 and have been used as the total error allowed when available. If CLIA 2024 values were unavailable for an assay, the following other sources were used: Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP),[5,6] American Association of Bioanalysts (AAB),[7] German Society for Clinical Chemistry and Laboratory Medicine (DGKL),[8] College of American Pathologists (CAP),[7] Canadian Fix Limits (CFX),[7] Richtlinien der Bundesärztekammer (RiliBÄK)[9] and Ricos Desirable Limits.[10]

For other manufacturers, performance data was collated from previously reported studies.[8,11] The peer means, %CV (Coefficient of Variation), and % Bias reported for the competitive systems come directly from the original papers. These papers were written prior to the CLIA 2024 TEa values so the updated limits were substituted into the calculations to ensure consistency. As such, the Sigma metrics were often different from those reported in the original studies. The TEa limits used for the assessments are provided alongside results in Appendix 1 and Appendix 2. Any Sigma metric that was calculated to be greater than 6 was capped at 6. This is because an assay performing at 12 Sigma for one manufacturer is not meaningfully different from one performing at 8 Sigma since both would well exceed performance expectations relative to proficiency limits.

Popular control fluids present in the E-Connectivity database during the study time frame were examined to identify a fluid similar in concentration to use for the comparison.

Results

Vitros Systems vs Abbott Alinity ci Systems

The results of Vitros systems compared to the Abbott Alinity ci system are shown in Appendix 1. A Sigma metric was considered "Comparable" if the Vitros Sigma metric and Alinity Sigma metric were within 0.5 Sigma of each other.

A simple count for the data from Appendix 1 indicates that more assays fall into the "Vitros better" category than the "Alinity better" category, see Table 1. However, laboratorians should interpret the results in the context of their clinical needs and patient populations.

Table 1: Count of Assay-by-Assay Competitive Assessment for Vitros Systems vs Alinity Systems

Assessment	Between Vitros and Alinity
Vitros better	12
Alinity better	9
Comparable	32

Vitros Systems vs Siemens Atellica Systems

Sigma metrics were also calculated for Siemens Atellica systems, using the %CV and % Bias from a published white paper.[8] A comparison of Sigma metrics was made between Vitros systems and Atellica systems and is shown in Appendix 2.

Table 2: Summary of Assay-by-Assay Competitive Assessment for Vitros Systems vs Siemens Atellica Systems

Assessment	Between Vitros and Atellica
Vitros better	30
Atellica better	4
Comparable	65

A simple count indicates that there are over seven times more assays that fall into the "Vitros better" category than the "Atellica better" category. While this is dramatic, laboratorians should interpret the results in the context of their clinical needs and patient populations.

Additional assays were also available in the Atellica white paper and were assessed for Sigma metrics using the TEa limits indicated, as shown in Table 3.

Table 3: Sigma Metrics for Additional Siemens Assays

Siemens Description	TEa Source	TEa Limit	Level	%CV	%Bias	Sigma Metric
AAG	Ricos	TV ±16.2%	43.2	2.29	2.31	6
B2M	AAB	TV ±30% or ±0.06 mg/dL	4.88	0.82	1.67	6
Fruc	RCPQA	TV ±6% or ±15 umol/L	324	0.90	2.79	3.6
Lp_a	RCPQA	TV ±20% or ±0.06 g/L	0.475	2.11	2.15	6
Pamy	Ricos	TV ±17.7%	75	1.20	1.35	6
aTG	Ricos	TV ±27.6%	49	3.31	5.29	6
aTPO	Ricos	TV ±46.2%	898	3.40	1.69	6
BNP	AAB	TV ±20% or ±5 pg/mL	36.2	3.20	4.68	4.8
Dgtn	RiliBÄK	TV ±30%	46.7	3.40	0.45	6
DHEAS	Ricos	TV ±13.08%	13.85	3.83	5.91	1.9
SHBG	RCPQA	TV ±12% or ±6 nmol/L	18.95	3.59	12.73	5.3
tIgE	RCPQA	TV ±15% or ±15 kU/L	87.1	2.70	4.19	4.8

Competitive Sigma values were recalculated using newer/updated TEa limits to match QuidelOrtho calculations and will differ from what is reported in the source references.

Overall

The total number of assays at each level for each manufacturer is shown in Table 4. For cases where different fluids were used for the Alinity system comparison than the Atellica system comparison, the lower Sigma metric of the two is compiled for Vitros systems in Table 4.

Table 4: Number of Assays at Each Sigma Level

Sigma Level	Description[2]	Vitros	Alinity[11]	Atellica[8]
>6	World Class	66	37	63
5	Excellent	17	3	12
4	Good	8	6	13
3	Marginal	4	5	10
2	Poor	0	0	9
1	Unacceptable	0	1	3
0	Unacceptable	1	1	1
Total Assays Assessed		**96**	**53**	**111**

Discussion

Vitros systems had 83 assays (86.4%) that are 5 or 6 Sigma, compared to 40 for Abbott Alinity systems (75.5%) and 75 for Siemens Atellica systems (67.6%) as shown in Table 6. The Vitros systems results are comparable to a more comprehensive assessment of Vitros Sigma levels which found 85% of Vitros assays have 5 or 6 Sigma quality.[12] That article included assessments for additional assays such as unconjugated bilirubin, c-peptide, haptoglobin, high-sensitivity troponin, insulin, pro B-natriuretic peptide, T3 uptake and assays in the XT format which combine two reagents onto the same slide.

The median Sigma metric for each assay is reported in Appendices 1 and 2 for Vitros systems. The tables also report the median values of the calculation components – bias and precision. These values can provide a sense of whether the bias or precision component had a stronger impact on the Sigma metrics. However, it should be noted that if one uses the median bias with the median precision to re-calculate a Sigma metric, the result may be different.

This is because the median values of the calculation components are independent of the median value for the Sigma metric. The inability to re-calculate the Sigma metrics with alternative TEa limits using the values provided in Appendices 1 and 2 is a limitation of this study.

The fluids available for the comparative assessment are limited to the levels selected by control fluid manufacturers and thus may not align with the levels used in the competitive studies. In addition, an assay does not have a single "Sigma level" for its performance. Rather, Sigma metrics can vary depending on the fluid selection plus factors such as TEa. For example, Vitros Estradiol was found to have a Sigma metric of 5.2 at 356.8 pmol/L for the Alinity comparison and a higher Sigma metric of >6 at 1107.5 pmol/L for the Atellica comparison. While both represent strong quality, the exact Sigma metric presented is different. As such, discrepancies in control fluid concentration may play a role in the differences in Sigma metrics reported between Vitros systems and the other IVD companies.

Overall, the findings show that for many assays, Sigma metrics are comparable across manufacturers. However, Vitros systems had the highest number of assays ranking 5 and 6 Sigma. Vitros systems also had the fewest number of assays ranking 3 Sigma or less. The Vitros data included results from as many analyzers as were available in the E-Connectivity database, in many cases numbering in the hundreds. For the Abbott Alinity study,[11] CLSI EP09-A3 was followed which typically indicates that three instruments were used in the assessment. For the Siemens white paper,[8] a single Atellica CH or IM system was run in duplicate for two runs per day for 20 days following CLSI EP05-A3.

In addition to potentially having a more significant component of instrument-to-instrument variability, the Vitros data included variability sources such as lab-to-lab, testing on different days, and included multiple reagent lots. Thus, variables in shipping, vial-to-vial and material handling by the lab were eliminated in the competitive studies but could not be eliminated in the Vitros data. All these aspects together have the potential for the competitive studies to be more favorable due to their ability to limit process factors that would otherwise negatively affect assay quality. Such factors should be considered when examining the comparison between Vitros systems and the other IVD companies.

While a perfect comparison of Sigma metrics is difficult to obtain, this analysis represents an assay-by-assay and broad-scale assessment of assay quality compared to published results from two competitive IVD manufacturers. Vitros systems were found to have the highest number of assays ranking 5 and 6 Sigma. Vitros systems also had the fewest number of assays ranking 3 Sigma or less. This strong performance is despite several additional sources of variation present in the Vitros data.

Appendix 1: Comparison of Sigma Metrics for Vitros vs Abbott Alinity

				Vitros Data					Alinity Data					
Vitros Assay Code	Units	TEa Source	TEa Limit	# of Analyzers	Level	%CV	%Bias	Sigma Metric	Alinity Description	Level	%CV	%Bias	Sigma Metric	Comparison
ALB	g/dL	CLIA	TV ±8%	635	2.4	1.32	2.00	4.4	ALB BCG	3.01	0.92	0	6	Alinity
ALB	g/dL	CLIA	TV ±8%	635	2.4	1.32	2.00	4.4	ALB BCP	2.91	1.11	0	6	Alinity
ALKP	U/L	CLIA	TV ±20%	404	104.2	2.21	4.66	6	Alkaline Phosphatase	187.25	1.59	3.44	6	Comparable
ALT2	U/L	CLIA	TV ±15% or ±6 U/L	25	28.5	1.75	1.70	6	ALT	30.2	2.83	0.26	6	Comparable
ALTV	U/L	CLIA	TV ±5% or ±6 U/L	592	166.3	1.60	1.72	6	Activated ALT	113.47	0.93	0.77	6	Comparable
AMYL	U/L	CLIA	TV ±20%	354	84.5	3.82	3.04	4.3	AMYL	114.32	0.78	0	6	Alinity
AST	U/L	CLIA	TV ±15% or ±6 U/L	257	45.2	2.07	2.57	5.9	Activated-AST	43.98	2.18	2.99	5.5	Comparable
ASTJ	U/L	CLIA	TV ±15% or ±6 U/L	19	27.3	1.83	1.65	6	AST	41.93	1.45	3.38	6	Comparable
Bc	mg/dL	AAB	TV ±20% or ±4 mg/dL	699	0.4	10.33	15.42	6	Bilirubin, Direct	0.4	3.9	1.01	6	Comparable
BhCG2	mIU/mL	CLIA	TV ±18% or ±3 mIU/mL	137	23.2	2.84	3.19	5.0	ß-hCG	24.45	5.46	0.08	3.3	Vitros
Ca	mg/dL	CLIA	TV ±1.0 mg/dL	396	11.6	1.06	1.24	6	Calcium	10.29	1	1.35	6	Comparable
CA125	U/mL	CLIA	TV ±20%	42	35.1	1.99	2.11	6	CA 125 II	39.33	4.81	5.54	3.0	Vitros
CA153	U/ml	RCPQA	TV ±3 up to 30 U/mL; 10% > 30 U/mL	24	21.5	2.29	2.89	4.5	CA 15-3	33.19	2.91	5.14	1.7	Vitros
CA19-9	U/mL	RCPQA	TV ±6 up to 40 U/mL; 15% > 40 U/mL	41	33.1	2.89	2.83	5.0	CA 19-9XR	37.22	9.1	9.62	0.7	Vitros
CHOL	mg/dL	CLIA	TV ±10%	389	146.7	1.42	1.72	5.6	Cholesterol, total	154.99	0.96	1.27	6	Comparable
CK	U/L	CLIA	TV ±20%	398	189.8	3.12	4.03	5.2	Creatinine Kinase	148.21	1.07	1.81	6	Alinity
Cl-	mmol/L	CLIA	TV ±5%	404	107.5	0.91	1.08	4.2	ICT Chloride	94.65	0.75	0.06	6	Alinity
Cort	nmol/L	CLIA	TV ±20%	43	589.9	2.39	2.26	6	Cortisol	417.4	2.66	1.06	6	Comparable
CREA	mg/dL	CLIA	TV ±0.2 mg/dL or ±10%	674	1.0	1.73	1.91	6	Creatinine - enzymatic	1.94	0.97	0.86	6	Comparable
CREA	mg/dL	CLIA	TV ±0.2 mg/dL or ±10%	674	1.0	1.73	1.91	6	Creatinine	2	1.88	1.94	4.3	Vitros
DGXN	ng/mL	CLIA	TV ±15% or ±0.2 ng/mL	95	1.2	3.27	3.19	4.1	Digoxin	1.39	1.39	9.93	3.6	Comparable
dHDL	mg/dL	CLIA	TV ±20% TV or ±6 mg/dL	373	49.5	2.29	2.67	6	HDL, Ultra	51.77	2.14	0.93	6	Comparable
dLDL	mg/dL	CLIA	TV ±20%	148	90.1	2.47	3.48	6	Direct LDL	78.44	1.6	1.24	6	Comparable
E2	pmol/L	CLIA	TV ±30%	55	356.8	4.60	5.38	5.2	Estradiol	688.4	2.6	9.77	6	Alinity
ECO2	mmol/L	CLIA	TV ±20%	262	26.6	3.35	2.54	5.1	CO2	22.34	3.91	3.1	4.3	Vitros
Fe	ug/dL	CLIA	TV ±15%	375	212.3	2.06	1.96	6	Iron	103.03	1.17	3.13	6	Comparable
fPSA	ng/mL	RCPQA	TV ±0.2 up to 1.4 ng/mL; 15% > 1.4 ng/mL	30	0.2	2.38	7.73	6	Free PSA	0.39	4.46	7.36	6	Comparable
FT3	pmol/L	AAB	TV ±2.3 pmol/L or ±30%	97	5.8	4.56	5.86	6	Free T3	9.45	3.71	5.43	6	Comparable
FT4	pmol/L	CLIA	TV ±3.86 pmol/L or ±15%	199	18.0	2.39	3.60	6	Free T4	14.93	1.97	4.26	6	Comparable
GGT	U/L	CLIA	TV ±5 U/L or ±15%	499	66.9	1.33	1.34	6	GGT	71.42	1.23	2.82	6	Comparable
GLU	mg/dL	CLIA	TV ±6 mg/dL or ±8%	407	90.5	1.13	1.67	5.3	Glucose	126.86	1.12	0.22	6	Alinity
hsCRP	mg/L	CLIA	TV ±1 mg/L or ±30%	21	6.1	1.43	2.06	6	CRP vario WR	4.03	3.09	1.91	6	Comparable
K+	mmol/L	CLIA	TV ±0.3 mmol/L	675	3.0	1.01	1.02	6	ICT Potassium	2.78	1.46	0.56	6	Comparable
LAC	mmol/L	RCPQA	TV ±0.5 up to 4.0 mmol/L; 12% > 4 mmol/L	89	1.0	1.28	1.24	6	Lactic Acid (plasma)	0.92	2.12	1.59	6	Comparable
LDH	U/L	CLIA	TV ±15%	583	178.0	2.04	1.80	6	LDH	127.98	3.39	1.35	4.0	Vitros
Li	mmol/L	CLIA	TV ±15% or ±0.3 mmol/L	37	1.6	2.74	2.05	6	Lithium	1.37	1.78	0.52	6	Comparable

Competitive Sigma values were recalculated using newer/updated TEa limits to match QuidelOrtho calculations and will differ from what is reported in the source references.

Appendix 1 (continued): Comparison of Sigma Metrics for Vitros vs Abbott Alinity

				Vitros Data					Alinity Data					
Vitros Assay Code	Units	TEa Source	TEa Limit	# of Analyzers	Level	%CV	%Bias	Sigma Metric	Alinity Description	Level	%CV	%Bias	Sigma Metric	Comparison
mALB	mg/dL	AAB	TV ±25% or ±1 mg/dL	114	1.7	3.26	2.80	6	Microalbumin (urine)	3.2	4.58	2.74	6	Comparable
Mg	mg/dL	CLIA	TV ±15%	338	1.9	1.91	2.46	6	Magnesium	2.22	1.43	0.01	6	Comparable
Na+	mmol/L	CLIA	TV ±4 mmol/L	686	117.8	0.70	0.81	3.5	ICT Sodium	112.03	0.82	0.1	4.2	Alinity
PHOS	mg/dL	CLIA	TV ±0.3 mg/dL or 10%	608	3.5	1.13	2.09	6	Phosphorous	4.24	1.83	0.05	5.4	Vitros
PHYT	ug/mL	CLIA	TV ±15% or ±2 ug/mL	41	12.9	2.62	2.81	4.5	Phenytoin	13.85	4.24	0.35	3.5	Vitros
Prol	mIU/L	CLIA	TV ±20%	61	841.6	1.77	2.90	6	Prolactin	824.47	2.79	4.81	5.4	Vitros
SALI	mg/dL	CLIA	TV ±15% or ±0.2 mg/dL	73	32.8	1.60	1.97	6	Salicylate	39.75	1	1.1	6	Comparable
TBIL	mg/dL	CLIA	TV ±20% or 0.4 mg/dL	672	1.4	3.97	4.23	6	Bilirubin, Total	2.78	2	1.76	6	Comparable
TP	g/dL	CLIA	TV ±8%	453	6.8	1.12	1.42	5.6	Protein, Total	5.09	1.23	0.56	6	Comparable
TRFRN	mg/dL	CAP	TV ±20%	31	378.0	3.00	2.83	5.7	Transferrin	362.43	1.29	1.88	6	Comparable
TRIG	mg/dL	CLIA	TV ±15%	606	122.7	1.27	1.59	6	Triglycerides	150.79	0.87	1.07	6	Comparable
TSH	mIU/L	CLIA	TV ±20% or ±0.2 mIU/L	164	0.6	2.63	3.08	6	TSH	0.31	1.77	4.48	6	Comparable
TT4	nmol/L	CLIA	TV ±20% or ±12.87 nmol/L	94	119.6	2.34	2.11	6	Total T4	53.8	4.52	1.96	4.9	Vitros
tVitD	ng/mL	RCPQA	TV ±9 up to 60 nmol/L; 15% > 60 nmol/L	72	20.9	9.50	10.53	0.7	25-OH Vitamin D	21.14	3.48	5.08	3.4	Alinity
UREA	mg/dL	CLIA	TV ±2 mg/dL or ±9%	590	53.8	1.20	1.25	6	Urea Nitrogen	38.82	1.84	1.19	4.2	Vitros
URIC	mg/dL	CLIA	TV ±10%	396	4.0	1.18	1.62	6	Uric Acid	2.49	1.01	1.23	6	Comparable
VANC	ug/mL	CLIA	TV ±15% or ±2 ug/mL	128	5.9	3.42	4.08	6	Vancomycin	0.346	1.08	5.2	6	Comparable

Competitive Sigma values were recalculated using newer/updated TEa limits to match QuidelOrtho calculations and will differ from what is reported in the source references.

Appendix 2: Comparison of Sigma Metrics for Vitros vs Siemens Atellica

				Vitros Data					Atellica Data					
Vitros Assay Code	Units	TEa Source	TEa Limit	# of Analyzers	Level	%CV	%Bias	Sigma Metric	Atellica Description	Level	%CV	%Bias	Sigma Metric	Comparison
A1C1	% NGSP	CLIA	TV ±8%	20	7.0	1.87	1.38	3.0	A1c_3	5.7	1.93	2.23	3.0	Comparable
AAT	mg/dL	CLIA	TV ±20%	7	174.1	1.90	3.91	6	AAT	352	1.80	2.21	6	Comparable
ACET	ug/mL	CLIA	TV ±15% or ±3 ug/mL	83	87.8	0.86	0.79	6	Acet	89.92	1.50	4.42	6	Comparable
AFP	IU/mL	CLIA	TV ±20%	10	25.8	2.18	1.71	6	AFP	35.1	4.90	4.20	3.2	Vitros
ALB	g/dL	CLIA	TV ±8%	635	2.4	1.32	2.00	4.4	Alb	3.4	2.06	2.02	2.9	Vitros
ALB	g/dL	CLIA	TV ±8%	635	2.4	1.32	2.00	4.4	AlbP	2.7	1.11	0.75	6	Atellica
ALC	mg/dL	CLIA	TV ±20%	120	90.2	1.69	1.70	6	ETOH	106.6	2.90	5.75	4.9	Vitros
ALKP	U/L	CLIA	TV ±20%	683	92.7	2.24	3.18	6	ALP_2c	87	1.30	0.38	6	Comparable
ALT2	U/L	CLIA	TV ±15% or ±6 U/L	18	166.0	1.16	1.30	6	ALT	79	2.20	1.28	6	Comparable
ALTV	U/L	CLIA	TV ±15% or ±6 U/L	635	30.5	2.05	2.12	6	ALTPLc	36	2.81	1.93	5.3	Vitros
AMON	umol/L	RCPQA	TV ±5 up to 50 µmol/L; 10% > 50 µmol/L	216	197.8	2.26	2.08	3.6	Amm	115	2.60	0.73	3.6	Comparable
AMYL	U/L	CLIA	TV ±20%	497	293.9	2.15	2.18	6	Amy	134	0.90	3.24	6	Comparable
ApoA1	mg/dL	RCPQA	TV ±20 up to 200 mg/dL; 10% > 200 mg/L	4	93.1	1.57	1.51	6	APO A1	83	2.41	3.49	6	Comparable
ApoB	mg/dL	RCPQA	TV ±20 up to 200 mg/dL; 10% > 200 mg/L	8	118.4	2.05	0.81	6	APO B	158	2.53	3.95	3.4	Vitros
ASO	IU/mL	DGKL	TV ±30%	49	319.7	2.17	2.66	6	ASO_2	402.1	2.30	0.74	6	Comparable
AST	U/L	CLIA	TV ±15% or ±6 U/L	257	45.2	2.07	2.57	5.9	ASTPLc	98	1.50	4.26	6	Comparable
ASTJ	U/L	CLIA	TV ±15% or ±6 U/L	17	158.9	1.50	2.07	6	AST	116	1.70	0.30	6	Comparable
B12	pg/mL	CLIA	TV ±25% or ±30 pg/mL	112	552.6	1.86	3.87	6	VB12	486	5.60	1.42	4.2	Vitros
Bc	mg/dL	AAB	TV ±20% or ±4 mg/dL	488	3.5	2.54	3.00	6	Dbil_2	3.51	1.60	2.83	6	Comparable
BhCG2	mIU/mL	CLIA	TV ±18% or ±3 mIU/mL	137	23.2	2.84	3.19	5.0	ThCG	23.6	3.81	10.78	1.9	Vitros
C3	mg/dL	CLIA	TV ±15%	42	128.1	1.57	1.75	6	C3	158.4	1.40	0.63	6	Comparable
C4	mg/dL	CLIA	TV ±20% or ±5 mg/dL	42	49.8	2.13	2.67	6	C4	42.3	1.30	3.30	6	Comparable
Ca	mg/dL	CLIA	TV ±1.0 mg/dL	244	8.3	0.95	1.40	6	Ca	6.1	2.95	2.01	4.9	Vitros
CA125	U/mL	CLIA	TV ±20%	55	21.2	2.41	2.88	6	CA125	0.03	2.71	4.07	5.9	Comparable
CA153	U/ml	RCPQA	TV ±3 up to 30 U/mL; 10% > 30 U/mL	24	21.5	2.29	2.89	4.5	CA15_3	21.1	2.80	6.72	2.7	Vitros
CA19-9	U/mL	RCPQA	TV ±6 up to 40 U/mL; 15% > 40 U/mL	26	25.5	3.26	3.15	6	CA19_9	25.56	5.99	5.06	3.1	Vitros
CEA	ng/mL	CLIA	TV ±15% or ±1 ng/mL	33	43.4	1.50	1.66	6	CEA	53.97	2.71	1.73	4.9	Vitros
CHE	U/mL	RCPQA	TV ±0.5 up to 5 U/mL; 10% > 5 U/mL	36	7.4	1.15	3.85	6	Che	12.5	1.40	5.10	3.5	Vitros
CHOL	mg/dL	CLIA	TV ±10%	389	146.7	1.42	1.72	5.6	Chol_2	170	1.00	2.55	6	Comparable
CK	U/L	CLIA	TV ±20%	398	189.8	3.12	4.03	5.2	CK_L	198	1.10	2.60	6	Atellica
CK-MB	ng/mL	CLIA	TV ±25% or ±3 ng/mL	92	41.8	2.05	4.09	6	CKMB	63.31	2.20	3.20	6	Comparable
Cl-	mmol/L	CLIA	TV ±5%	404	107.5	0.91	1.08	4.2	Cl	102	1.00	0.00	5.0	Atellica
Cort	nmol/L	CLIA	TV ±20%	65	873.7	2.53	2.46	6	Cor	872.93	7.59	2.35	2.3	Vitros
CRBM	ug/mL	CLIA	TV ±20% or ±1 ug/mL	56	7.7	3.58	2.80	4.8	Carb	6.4	1.25	1.91	6	Atellica
CREA	mg/dL	CLIA	TV ±10% or ±0.2 mg/dL	674	1.0	1.73	1.91	6	Ecre_2	1.9	2.63	0.00	4.0	Vitros

Competitive Sigma values were recalculated using newer/updated TEa limits to match QuidelOrtho calculations and will differ from what is reported in the source references.

Appendix 2 (continued): Comparison of Sigma Metrics for Vitros vs Siemens Atellica

				Vitros Data					Atellica Data					
Vitros Assay Code	Units	TEa Source	TEa Limit	# of Analyzers	Level	%CV	%Bias	Sigma Metric	Atellica Description	Level	%CV	%Bias	Sigma Metric	Comparison
CREA	mg/dL	CLIA	TV ±10% or ±0.2 mg/dL	477	5.6	1.36	1.69	5.8	Crea_2	6.35	0.94	2.09	6	Comparable
CRP	mg/L	CLIA	TV ±30% or ±1 mg/L	168	31.7	3.56	3.90	6	CRP_2	33	1.39	5.57	6	Comparable
DGXN	ng/mL	CLIA	TV ±15% or ±0.2 ng/mL	95	1.2	3.27	3.19	4.1	Dgn	1.51	2.65	9.04	2.3	Vitros
DGXN	ng/mL	CLIA	TV ±15% or ±0.2 ng/mL	47	3.0	2.21	3.21	5.1	Dig	2.1	2.38	1.94	5.5	Comparable
dHDL	mg/dL	CLIA	TV ±20% TV or ±6 mg/dL	613	48.5	2.41	2.61	6	D_HDL	37.5	2.00	0.74	6	Comparable
dLDL	mg/dL	CLIA	TV ±20%	98	99.1	2.64	4.07	5.7	DLDL	106.6	2.90	5.75	4.9	Vitros
dTIBC	ug/dL	CLIA	TV ±20%	227	313.5	1.29	1.56	6	TIBC	369.9	0.69	0.39	6	Comparable
E2	pmol/L	CLIA	TV ±30%	69	1107.5	3.97	4.46	6	eE2	944.68	3.30	4.89	6	Comparable
ECO2	mmol/L	CLIA	TV ±20%	262	26.6	3.35	2.54	5.1	CO2_c	24.4	4.14	4.10	3.8	Vitros
Fe	ug/dL	CLIA	TV ±15%	375	212.3	2.06	1.96	6	Iron_2	157	1.10	2.35	6	Comparable
Ferr	ng/mL	CLIA	TV ±20%	195	22.4	2.37	3.60	6	Fer	41.9	4.20	1.50	4.4	Vitros
Fol	ng/mL	CLIA	TV ±30% or ±1 ng/mL	152	3.3	5.06	5.99	4.6	Fol	4.13	5.81	6.99	4.0	Vitros
fPSA	ng/mL	RCPQA	TV ±0.2 up to 1.4 ng/L; 15% > 1.4 ng/L	31	1.5	1.72	2.25	6	fPSA	3.6	2.78	9.09	2.1	Vitros
FSH	mIU/mL	CLIA	TV ±18% or ±2 mIU/mL	58	35.6	2.06	2.42	6	FSH	50.78	2.89	1.78	5.6	Comparable
FT3	pmol/L	AAB	TV ±30% or ±2.3 pmol/L	97	5.8	4.56	5.86	6	FT3	9.74	1.58	0.96	6	Comparable
FT4	pmol/L	CLIA	TV ±15% or ±3.86 pmol/L	182	23.8	2.17	3.24	5.7	FT4	25.74	2.00	0.99	6	Comparable
GENT	ug/mL	CLIA	TV ±25%	41	7.1	2.66	2.17	6	Gent	7.8	1.79	1.83	6	Comparable
GGT	U/L	CLIA	TV ±15% or ±5 U/L	499	66.9	1.33	1.34	6	GGT	81	1.51	2.75	6	Comparable
GLU	mg/dL	CLIA	TV ±8% or ±6 mg/dL	439	289.8	1.03	1.29	6	GluH_3	292	1.10	2.51	5.0	Vitros
GLU	mg/dL	CLIA	TV ±8% or ±6 mg/dL	439	289.8	1.03	1.29	6	GluO	261	2.00	2.22	2.9	Vitros
HCY 2	umol/L	RCPQA	TV ±1.5 up to 15 umol/L; 10% > 15 umol/L	23	23.8	1.38	1.18	6	HCY	26.38	2.50	6.05	1.6	Vitros
hsCRP	mg/L	CLIA	TV ±30% or ±1 mg/L	53	1.8	1.41	2.66	6	hsCRP	1.52	1.97	2.70	6	Comparable
IgA	mg/dL	CLIA	TV ±20%	47	357.2	2.76	2.31	6	IgA_2	266.8	0.70	3.35	6	Comparable
IgG	mg/dL	CLIA	TV ±20%	22	772.9	2.25	2.16	6	IgG_2	1112	1.40	0.65	6	Comparable
IgM	mg/dL	CLIA	TV ±20%	23	204.8	1.83	1.21	6	IgM_2	260.5	1.30	1.90	6	Comparable
iPTH	pg/mL	CLIA	TV ±30%	69	186.6	1.97	3.69	6	PTH	240.47	2.90	1.58	6	Comparable
K+	mmol/L	CLIA	TV ±0.3 mmol/L	247	3.9	1.11	1.07	5.8	K	3.95	1.01	0.00	6	Comparable
LAC	mmol/L	RCPQA	TV ±0.5 up to 4.0 mmol/L; 12% > 4 mmol/L	88	4.2	0.81	1.06	6	Lac	112.61	4.88	0.56	2.3	Vitros
LDH	U/L	CLIA	TV ±15%	347	187.8	2.01	1.65	6	LDLP	189	1.00	0.87	6	Comparable
LH	mIU/mL	CLIA	TV ±20%	54	60.8	1.83	2.61	6	LH	63.64	2.20	8.02	5.5	Vitros
Li	mmol/L	CLIA	TV ±15% or ±0.3 mmol/L	37	1.6	2.74	2.05	6	Li	1.99	1.51	1.02	6	Comparable
LIPA	U/L	RCPQA	TV ±12 up to 60 U/L; 20% > 60 U/L	502	145.6	2.11	2.24	6	Lip	204	2.80	3.73	5.8	Comparable
mALB	mg/dL	AAB	TV ±25% or ±1 mg/dL	114	1.7	3.26	2.80	6	uALB_2	3	3.60	4.82	6	Comparable
Mg	mg/dL	CLIA	TV ±15%	570	2.0	1.85	2.22	6	Mg	2.53	1.98	2.85	6	Comparable
Myog	ng/mL	Rico	TV ±19.6%	16	105.8	2.30	2.40	6	MYO	155.95	2.90	2.35	6.0	Comparable
Na+	mmol/L	CLIA	TV ±4 mmol/L	686	117.8	0.70	0.81	3.5	Na	73.6	0.80	2.65	3.5	Comparable

Competitive Sigma values were recalculated using newer/updated TEa limits to match QuidelOrtho calculations and will differ from what is reported in the source references.

Appendix 2 (continued): Comparison of Sigma Metrics for Vitros vs Siemens Atellica

Vitros Assay Code	Units	TEa Source	TEa Limit	Vitros Data					Atellica Data					Comparison
				# of Analyzers	Level	%CV	%Bias	Sigma Metric	Atellica Description	Level	%CV	%Bias	Sigma Metric	
NBNP2	pg/mL	CLIA	TV ±30%	41	170.8	3.21	4.37	6	NTpro	173	3.10	10.67	6	Comparable
PALB	mg/dL	Rico	TV ±14.5%	55	36.7	2.16	1.74	5.9	PreAlb	40.3	1.71	4.55	5.8	Comparable
PCT	ng/mL	RCPQA	TV ±0.05 up to 0.15 ng/mL; 30% > 0.15 ng/mL	109	0.5	2.65	3.00	6	PCT	0.31	3.23	11.43	5.8	Comparable
PHBR	ug/mL	CLIA	TV ±15% or ±2 ug/mL	9	31.5	2.31	2.63	5.2	Phnb	47	1.60	7.63	4.6	Vitros
PHOS	mg/dL	CLIA	TV 10% or ±0.3 mg/dL	236	3.2	1.15	2.42	6	IP	3	2.67	3.81	2.3	Vitros
PHYT	ug/mL	CLIA	TV ±15% or ±2 ug/mL	44	21.2	2.94	3.77	3.6	Phny	19.7	2.28	6.14	3.9	Comparable
Prog	nmol/L	CLIA	TV ±25%	55	30.8	2.35	2.76	6	PRGE	17.77	4.29	1.82	5.4	Vitros
Prol	mIU/L	CLIA	TV ±20%	61	841.6	1.77	2.90	6	PRL	789.28	2.30	5.98	6	Comparable
RF	IU/mL	RCPQA	TV ±12 up to 60 IU/mL; 20% > 60 IU/L	54	38.4	1.41	1.83	6	RF	50.9	1.00	0.76	6	Comparable
SALI	mg/dL	CLIA	TV ±15% or ±0.2 mg/dL	73	32.8	1.60	1.97	6	Sal	30.9	1.39	3.74	6	Comparable
TBIL	mg/dL	CLIA	TV ±20% or 0.4 mg/dL	672	1.4	3.97	4.23	6	Tbil_2	1.5	3.33	4.17	6	Comparable
Testo	nmol/L	CLIA	TV ±30% or ±0.69 nmol/L	43	4.3	3.09	3.05	6	TSTII	2.88	2.70	0.57	6	Comparable
THEO	ug/mL	CLIA	TV ±20%	37	12.6	2.48	2.71	6	Theo	14.9	2.21	3.91	6	Comparable
TOBRA	ug/mL	CLIA	TV ±20%	20	6.5	1.44	1.63	6	Tob	5.3	1.51	2.21	6	Comparable
TP	g/dL	CLIA	TV ±8%	641	3.7	1.08	1.70	5.6	TP	0	1.00	0.50	6	Comparable
tPSA	ng/mL	CLIA	TV 20% or ±0.2 ng/mL	46	3.2	1.56	2.62	6	PSA	4.76	2.10	2.15	6	Comparable
TRFRN	mg/dL	CAP	TV ±20%	18	276.2	2.86	2.69	6	Trf	257	1.20	3.34	6	Comparable
TRIG	mg/dL	CLIA	TV ±15%	416	232.0	1.33	2.23	6	Trig	228	1.30	1.85	6	Comparable
TrpES	ng/mL	CLIA	TV 30% or ±0.9 ng/dL	129	0.2	2.75	3.18	6	TnI_UL	2.59	2.32	2.38	6	Comparable
TSH	mIU/L	CLIA	TV ±20% or ±0.2 mIU/L	141	4.8	2.13	2.22	6	TSH3UL	5.35	2.62	4.47	6	Comparable
TT3	nmol/L	CLIA	TV ±30%	85	3.3	2.46	3.85	6	T3	3.98	3.86	6.16	6	Comparable
TT4	nmol/L	CLIA	TV ±20% or ±12.87 nmol/L	94	119.6	2.34	2.11	6	T4	56.63	4.09	3.51	4.7	Vitros
tVitD	ng/mL	RCPQA	TV ±9 up to 60 nmol/L; 15% > 60 nmol/L	192	23.7	8.48	8.47	0.7	VitD	28.4	5.21	10.72	0.8	Comparable
UPRO	mg/dL	CAP	TV ±44%	234	41.9	3.11	3.70	6	Upro	54.9	1.90	0.09	6	Comparable
UREA	mg/dL	CLIA	TV ±9% or ±2 mg/dL	481	54.3	1.17	1.17	6	UN	67	1.60	1.07	5.0	Vitros
URIC	mg/dL	CLIA	TV ±10%	460	10.6	1.10	1.12	6	UA	10.6	0.57	1.05	6	Comparable
VALP	ug/mL	CLIA	TV ±20%	90	103.6	2.69	2.44	6	VPA	97.5	1.70	0.43	6	Comparable
VANC	ug/mL	CLIA	TV ±15% or ±2 ug/mL	65	28.3	2.20	1.73	5.8	Vanc	32.7	1.99	0.79	6	Comparable

Competitive Sigma values were recalculated using newer/updated TEa limits to match QuidelOrtho calculations and will differ from what is reported in the source references.

References

1. Coskun A, Unsal I, Serteser M, Inal T. Six Sigma as a Quality Management Tool: Evaluation of Performance in Laboratory Medicine Quality Management and Six Sigma. In: Coskun A, editor. *Quality Management and Six Sigma.* Rijeka (Croatia): InTechOpen. 2010:248–61.

2. Westgard S, Bayat H, Westgard JO. Analytical Sigma Metrics: A review of Six Sigma implementation tools for medical laboratories. *Biochem Med (Zagreb)*. 2018 Jun 15; 28(2):020502. doi: 10.11613/BM.2018.020502. PMID: 30022879; PMCID: PMC6039161.

3. Westgard S. *Quantitating Quality: Best Practices for Estimating the Sigma metric.* Abbott Laboratories. Document number: MS_10_38704/v1, AZ2215-3. 2016. https://static.secure.website/wscfus/4091441/uploads/MS_10_38704_Six_Sigma_Whitepaper_032111_8pgs_POSTED.pdf [Accessed 2 November 2022]

4. Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments of 1988 (CLIA) Proficiency Testing Regulations Related to Analytes and Acceptable Performance. Federal Register, United States Government National Archives. July 11, 2022. https://www.federalregister.gov/d/2022-14513

5. Royal College of Pathologists of Australasia Quality Assurance Programs. *Chemical Pathology Analytical Performance Specifications.* https://rcpaqap.com.au/resources/chemical-pathology-analytical-performance-specifications/ [Accessed 16 November 2022]

6. Royal College of Pathologists of Australasia Quality Assurance Programs. *Immunology Analytical Performance Specifications.* https://rcpaqap.com.au/immunology-aps/ [Accessed 16 November 2022]

7. Sun Diagnostics. *Recommended Total Allowable Error Limits.* http://rmbiolab.com/UpFiles/Documents/808edaad-0fb5-4412-9235-2921bf9e8b62.pdf [Accessed 16 November 2022]

8. Pierson-Perry J. Sigma Metrics for Atellica Solution Assays. Tarrytown (NY): Siemens Healthineers (Order No. 30-18-12850-02-76); 2018

9. WestgardQC. *Rilibak - German Guidelines for Quality.* www.westgard.com/rilibak.htm [Accessed 16 November 2022]

10. WestgardQC. *Desirable Biological Variation Database specifications.* https://www.westgard.com/biodatabase1.htm [Accessed 17 November 2022]

11. Westgard, S, et al. Assessing Precision, Bias and Sigma-Metrics of 53 Measurands of the Alinity Ci System. *Clinical Biochemistry.* 2017; 18: 1216-21. doi: 10.1016/j.clinbiochem.2017.09.005.

12. Miller J, Gammie A. A novel approach for automatically assessing laboratory Sigma metrics for a broad range of Vitros® Assays. PR-14234.

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