Stability and performance evaluation of liquid stable cardiac controls for in vitro diagnostic applications

R. Lu[1], K.Cristobal[1], E. Frew[1], M. Anderson[1]

[1] Bio-Techne Diagnostics, Minneapolis, MN, USA

CONTACT INFORMATION

Raymond Lu, R&D Manager

O: +1 760 571 5228

Raymond.Lu@bio-techne.com

INTRODUCTION

Reliable quality control (QC) materials are essential for ensuring the analytical performance of cardiac and related biomarker assays used in in vitro diagnostic (IVD) testing. In addition to manufacturers provided controls, independent third-party QC materials are recommended to provide an objective assessment of assay performance and to detect changes related to reagent lots, calibration shifts, or platform variability. Liquid ready-to-use cardiac controls that closely resemble patient specimens and maintain stability throughout their intended use offer advantages over lyophilized or frozen materials, including reduced risk of reconstitution-related errors, improved ease of use, and lower shipping and storage burden. These materials are increasingly relevant across a broad range of testing environments, spanning high throughput chemiluminescent analyzers to emerging point-of-care modalities. Liquid cardiac quality controls are particularly important for routine laboratory workflows, high-sensitivity cardiac assays, and adjunct biomarkers used in cardiovascular risk assessment and differential diagnosis.

PURPOSE

This study describes the target concentration and stability characterization of multi-level liquid cardiac controls designed for IVD use.

METHODS

Human serum-based liquid cardiac controls Liquid QC™ Cardiac Marker Control Complete were formulated at clinically relevant concentrations of cardiac associated biomarkers, including cardiac troponin I/T, creatine kinase-MB, myoglobin, B-type natriuretic peptide (NT-proBNP), D-dimer, and C reactive protein. Commutability through assay specific value assignment was evaluated on select automated immunoassay platforms. Stability studies supporting IVD use included real-time and accelerated stability under recommended storage conditions, open-vial stability following repeated use, freeze-thaw robustness, and simulated shipping stress at elevated temperature.

RESULTS

Table 1: 1 lot demonstrating commutability and assay specific value assignment across multiple platforms.

Analyte / Instrument	Units	Level 1 Mean	Level 1 Range	Level 2 Mean	Level 2 Range	Level 3 Mean	Level 3 Range	Units	Level 1 Mean	Level 1 Range	Level 2 Mean	Level 2 Range	Level 3 Mean	Level 3 Range
CKMB, mass														
Abbott Architect	ng/mL	2.78	2.23 - 3.34	13.2	10.6 - 15.9	53.8	43.0 - 64.5	µg/L	2.78	2.23 - 3.34	13.2	10.6 - 15.9	53.8	43.0 - 64.5
Beckman Coulter Access	ng/mL	4.19	3.35 - 5.03	19.1	15.3 - 22.9	73.8	59.0 - 88.6	µg/L	4.19	3.35 - 5.03	19.1	15.3 - 22.9	73.8	59.0 - 88.6
Ortho Vitros ECI	ng/mL	1.78	1.43 - 2.14	8.97	7.18 - 10.8	35.6	28.5 - 42.7	µg/L	1.78	1.43 - 2.14	8.97	7.18 - 10.8	35.6	28.5 - 42.7
Roche cobas e series	ng/mL	3.23	2.59 - 3.88	12.8	10.2 - 15.4	49.1	39.3 - 58.9	µg/L	3.23	2.59 - 3.88	12.8	10.2 - 15.4	49.1	39.3 - 58.9
Siemens Advia Centaur Systems	ng/mL	4.10	3.28 - 4.91	18.0	14.4 - 21.6	68.4	54.7 - 82.1	µg/L	4.10	3.28 - 4.91	18.0	14.4 - 21.6	68.4	54.7 - 82.1
Siemens Dimension EXL	ng/mL	3.12	2.49 - 3.74	16.2	12.9 - 19.4	74.7	59.8 - 89.6	µg/L	3.12	2.49 - 3.74	16.2	12.9 - 19.4	74.7	59.8 - 89.6
D-DIMER														
bioMérieux VIDAS Systems	ng/mL	267	213 - 320	742	593 - 890	1920	1536 - 2304	ng/mL	267	213 - 320	742	593 - 890	1920	1536 - 2304
Roche cobas Integra	µg/L	0.225	0.180 - 0.270	0.632	0.505 - 0.758	1.64	1.31 - 1.97	µg/L	0.225	0.180 - 0.270	0.632	0.505 - 0.758	1.64	1.31 - 1.97
hsCRP														
Beckman AU Systems	mg/dL	0.120	0.096 - 0.144	0.458	0.366 - 0.549	0.717	0.574 - 0.861	mg/L	1.20	0.963 - 1.44	4.58	3.66 - 5.49	7.17	5.74 - 8.61
Beckman Coulter Immage	mg/dL	0.131	0.105 - 0.157	0.538	0.431 - 0.646	0.843	0.674 - 1.01	mg/L	1.31	1.05 - 1.57	5.38	4.31 - 6.46	8.43	6.74 - 10.1
Roche cobas Integra	mg/dL	0.112	0.090 - 0.135	0.359	0.287 - 0.431	0.533	0.426 - 0.640	mg/L	1.12	0.899 - 1.35	3.59	2.87 - 4.31	5.33	4.26 - 6.40
Siemens Dimension EXL	mg/dL	0.157	0.126 - 0.189	0.505	0.404 - 0.606	0.728	0.582 - 0.874	mg/L	1.57	1.26 - 1.89	5.05	4.04 - 6.06	7.28	5.82 - 8.74
MYOGLOBIN														
Abbott Architect	ng/mL	48.8	34.2 - 63.5	170	119 - 221	410	287 - 533	µg/L	48.8	34.2 - 63.5	170	119 - 221	410	287 - 533
Beckman Coulter Access	ng/mL	43.3	30.3 - 56.2	144	101 - 187	330	231 - 430	µg/L	43.3	30.3 - 56.2	144	101 - 187	330	231 - 430
Ortho Vitros ECI	ng/mL	124.7	87.3 - 162	348	244 - 453	724	506 - 941	µg/L	124.7	87.3 - 162	348	244 - 453	724	506 - 941
Roche cobas e series	ng/mL	50.2	35.1 - 65.2	150	105 - 195	343	240 - 446	µg/L	50.2	35.1 - 65.2	150	105 - 195	343	240 - 446
Siemens Advia Centaur Systems	ng/mL	51.0	35.7 - 66.4	191	134 - 249	467	327 - 607	µg/L	51.0	35.7 - 66.4	191	134 - 249	467	327 - 607
Siemens Dimension EXL	ng/mL	56.9	39.8 - 74.0	225	157 - 292	563	394 - 731	µg/L	56.9	39.8 - 74.0	225	157 - 292	563	394 - 731
NT ProBNP														
Roche cobas e series	pg/mL	104	82.9 - 124	476	381 - 572	1423	1138 - 1707	pmol/L	12.2	9.78 - 14.7	56.2	45.0 - 67.5	168	134 - 201
Siemens Dimension EXL	pg/mL	29.5	23.6 - 35.4	155	124 - 186	519	415 - 623	pmol/L	3.48	2.78 - 4.18	18.3	14.6 - 21.9	61.3	49.0 - 73.5
TROPONIN T														
Roche cobas e series	ng/mL	0.016	0.013 - 0.019	0.207	0.166 - 0.249	0.912	0.729 - 1.09	µg/L	0.016	0.013 - 0.019	0.207	0.166 - 0.249	0.912	0.729 - 1.09
TROPONIN T hs														
Roche cobas e series	pg/mL	17.3	13.8 - 20.7	198	158 - 238	919	735 - 1103	pg/mL	17.3	13.8 - 20.7	198	158 - 238	919	735 - 1103

Figure 1: N=2 vials of 1 lot of each level of Liquid QC Cardiac Marker Control Complete were set up at -70°C and 2-8°C and tested periodically for each analyte across the platforms listed in Table 5 below out to 24.1 months. Two additional lots were tested with similar results (data not shown). All results were within +/- 20% recovery samples stored at -70°C.

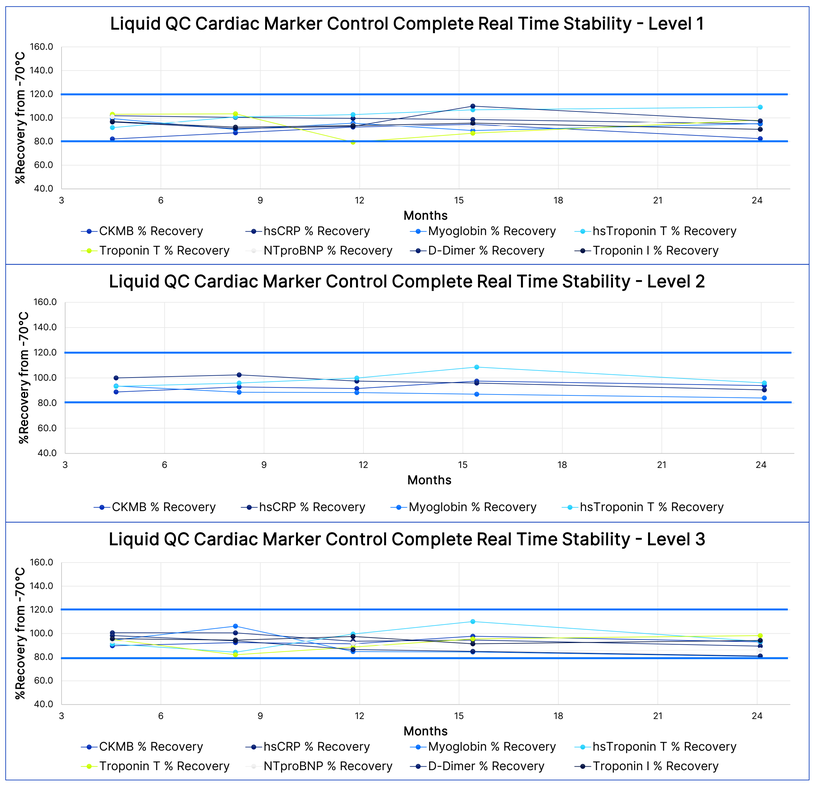

Table 5: Platforms used to test each analyte in Liquid QC Cardiac Marker Control Complete for real time stability assessment.

Liquid QC Cardiac Marker Control Complete Real Time Stability Months at 5°C								
	CKMB	hsCRP	Myoglobin	hsTnT	TnT	NTproBNP	D-Dimer	TnI
Test method	Ortho Vitros Eci	Beckman AU400	Roche e411	Roche e411	Roche e411	Roche e411	Roche Integra	Roche e411

Figure 2: N=4 vials of 1 lot of each level of custom hsTroponin I controls were set up at -70°C and 2-8°C and tested on a POC test system at time 0, 6, and 12 months. Two additional lots were tested with similar results (data not shown). All results were within +/- 20% recovery samples stored at -70°C.

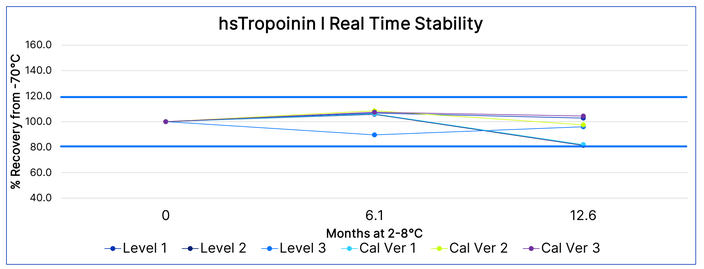

Table 6: N=2 vials of 2 lots of each level of Liquid QC Cardiac Marker Control Complete were set up at 45°C, 37°C, and 25°C and tested periodically for each analyte across the platforms listed in Table 5. The Arrhenius equation was used to calculate the estimated time to failure at 5°C defined as a %15 change in recovery from time 0.

Accelerated Stability (Equivalent Months at 5°C)								
	CKMB	hsCRP	Myo	hsTnT	TnT	NTproBNP	D-Dimer	TnI
L1	99	13	15	19	29	28	26	32
L2	66	20	21	29	13	29	29	83
L3	52	11	18	29	29	29	25	37

Table 2: N=2 vials of 2 lots of each level of Liquid QC Cardiac Marker Control Complete were opened, sample was removed, vial closed and set up at 5°C. Periodic open vial testing for each analyte across the platforms listed in Table 5 was performed out to 3 months. Results are the average % recovery from time 0. TnT L1 was below dynamic range of the test platform utilized and not reported.

Open Vial Stability, 3 Months at 5°C (% Recovery from Time 0)								
	CKMB	hsCRP	Myo	hsTnT	TnT	NTproBNP	D-Dimer	TnI
L1	89	101	98	99	n/a	100	102	93
L2	95	99	96	96	98	102	100	97
L3	94	100	94	97	103	103	93	98

Table 3: N=2 vials of 2 lots of each level of Liquid QC Cardiac Marker Control Complete were subjected to 5 freeze thaw cycles to simulate transport excursion temperatures. Testing was performed for each analyte across the platforms listed in Table 5 . Results are the average % recovery from samples stored at 5°C. TnT L1 was below dynamic range of the test platform utilized and not reported.

Freeze / Thaw Stability (% Recovery from 5°C)								
	CKMB	hsCRP	Myo	hsTnT	TnT	NTproBNP	D-Dimer	TnI
L1	94	100	95	109	n/a	104	99	94
L2	93	101	96	98	122	106	101	101
L3	92	101	92	96	103	104	94	93

Table 4: N=2 vials of 2 lots of each level of Liquid QC Cardiac Marker Control Complete were set up at 45°C and tested after 5 days to simulate transport excursion temperatures. Testing was performed for each analyte across the platforms listed in Table 5; results are the average % recovery from time 0. Analytes marked with * were tested after 5 days at 32°C; TnT L1 was below dynamic range of the test platform utilized and not reported.

Elevated Temperature Transport Stability (% Recovery from 5°C)				
	CKMB*	hsCRP	Myo*	hsTnT
L1	79	100	79	97
L2	84	98	81	95
L3	86	94	79	96
	TnT	NTproBNP	D-Dimer	TnI
L1	n/a	94	95	98
L2	77	93	94	80
L3	101	92	91	90

CONCLUSIONS

Liquid QC™ Cardiac Marker Control Complete demonstrates robust stability and consistent performance under conditions representative of routine IVD laboratory use. Stability across storage, handling, and analyzer operating conditions supports their use in quality assurance of high-sensitivity cardiac biomarker assays. The liquid-stable, ready-to-use format enhances laboratory efficiency and reliability by eliminating the need for frozen shipping and reconstitution, while supporting both core lab and point-of-care platforms.

These controls are well-suited for use as independent third-party quality controls, providing laboratory clinicians with an unbiased tool to monitor assay performance, detect shifts, and ensure comparability across instruments, sites, and reagent lots. In parallel, the technology offers flexibility for customization to meet the specific design, matrix, and performance requirements of IVD OEM partners, enabling tightly aligned system controls for assay development, validation, and ongoing quality monitoring (see custom hsTnI control example in Figure 2).

Together, these attributes support regulatory expectations and empower both laboratories and assay developers to maintain confidence in consistent, accurate, and reliable cardiac biomarker testing across diverse clinical settings.

Product availability, specifications, and regulatory status may vary by country.