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Run 24 Assessor's Report

The following report is based on independent assessment of slides by John Garratt, Blake Gilks and Jason Morin, done at Vancouver General Hospital, on Tuesday, September 18, 2012.

This assessment is based only on those slides returned to CIQC in time for the assessment meeting. With the use of the website, it is now possible for participating labs to perform self-assessment of their results immediately, comparing their staining to that of the reference lab (available through a link on the CIQC website), so the run should be of value even for those labs whose slides were not available at the time of our review meeting in Vancouver. Although external review and assessment is provided, it is not a substitute for self-assessment, with comparison of your results to reference results. Self assessments are immediately available in the TMA Scorer web site once you have entered your results. http://www.tmascorersystem.ca/login.php
The assessment team graded laboratory results as adequate, suboptimal, and unacceptable. Only two slides were considered unacceptable (one each for HER2 and PR), and these are noted below. Similarly, suboptimal staining results are noted below. Many discordant results (compared to reference lab results) noted on self-assessment were found on review to be due to cores without tumor cells (i.e. uninterpretable) or interpretive/data entry errors (i.e. clearly positive result, but recorded as negative), so that the overall technical quality seen on this run was excellent, and noticeably better than early CIQC runs.

RESULTS

HER2: The HER2 testing results continue to be excellent in Canada. This run was not ideal as a test of HER2 staining as only three HER2 positive cases were present on the array (cores 9, 31 and 40, with core 40 being uninterpretable on the slide used by many labs as there were no tumor cells present in the tissue core on deeper sectioning into the block. Core 17 was problematic with a range of staining seen in different laboratories, and few tumor cells present, so we disregarded that core in our review assessment. A single lab (179) had inadequate staining, with strong staining of many cores i.e. many false positive results. False positive results were noted on the self-assessment results for labs 102 (cores 2 and 45), 105 (core 8), and 190 (core 10), but these cores were interpreted as not showing 3+ staining on review. Thus, for the labs where slides were available for review, apart from lab 179, there were **no false positive results**. There were similarly **no false negative results on review**, as those labs that had recorded a negative result for core 40 had uniformly, based on review, assessed cores that were technically uninterpretable, as there were no tumor cells present in the tissue on their slides (e.g. labs 103, 10, 120, 152). Labs 113 and 188 had overall weak staining, but based on the correct interpretations in the self-assessment they are proficient in interpretation of their staining results. Both 113 and 188 had recorded core 40 as being negative, but on review it was considered uninterpretable in both instances, as no tumor cells were present. Finally, lab 186 showed weak staining of many cases; again, their self-assessment results were fine, indicating that they are proficient at interpretation of their staining results. HER2 is unique in that there is some latitude allowed in staining intensity; what is 3+ and 2+ positivity can show some subtle variation between laboratories, and not negatively effect their performance.

Fig. 1 Heat Map, Fig 4 Statistical Analysis

ER: This run was a good challenge of ER staining, with a nice mix of ER+ and negative cases. Cores 9, 14, 16, 22, 25, 33, 40, 43, 44, and 45 were ER-, while cores 11 and 31 were weak ER+ cores, and thus presented a particular challenge with respect to test sensitivity. No laboratories had unacceptable results, based on independent review. Lab 102 appeared to have false positive results based on self-assessment, but on review cores 25 and 43 were uninterpretable, and core 33 was negative. Lab 124 recorded 11 and 31 as negative, but both were considered positive on review, and cores 38 and 40 were uninterpretable. Staining was therefore adequate for both of these laboratories. Labs 170, 172, and 188 recorded negative results for cores that on review were considered uninterpretable or weakly positive, and these labs were all considered to have technically adequate staining. Lab 177 had a single false negative result on the weakly positive core 31, and lab 188 had false negative results on both weakly positive cores, 11 and 31, so that these labs were considered to have suboptimal staining. Overall, the staining for ER was excellent in this run.

Fig. 2 Heat Map, Fig 5 Statistical Analysis

PR: Unlike ER, where lack of sensitivity is the only problem, there were some issues around false positive staining for PR. According to the reference lab results, cores 7-9, 12, 14, 16, 22, 25, 33, 34, 40, 43-45 were PR negative. Core 8 did have a few positive cells on some slides, so we accepted that as a true result, ascribing the variable staining to a combination of intratumoral heterogeneity and weak staining. Based on the reference lab results, there were no PR+, ER- cases, as expected, as this immunostaining profile should be rare. Lab 187 did have weak staining of cores 14 and 16, which were ER- cases; we consider those to be false positive results, and this is therefore a suboptimal result. Lab 191 had identical results, with weak staining of cores 14 and 16. These were the only labs with false positive results, based on review assessment. A number of labs which showed discrepant results based on self-assessment were considered to have adequate staining based on review, including labs 157, 162, 123, 178, 167, 170, 153 and 186. The discrepant results were due to either reporting results on cores that were considered uninterpretable based on review, due to no tumor cells, or cores with weak staining that were scored as negative on self-assessment. Lab 194 showed overall weak staining, with only occasional positive cells in cores 4, 11, and 31, and a false negative result for core 46 (a core with weak staining). Lab 173 also had weak staining overall, with two false negative results (cores 11 and 46, both of which were weak positive cases), while lab 126 had three false negative results, all of which were cases with weak PR positivity. The only unacceptable result was for lab 177, which had weak staining, with five false negative results on review (cores 24, 30, 31, 41, 42). As we have observed in the past, there was more variability in PR staining, compared to ER and HER2, but overall results were very good, and significantly improved over earlier runs.

Fig. 3 Heat Map, Fig 6 Statistical Analysis


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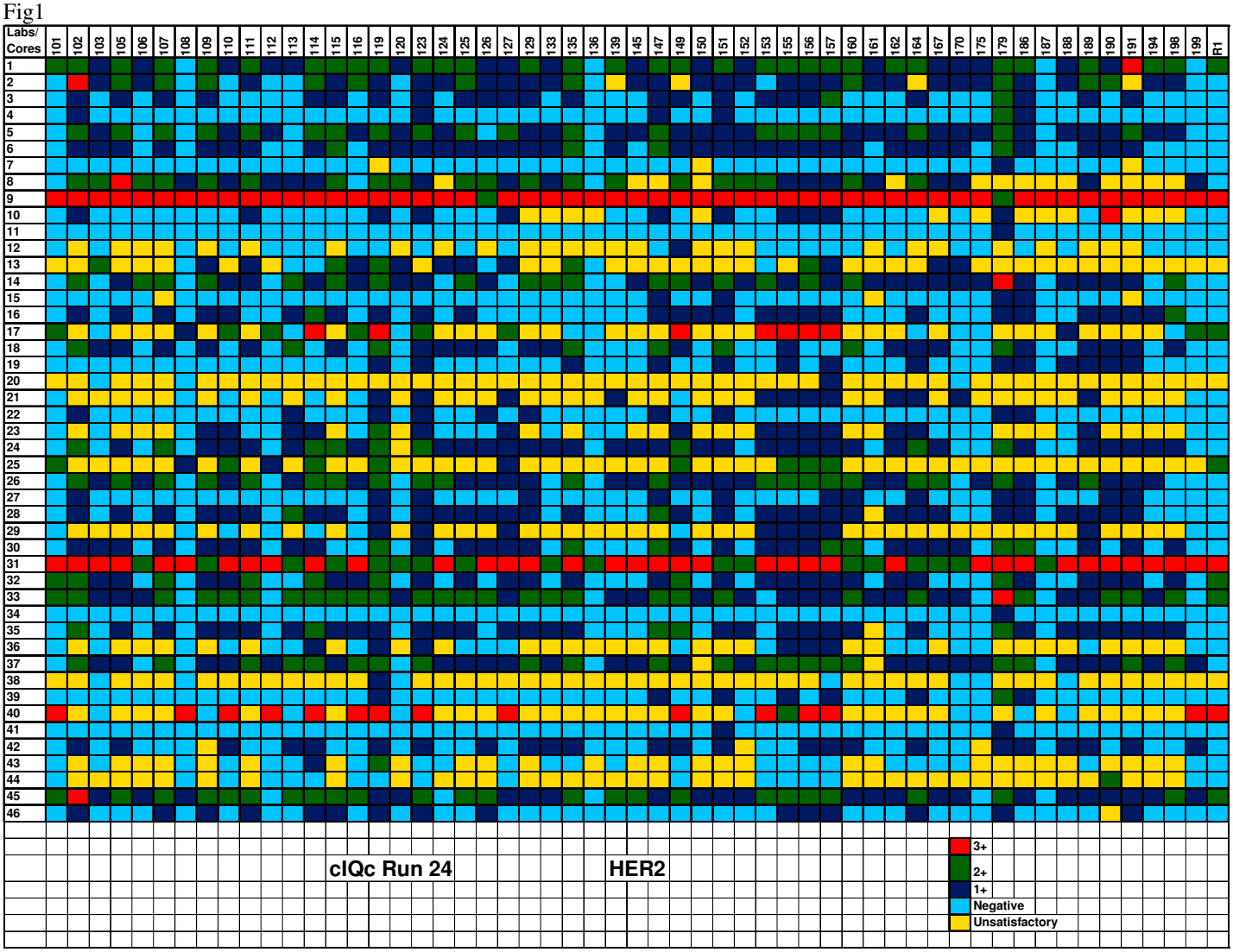
Fig1


Labs/ Cores
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cIQc Run 24
HER2
3+
2+
1+
Negative
Unsatisfactory


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Fig2


Labs/ Core
101 102 103 105 106 107 108 109 111 112 113 114 115 116 119 120 122 123 124 125 126 127 128 129 132 133 134 135 136 138 139 141 143 144 145 146 147 149 150 151 152 153 155 156 157 159 160 161 162 163 164 165 167 168 170 172 173 175 177 178 179 180 183 184 186 187 188 189 190 191 192 194 198 199 R1
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cIQc Run 24
ER
P Positive
N Negative
U Unsatisfactory


cIQc
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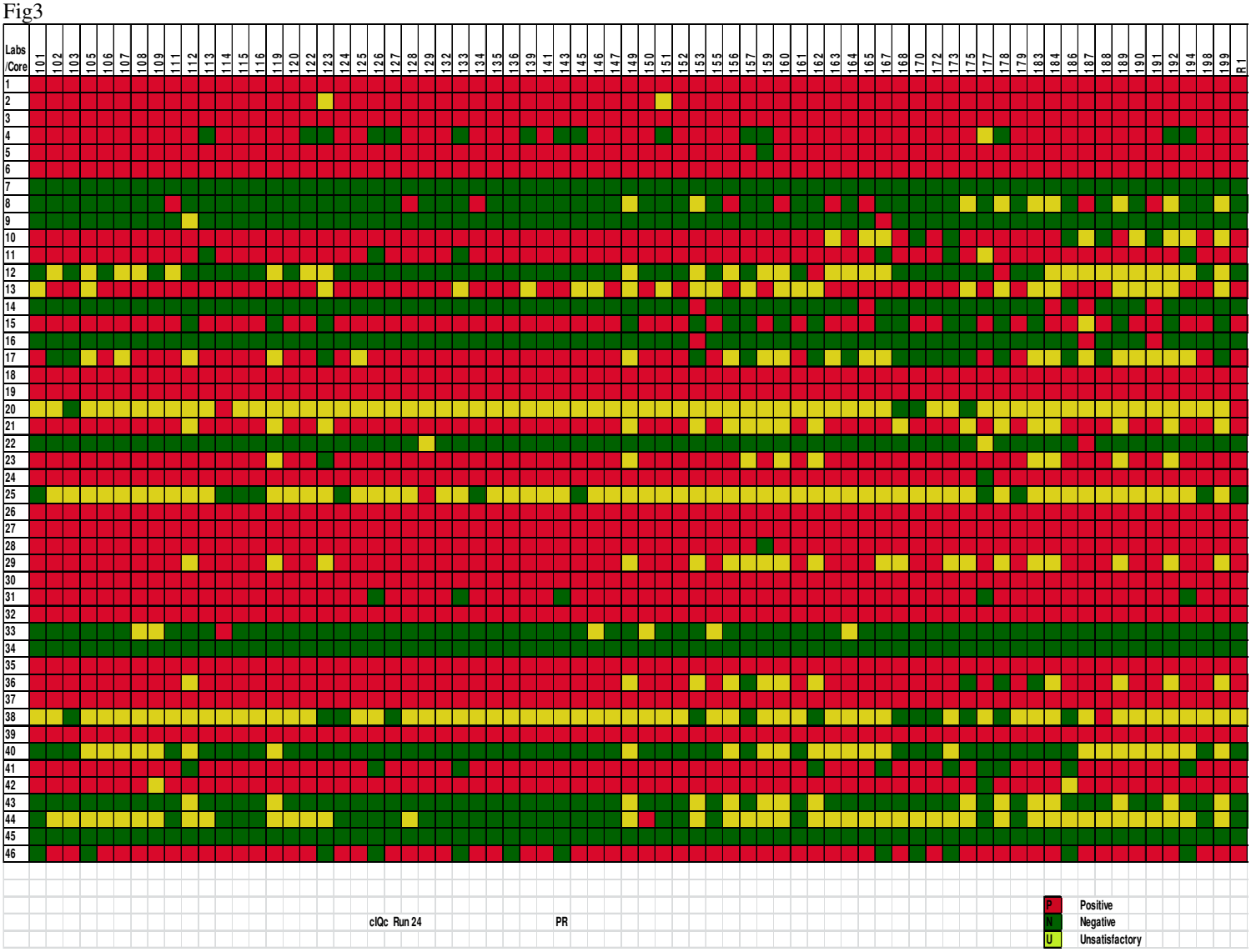
Fig3


Labs /Core
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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46
cIQc Run 24
PR
P Positive
N Negative
U Unsatisfactory

Fig 4

Descriptive Statistics Run 24 cIQc HER2

Test lab name	total n	% scorable	pairwise complete observations	concordance with reference (%)	sensitivity	specificity	PPV (positive predictive value)	NPV (negative predictive value)	Cohen's kappa
101	46	93.48	43	43/43 (100%)	1	1	1	1	1
102	46	69.57	32	30/32 (94%)	1	0.93	0.5	1	0.64
103	46	91.3	39	38/39 (97%)	0.67	1	1	0.97	0.79
105	46	71.74	33	32/33 (97%)	1	0.97	0.67	1	0.78
106	46	71.74	33	33/33 (100%)	1	1	1	1	1
107	46	69.57	32	32/32 (100%)	1	1	1	1	1
108	46	100	43	43/43 (100%)	1	1	1	1	1
109	46	76.09	34	33/34 (97%)	0.67	1	1	0.97	0.78
110	46	93.48	43	43/43 (100%)	1	1	1	1	1
111	46	76.09	34	34/34 (100%)	1	1	1	1	1
112	46	93.48	43	43/43 (100%)	1	1	1	1	1
113	46	89.13	40	39/40 (98%)	0.67	1	1	0.97	0.79
114	46	95.65	43	42/43 (98%)	1	0.98	0.75	1	0.84
115	46	73.91	33	33/33 (100%)	1	1	1	1	1
116	46	93.48	42	42/42 (100%)	1	1	1	1	1
119	46	95.65	42	41/42 (98%)	1	0.97	0.75	1	0.84
120	46	78.26	34	33/34 (97%)	0.67	1	1	0.97	0.78
123	46	91.3	42	42/42 (100%)	1	1	1	1	1
124	46	76.09	34	34/34 (100%)	1	1	1	1	1
125	46	80.43	36	36/36 (100%)	1	1	1	1	1
126	46	78.26	35	35/35 (100%)	1	1	1	1	1
127	46	95.65	43	43/43 (100%)	1	1	1	1	1
129	46	69.57	32	32/32 (100%)	1	1	1	1	1
133	46	73.91	34	34/34 (100%)	1	1	1	1	1
135	46	76.09	34	34/34 (100%)	1	1	1	1	1
136	46	76.09	34	34/34 (100%)	1	1	1	1	1
139	46	76.09	35	35/35 (100%)	1	1	1	1	1
145	46	69.57	32	32/32 (100%)	1	1	1	1	1
147	46	71.74	33	33/33 (100%)	1	1	1	1	1
149	46	91.3	42	41/42 (98%)	1	0.97	0.75	1	0.84
150	46	63.04	29	29/29 (100%)	1	1	1	1	1
151	46	71.74	33	33/33 (100%)	1	1	1	1	1
152	46	71.74	33	32/33 (97%)	0.67	1	1	0.97	0.78
153	46	93.48	42	41/42 (98%)	1	0.97	0.75	1	0.84
155	46	93.48	43	42/43 (98%)	1	0.98	0.75	1	0.84
156	46	95.65	43	42/43 (98%)	1	0.98	0.75	1	0.84
157	46	100	43	42/43 (98%)	1	0.98	0.75	1	0.84
160	46	73.91	34	34/34 (100%)	1	1	1	1	1
161	46	63.04	29	29/29 (100%)	1	1	1	1	1
162	46	80.43	37	37/37 (100%)	1	1	1	1	1
164	46	80.43	37	37/37 (100%)	1	1	1	1	1
167	46	76.09	34	34/34 (100%)	1	1	1	1	1
170	46	93.48	40	39/40 (98%)	0.67	1	1	0.97	0.79
175	46	78.26	35	34/35 (97%)	0.67	1	1	0.97	0.79
179	46	69.57	32	30/32 (94%)	1	0.93	0.5	1	0.64
186	46	71.74	33	32/33 (97%)	0.67	1	1	0.97	0.78
187	46	67.39	31	31/31 (100%)	1	1	1	1	1
188	46	78.26	35	34/35 (97%)	0.67	1	1	0.97	0.79
189	46	82.61	38	38/38 (100%)	1	1	1	1	1
190	46	69.57	32	31/32 (97%)	1	0.97	0.67	1	0.78
191	46	60.87	28	27/28 (96%)	1	0.96	0.67	1	0.78
194	46	69.57	32	32/32 (100%)	1	1	1	1	1
198	46	71.74	33	33/33 (100%)	1	1	1	1	1
199	46	91.3	42	42/42 (100%)	1	1	1	1	1

Fig 5

Descriptive Statistics Run 24 cIQc ER

Test lab name	total n	% scorable	pairwise complete observations	concordance with reference (%)	sensitivity	specificity	PPV (positive predictive value)	NPV (negative predictive value)	Cohen's kappa
101	46	95.65	44	44/44 (100%)	1	1	1	1	1
102	46	100	45	42/45 (93%)	1	0.7	0.92	1	0.78
103	46	100	45	45/45 (100%)	1	1	1	1	1
105	46	93.48	43	43/43 (100%)	1	1	1	1	1
106	46	97.83	44	43/44 (98%)	1	0.9	0.97	1	0.93
107	46	93.48	43	43/43 (100%)	1	1	1	1	1
108	46	73.91	34	34/34 (100%)	1	1	1	1	1
109	46	91.3	42	42/42 (100%)	1	1	1	1	1
111	46	93.48	43	43/43 (100%)	1	1	1	1	1
112	46	89.13	41	39/41 (95%)	0.94	1	1	0.8	0.86
113	46	95.65	44	43/44 (98%)	1	0.9	0.97	1	0.93
114	46	97.83	45	45/45 (100%)	1	1	1	1	1
115	46	91.3	42	41/42 (98%)	1	0.88	0.97	1	0.92
116	46	76.09	35	33/35 (94%)	1	0.71	0.93	1	0.8
119	46	91.3	42	42/42 (100%)	1	1	1	1	1
120	46	100	45	44/45 (98%)	0.97	1	1	0.91	0.94
122	46	95.65	44	41/44 (93%)	0.97	0.8	0.94	0.89	0.8
123	46	89.13	41	40/41 (98%)	1	0.9	0.97	1	0.93
124	46	95.65	44	40/44 (91%)	0.91	0.89	0.97	0.73	0.74
125	46	95.65	44	41/44 (93%)	1	0.67	0.92	1	0.76
126	46	97.83	45	45/45 (100%)	1	1	1	1	1
127	46	58.7	27	26/27 (96%)	0.95	1	1	0.83	0.89
128	46	97.83	45	45/45 (100%)	1	1	1	1	1
129	46	91.3	42	41/42 (98%)	0.97	1	1	0.89	0.93
132	46	95.65	44	41/44 (93%)	0.94	0.9	0.97	0.82	0.81
133	46	86.96	40	40/40 (100%)	1	1	1	1	1
134	46	93.48	43	42/43 (98%)	0.97	1	1	0.9	0.93
135	46	93.48	43	43/43 (100%)	1	1	1	1	1
136	46	91.3	42	39/42 (93%)	0.91	1	1	0.75	0.81
138	46	89.13	41	38/41 (93%)	0.91	1	1	0.75	0.81
139	46	91.3	42	41/42 (98%)	0.97	1	1	0.89	0.93
141	46	91.3	42	40/42 (95%)	0.94	1	1	0.82	0.87
143	46	91.3	42	41/42 (98%)	0.97	1	1	0.9	0.93
144	46	93.48	43	42/43 (98%)	0.97	1	1	0.91	0.94
145	46	93.48	43	41/43 (95%)	0.94	1	1	0.82	0.87
146	46	89.13	41	41/41 (100%)	1	1	1	1	1
147	46	93.48	43	43/43 (100%)	1	1	1	1	1
149	46	93.48	43	43/43 (100%)	1	1	1	1	1
150	46	93.48	43	43/43 (100%)	1	1	1	1	1
151	46	93.48	43	41/43 (95%)	1	0.8	0.94	1	0.86
152	46	93.48	43	43/43 (100%)	1	1	1	1	1
153	46	97.83	44	42/44 (95%)	0.94	1	1	0.82	0.87
155	46	71.74	33	33/33 (100%)	1	1	1	1	1
156	46	93.48	43	43/43 (100%)	1	1	1	1	1
157	46	95.65	44	42/44 (95%)	0.94	1	1	0.82	0.87
159	46	97.83	44	44/44 (100%)	1	1	1	1	1
160	46	97.83	44	44/44 (100%)	1	1	1	1	1
161	46	84.78	39	39/39 (100%)	1	1	1	1	1
162	46	86.96	40	38/40 (95%)	0.97	0.86	0.97	0.86	0.83
163	46	93.48	43	43/43 (100%)	1	1	1	1	1
164	46	93.48	43	43/43 (100%)	1	1	1	1	1
165	46	82.61	38	36/38 (95%)	0.94	1	1	0.78	0.84
167	46	84.78	39	37/39 (95%)	0.94	1	1	0.78	0.84
168	46	95.65	43	37/43 (86%)	0.83	1	1	0.57	0.64
170	46	93.48	42	39/42 (93%)	0.91	1	1	0.7	0.78
172	46	93.48	43	38/43 (88%)	0.89	0.88	0.97	0.64	0.66
173	46	95.65	44	44/44 (100%)	1	1	1	1	1
175	46	100	45	43/45 (96%)	0.97	0.9	0.97	0.9	0.87
177	46	71.74	33	30/33 (91%)	0.89	1	1	0.67	0.74
178	46	100	45	42/45 (93%)	0.91	1	1	0.77	0.83
179	46	69.57	32	32/32 (100%)	1	1	1	1	1
180	46	89.13	41	39/41 (95%)	0.94	1	1	0.8	0.86
183	46	86.96	40	36/40 (90%)	0.91	0.88	0.97	0.7	0.71
184	46	73.91	34	32/34 (94%)	0.93	1	1	0.75	0.82
186	46	89.13	41	38/41 (93%)	0.91	1	1	0.73	0.8
187	46	84.78	39	37/39 (95%)	0.94	1	1	0.78	0.84
188	46	89.13	41	38/41 (93%)	0.91	1	1	0.7	0.78
189	46	80.43	37	37/37 (100%)	1	1	1	1	1
190	46	84.78	38	38/38 (100%)	1	1	1	1	1
191	46	86.96	40	38/40 (95%)	1	0.75	0.94	1	0.83
192	46	69.57	32	31/32 (97%)	1	0.83	0.96	1	0.89
194	46	71.74	33	31/33 (94%)	0.93	1	1	0.75	0.82
198	46	97.83	45	40/45 (89%)	0.86	1	1	0.67	0.73
199	46	80.43	37	32/37 (86%)	0.84	1	1	0.55	0.63

Fig 6

Descriptive Statistics Run 24 cIQc PR

Test lab name	total n	% scorable	pairwise complete observations	concordance with reference (%)	sensitivity	specificity	PPV (positive predictive value)	NPV (negative predictive value)	Cohen's kappa
101	46	93.48	43	42/43 (98%)	0.97	1	1	0.93	0.95
102	46	89.13	41	40/41 (98%)	0.97	1	1	0.92	0.94
103	46	95.65	43	41/43 (95%)	0.94	1	1	0.86	0.89
105	46	82.61	38	37/38 (97%)	0.96	1	1	0.91	0.93
106	46	89.13	41	41/41 (100%)	1	1	1	1	1
107	46	84.78	39	39/39 (100%)	1	1	1	1	1
108	46	84.78	39	39/39 (100%)	1	1	1	1	1
109	46	84.78	39	39/39 (100%)	1	1	1	1	1
111	46	91.3	42	41/42 (98%)	1	0.92	0.97	1	0.94
112	46	76.09	35	33/35 (94%)	0.92	1	1	0.82	0.86
113	46	91.3	42	40/42 (95%)	0.93	1	1	0.86	0.89
114	46	97.83	45	44/45 (98%)	1	0.93	0.97	1	0.95
115	46	95.65	44	44/44 (100%)	1	1	1	1	1
116	46	95.65	44	44/44 (100%)	1	1	1	1	1
119	46	76.09	35	34/35 (97%)	0.96	1	1	0.9	0.93
120	46	91.3	42	42/42 (100%)	1	1	1	1	1
122	46	89.13	41	40/41 (98%)	0.97	1	1	0.92	0.94
123	46	82.61	37	32/37 (86%)	0.81	1	1	0.69	0.71
124	46	97.83	44	44/44 (100%)	1	1	1	1	1
125	46	91.3	42	42/42 (100%)	1	1	1	1	1
126	46	93.48	43	38/43 (88%)	0.83	1	1	0.72	0.75
127	46	95.65	43	42/43 (98%)	0.97	1	1	0.93	0.95
128	46	91.3	42	41/42 (98%)	1	0.92	0.97	1	0.94
129	46	93.48	43	42/43 (98%)	1	0.92	0.97	1	0.94
132	46	93.48	43	43/43 (100%)	1	1	1	1	1
133	46	91.3	42	37/42 (88%)	0.83	1	1	0.72	0.75
134	46	95.65	44	43/44 (98%)	1	0.93	0.97	1	0.95
135	46	93.48	43	43/43 (100%)	1	1	1	1	1
136	46	93.48	43	42/43 (98%)	0.97	1	1	0.93	0.95
139	46	91.3	42	41/42 (98%)	0.97	1	1	0.93	0.95
141	46	93.48	43	43/43 (100%)	1	1	1	1	1
143	46	93.48	43	40/43 (93%)	0.9	1	1	0.81	0.84
145	46	93.48	43	42/43 (98%)	0.97	1	1	0.93	0.95
146	46	89.13	41	41/41 (100%)	1	1	1	1	1
147	46	93.48	43	43/43 (100%)	1	1	1	1	1
149	46	69.57	32	31/32 (97%)	0.96	1	1	0.89	0.92
150	46	91.3	42	41/42 (98%)	1	0.92	0.97	1	0.94
151	46	89.13	41	40/41 (98%)	0.96	1	1	0.93	0.94
152	46	93.48	43	43/43 (100%)	1	1	1	1	1
153	46	78.26	35	31/35 (89%)	0.92	0.78	0.92	0.78	0.7
155	46	89.13	41	41/41 (100%)	1	1	1	1	1
156	46	76.09	35	33/35 (94%)	0.96	0.89	0.96	0.89	0.85
157	46	84.78	38	34/38 (89%)	0.85	1	1	0.75	0.78
159	46	76.09	35	32/35 (91%)	0.88	1	1	0.75	0.8
160	46	71.74	33	31/33 (94%)	0.96	0.89	0.96	0.89	0.85
161	46	91.3	42	42/42 (100%)	1	1	1	1	1
162	46	78.26	35	31/35 (89%)	0.88	0.9	0.96	0.75	0.74
163	46	82.61	38	37/38 (97%)	1	0.9	0.97	1	0.93
164	46	84.78	39	38/39 (97%)	0.97	1	1	0.9	0.93
165	46	82.61	38	36/38 (95%)	1	0.8	0.93	1	0.85
167	46	80.43	37	32/37 (86%)	0.85	0.9	0.96	0.69	0.69
168	46	91.3	41	38/41 (93%)	0.9	1	1	0.8	0.84
170	46	95.65	43	39/43 (91%)	0.87	1	1	0.75	0.79
172	46	93.48	42	41/42 (98%)	0.97	1	1	0.92	0.94
173	46	86.96	40	34/40 (85%)	0.79	1	1	0.65	0.68
175	46	84.78	38	34/38 (89%)	0.86	1	1	0.71	0.76
177	46	89.13	41	37/41 (90%)	0.86	1	1	0.76	0.79
178	46	82.61	37	31/37 (84%)	0.81	0.9	0.96	0.64	0.63
179	46	95.65	44	44/44 (100%)	1	1	1	1	1
183	46	76.09	35	33/35 (94%)	0.92	1	1	0.83	0.87
184	46	71.74	33	32/33 (97%)	1	0.89	0.96	1	0.92
186	46	89.13	40	36/40 (90%)	0.86	1	1	0.73	0.77
187	46	80.43	37	33/37 (89%)	1	0.6	0.87	1	0.69
188	46	89.13	40	38/40 (95%)	0.93	1	1	0.83	0.87
189	46	69.57	32	31/32 (97%)	0.96	1	1	0.89	0.92
190	46	80.43	37	37/37 (100%)	1	1	1	1	1
191	46	82.61	38	34/38 (89%)	0.96	0.7	0.9	0.88	0.71
192	46	67.39	31	29/31 (94%)	0.91	1	1	0.8	0.84
194	46	82.61	38	33/38 (87%)	0.82	1	1	0.67	0.71
198	46	95.65	44	44/44 (100%)	1	1	1	1	1
199	46	71.74	33	31/33 (94%)	0.92	1	1	0.8	0.85