Supplemental Data Table S1. Information of traceability and calibrator uncertainty

Analyte	Reagent kit	Calibrator	Reference method	Reference material	Calibrator value	Uncertainty (expanded uncertainty; $k=2$)	Unit	Routine method
Albumin	ALBP	C.f.a.s.		ERM-DA470k/IFCC	2.82	0.0264	g/dL	BCP
ALP	ALP2	C.f.a.s.	Original formulation IFCC5 (Tietz, 1983), manual measurement		211	1.25	U/L	IFCC Gen. 2
ALT	ALT	C.f.a.s.	Original formulation IFCC5 (2002) modified, manual measurement		96.2	0.638	U/L	IFCC without pyridoxal phosphate activation
AST	AST	C.f.a.s.	Original formulation IFCC5 (2002) modified, manual measurement		105	0.859	U/L	IFCC without pyridoxal phosphate activation
HDL	HDLC4	C.f.a.s.	According to the CDC reference method ([pPrecipitation by dextran sulphate and Abell—Kendall])		65.3	1.17	mg/dL	Eenzymatic colorimetric Gen. 4
LDL	LDLC3	C.f.a.s.	According to CDC beta quantification method ([pPrecipitation by heparin-manganese (ultracentrifugation) and Abell—Kendall])		137	1.55	mg/dL	Gen. 3
Total cholesterol	CHOL2	C.f.a.s.	ID-MS		158	1.35	mg/dL	CHOD-PAP Gen. 2 stand. ID/MS
Creatinine	CREJ2	C.f.a.s.	ID-MS		4.06	0.0576	mg/dL	Jaffé rate-blanked and compensated Gen. 2 serum, plasma
Glucose	GLUC3	C.f.a.s.	ID-MS		193	1.60	mg/dL	HK
Protein	TP2	C.f.a.s.		SRM 927d	5.05	0.0269	g/dL	Biuret Gen. 2
TG	TRIGL	C.f.a.s.	ID-MS		59.5	0.700	mg/dL	GPO-PAPGlycerine phosphate oxidase peroxidase
K	ISE	ISE Standard Low/High	ISE Standard: pPrimary calibrators prepared gravimetrically from p.a. quality salts		3.00/7.00	0.0122/0.0285	mmol/L	ISE
Na	ISE	ISE Standard Low/High	ISE Standard: pPrimary calibrators prepared gravimetrically from p.a. quality salts		120/160	0.439/0.640	mmol/L	ISE
BUN	UREAL	C.f.a.s.	ID -MS		47.3	0.880	mg/dL	Urease/GLDH glutamate dehydrogenase serum, plasma

*All reagent kits and calibrators were manufactured by Roche Diagnostics (Roche, Rotkreuz, Switzerland).
Abbreviations: C.f.a.s, calibrator for automated system; IFCC, the method authorized by the International Federation of Clinical Chemistry and Laboratory Medicine; ID-MS, isotope dilution-mass spectrometry; ERM, European Reference Materials; CDC, Centers for Disease Control; ISE, ion-selective electrode; p.a., pro analysis (for analysis); ALP, alkaline phosphatase; K, potassium; Na, sodium; TG, triglyceride; BUN, blood urea nitrogen.

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Supplemental Data Table S2. Reagent lot-to-lot validation results with QC materials and patient samples for each test item

Analyte	No. of reagent lots used		%Mean difference ((new value – old value)/(old value) × 100)			%U_{rel} (k = 2)		
	No. of lot changes		1	2	3	U_{rel_sub}	U_{rel_tot}	U_{rel_tot}-U_{rel_sub}
Albumin	3	QC level 1	-0.75	0.00		2.88	2.94	0.06
		QC level 2	0.49	–1.96		2.47	2.57	0.09
		Patient	0.40	–1.20				
ALP	3	QC level 1	1.53	–2.73		4.01	4.26	0.25
		QC level 2	0.76	–2.27		3.59	4.09	0.50
		Patient	–0.30	–2.50				
ALT	2	QC level 1	3.32			8.00	8.01	0.01
		QC level 2	1.28			2.57	2.59	0.02
		Patient	1.10					
AST	3	QC level 1	2.70	–3.51		5.38	5.43	0.04
		QC level 2	1.70	3.32		2.91	2.94	0.03
		Patient	0.60	0.40				
HDL	3	QC level 1	0.46	0.95		4.17	4.66	0.49
		QC level 2	1.82	0.34		4.52	5.35	0.83
		Patient	0.70	0.40				
LDL	2	QC level 1	–2.12			4.31	4.41	0.10
		QC level 2	–2.26			3.84	3.93	0.09
		Patient	–1.30					
Total cholesterol	3	QC level 1	–1.16	–0.95		3.49	3.55	0.06
		QC level 2	0.61	–0.45		3.49	3.57	0.08
		Patient	0.90	0.20				
Creatinine	3	QC level 1	–0.08	0.55		5.81	5.85	0.03
		QC level 2	–3.67	3.29		4.33	4.35	0.01
		Patient	–1.00	0.20				
Glucose	4	QC level 1	0.73	0.85	–1.20	2.09	2.16	0.07
		QC level 2	0.18	0.36	–0.04	2.07	2.14	0.08
		Patient	0.20	0.01	0.10			
Total protein	4	QC level 1	–1.16	–0.95	0.12	2.31	2.36	0.05
		QC level 2	0.61	–0.45	1.20	2.26	2.29	0.03
		Patient	0.90	0.20	0.40			
Triglyceride	3	QC level 1	0.90	–0.69		2.58	2.58	0.002
		QC level 2	0.16	1.40		2.53	2.53	0.002
		Patient	0.40	0.10				
BUN	4	QC level 1	–3.73	–0.65	–2.61	4.31	4.37	0.06
		QC level 2	–0.42	–2.49	0.64	3.46	3.48	0.02
		Patient	–0.70	0.40	0.30			
Minimum (absolute difference)		QC level 1 QC level 2 Patient	–0.08 –0.04 0.01		(cCreatinine) (gGlucose) (gGlucose)	2.07 (gGlucose)	2.14 (gGlucose)	0.002 (tTriglyceride)
Maximum (absolute difference)		QC level 1 QC level 2 Patient	–3.73 –3.67 –2.50		(BUN) (cCreatinine) (ALP)	7.995 (ALT)	8.01 (ALT)	0.825 (HDL)
Mean		QC level 1 QC level 2 Patient	–0.41 0.17 0.04					0.125

*The data for potassium and sodium are not included in this table because of the lack of comparison data with patient samples.
Abbreviations: IQC, internal quality control; QC, quality control; U_{rel}, relative expanded uncertainty; U_{rel_tot}, expanded relative uncertainty (coverage factor, k = 2) calculated regardless of reagent lot change, akin to CV; U_{rel_sub}, expanded relative uncertainty (coverage factor, k = 2) calculated from values obtained from each subgroup, akin to CV; ALP, alkaline phosphatase; BUN, blood urea nitrogen.

Supplemental Data Table S3. Worked-out examples of MU estimation of two chemistry analytes (albumin and creatinine)

(A) Albumin

Component (aAnalyte)	Albumin (Alb)			
Measurement unit	g/dL			
Reference range	3.5–5.2			
Measurement method	Colorimetric assay-BCP			
Measurement system	Roche Cobas 8000			
Calibrator uncertainty				
Assigned value	2.82			
U_{cal} ($k=2$)	0.0264			
U_{rel} *(cal)* ($k=2$)	0.0094			
Long-term precision	Level 1		Level 2	
Total period	2020.03.09–2021.02.28			
N, enrolled data	1,060		1,060	
N, outliers	16		20	
N, total data	1,044		1,040	
N, used reagent lot	3		3	
Data cellectioncollection per reagent lot	Subgrouping	Total	Subgrouping	Total
Period 1	2020.03.09–2020.07.08	SD (u_{rw})	2020.03.09–2020.07.08	SD (u_{rw})
N	325	=0.0357	325	=0.0485
Mean	2.57		4.08	
u 1	0.0385		0.0485	
Period 2	2020.06.11–2020.11.30		2020.06.11–2020.11.30	
N	459		468	
Mean	2.55		4.05	
u 2	0.0315		0.0440	
Period 3	2020.12.01–2021.02.28		2020.12.01–2021.02.28	
N	260		247	
Mean	2.56		4.06	
u 3	0.0358		0.0489	
u Rw, U/L (pooled average)	0.0348		0.0466	
Total mean	2.56		4.06	
Uncertainty estimation				
Standard (Rw)				
u_{Rw}	0.0348	0.0357	0.0466	0.0485
U_{Rw} ($k=2$)	0.0697	0.0714	0.0932	0.0969
U_c at IQC mean=$\sqrt{(U2cal+U2Rw)}$ ($k=2$)	0.075	0.076	0.097	0.100
Relative (rel)				
$u_{rel(Rw)}$	0.0136	0.0140	0.0115	0.0119
$U_{rel(Rw)}$ ($k=2$)	0.0272	0.0279	0.0230	0.0239
$U_{rel,\,c}=\sqrt{(U2rel(cal)+U2rel(Rw))}$ ($k=2$)	0.0288	0.0294	0.0248	0.0256
$U_{rel,\,c}$ ($k=2$)	2.88	2.94	2.48	2.56
Applied to patients' resultsdata (95% confidencet interval)	2.56±0.0745 g/dL or (2.88%)	2.56±0.0761 g/dL or (2.94%)	4.06±0.0969 g/dL or (2.48%)	4.06±0.100 g/dL or (2.56%)

Abbreviations: MU, measurement uncertainty; BCP, bromocresol purple; U_{cal}, expanded uncertainty of end-user calibrator; $U_{rel(cal)}$, relative expanded uncertainty of end-user calibrator; ui, standard uncertainty in the ith group; u_{Rw}, standard uncertainty obtained by repetitive measurement; U_{Rw}, expanded uncertainty obtained by repetitive measurement; U_c, expanded combined uncertainty; $u_{rel(Rw)}$, relative uncertainty obtained by repetitive measurement; $U_{rel(Rw)}$, relative expanded uncertainty obtained by repetitive measurement; $U_{rel,\,c}$, relative expanded combined uncertainty.

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(B) Creatinine

Component (aAnalyte)	Creatinine (Cr)			
Measurement unit	mg/dL			
Reference range	0.7–1.4			
Measurement method	Jaffé method, kinetic colorimetric assay			
Measurement system	Roche Cobas 8000			
Calibrator uncertainty				
Assigned value	4.06			
U_{cal} $(k=2)$	0.0576			
$U_{rel(cal)}$ $(k=2)$	0.0142			
Long-term precision	Level 1		Level 2	
Total period	2020.03.09–2021.02.28			
N, enrolled data	1,065		1,060	
N, outliers	41		29	
N, total data	1,024		1,031	
N, used reagent lot	3		3	
Data cellectioncollection per reagent lot	Subgrouping	Total	Subgrouping	Total
Period 1	2020.03.09–2020.05.17	SD (u_{rw})	2020.03.09–2020.05.17	SD (u_{rw})
N	166	= 0.0355	164	=0.107
Mean	1.25		5.23	
u 1	0.0334		0.103	
Period 2	2020.05.18 – -2020.11.18		2020.05.18–2020.11.18	
N	569		575	
Mean	1.25		5.21	
u 2	0.0360		0.107	
Period 3	2020.11.19–2021.02.28		2020.11.19–2021.02.28	
N	289		292	
Mean	1.26		5.23	
u 3	0.0349		0.108	
u_{Rw}, *U/L (pooled average)*	0.0353		0.107	
Total mean	1.25		5.22	
Uncertainty estimation				
Standard (Rw)				
u_{Rw}	0.0353	0.0355	0.107	0.107
U_{Rw} $(k=2)$	0.0706	0.0710	0.214	0.214
U_c at IQC mean $=\sqrt{(U2cal+U2Rw)}$ $(k=2)$	0.0911	0.0915	0.221	0.222
Relative (rel)				
$u_{rel(Rw)}$	0.0282	0.0284	0.020	0.021
$U_{rel(Rw)}$ $(k=2)$	0.0564	0.0567	0.041	0.041
$U_{rel,\,c}=\sqrt{(U2rel(cal)+U2rel(Rw))}$ $(k=2)$	0.0581	0.0585	0.043	0.043
$U_{rel,\,c}$ $(k=2)$	5.81	5.85	4.33	4.34
Applied to patients' resultsdata (95% confidencet interval)	2.56 ± 0.0745 g/dL or (2.88%)	2.56 ± 0.0761 g/dL or (2.94%)	4.06 ± 0.0969 g/dL or (2.48%)	4.06 ± 0.100 g/dL or (2.56%)

Supplemental Data Table S4. Mean values and MU (SD and CV (%)) of IQC data of 14 analytes with two different QC lots used for two consecutive years (lot 1: March 2019 to February 2020, lot 2: March 2020 to February 2021)

Year	MU	2019		2020		%Diff. (2020 – 2019)	
Level		1	2	1	2	1	2
Albumin	mean	2.66	4.14	2.56	4.06	–3.92	–1.97
	SD	0.0373	0.0544	0.0360	0.0480	–3.68	–13.33
	CV(%)	1.40	1.31	1.41	1.18	0.236	–11.1
ALP	mean	92.1	382	94.7	365	2.76	–4.69
	SD	1.84	7.01	1.98	7.37	7.13	4.86
	CV(%)	1.99	1.84	2.09	2.02	4.49	9.12
ALT	mean	29.1	97.5	26.9	93.9	–8.23	–3.91
	SD	1.21	1.64	1.07	1.18	–12.5	–39.6
	CV(%)	4.15	1.68	3.99	1.25	–3.92	–34.4
AST	mean	39.4	196	40.2	200	2.06	2.34
	SD	1.13	2.76	1.08	2.83	–5.16	2.38
	CV(%)	2.88	1.41	2.68	1.41	–7.38	0.03
HDL	mean	22.3	59.9	21.1	58.9	–5.69	–1.67
	SD	0.664	2.12	0.45	1.48	–46.5	–43.0
	CV(%)	2.98	3.54	2.15	2.52	–38.6	–40.7
LDL	mean	61.3	135.3	61.6	136	0.563	0.703
	SD	1.58	3.41	1.31	2.56	–20.1	–33.3
	CV(%)	2.58	2.52	2.13	1.88	–20.8	–34.3
T-chol	mean	96.9	237	101	253	3.75	6.42
	SD	1.51	3.44	4.40	4.38	65.7	21.4
	CV(%)	1.56	1.45	4.37	1.73	64.3	16.0
Creatinine	mean	1.26	5.06	1.25	5.22	–0.78	3.04
	SD	0.04	0.10	0.04	0.11	–3.37	2.25
	CV(%)	2.91	2.07	2.83	2.05	–2.57	–0.82
Glucose	mean	83.7	284	82.5	275	–1.47	–3.40
	SD	1.18	3.40	1.04	2.72	–12.8	–25.1
	CV(%)	1.40	1.20	1.26	0.99	–11.1	–21.0
T-Protein	mean	4.31	6.64	4.19	6.66	–2.80	0.29
	SD	0.0550	0.0778	0.0472	0.0735	–16.5	–5.82
	CV(%)	1.28	1.17	1.13	1.10	–13.3	–6.13
K	mean	4.01	6.16	3.97	6.17	–1.07	0.16
	SD	0.0281	0.0355	0.0294	0.0376	4.39	5.60
	CV(%)	0.702	0.576	0.742	0.609	5.40	5.45
Na	mean	123	144	126	146	1.92	1.14
	SD	0.834	0.931	0.951	0.944	12.4	1.41
	CV(%)	0.676	0.647	0.756	0.649	10.7	0.27
TG	mean	98.9	181	103	187	3.80	3.50
	SD	1.26	2.03	1.18	2.10	–6.44	3.37
	CV(%)	1.27	1.12	1.15	1.12	–10.6	–0.136
BUN	mean	15.7	46.0	15.1	47.5	–4.21	3.15
	SD	0.326	0.867	0.297	0.694	–10.0	–24.9
	CV(%)	2.08	1.89	1.97	1.46	–5.60	–28.9
Total Diff.	mean					–0.951 (–8.23 to 3.80)	0.364 (–4.69 to 6.42)
	SD					–3.39 (–46.5 to 65.7)	–10.3 (–43.0 to 21.4)
	CV(%)					–2.06 (–38.6 to 64.3)	–10.5 (–40.7 to 16.0)

Abbreviations: MU, measurement uncertainty; IQC, internal quality control; QC, quality control material; ALP, alkaline phosphatase; T-chol, total cholesterol; K, potassium; Na, sodium; TG, triglyceride; BUN, blood urea nitrogen.

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