Assessor's report for CIQC Run 22: ER, PR and HER2

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Assessment done Tues May 8, 2012, at Vancouver General Hospital

Overview

This run was a departure from previous CIQC runs in that you were asked to stain a TMA consisting not of formalin-fixed paraffin-embedded tissue samples, but of cell line samples. Heather Neufeld of the University of Saskatchewan selected 9 breast cancer cell lines, including lines expressing and not expressing ER, PR and HER2, grew them up in bulk, and prepared formalin-fixed paraffin-embedded pellets from these cell lines. The microarray consisted of two cores from each of these nine cell lines.

The advantages of cell lines over tissue samples include renewability and the ability to do very detailed characterization of the cell line samples. RT-PCR levels for mRNA expression, and HER2 FISH have been done on these samples, and offer an independent method of assessing ER, PR and HER2 status in these samples. Although these assessments are also possible on tissue samples, the cost of doing this on 40 samples for every CIQC run is prohibitive at present. Disadvantages of using cell lines include the inability to calculate test sensitivity and specificity, and negative and positive predictive values, which requires that you have tested a sufficiently large set of clinical samples that are representative of what you would encounter in practice. As well, the specimen handling for the cell lines is not identical to that used for clinical samples, and criteria for assessment of HER2 membranous staining in cell line samples are not established.

One advantage of cell lines is that it may make it possible to allow each lab in Canada to have their own cell line TMA in house, from which they can cut sections for regular (e.g. weekly) monitoring of ER, PR and HER2 staining, to allow them to detect subtle drift in staining results. New batches of Ab could also be assessed with these TMAs. In this way, the cell line TMAs could complement the three times yearly tissue-based TMA external proficiency testing that does allow calculation of statistical indicators reflecting performance across a series of clinical samples (test sensitivity, specificity, etc.), which is a unique aspect of the CIQC program. This strategy is evolving, as we assess the performance of the cell line TMAs, and

we would be interested in your feedback on whether such a resource (i.e. a TMA block for your own laboratory, consisting of cell line samples, that would allow you to cut sections as needed for internal quality assessment in your lab) would be of potential value to you.

With regards to Run 22, the results by participating laboratories were very good, overall. Results of our re-assessment of the slides in Vancouver largely confirmed your assessments. One problem with this particular array was that the first core fell off many of the slides, and this did create alignment/result entry problems, which we were able to correct on review.

ER: Three of the cell lines (cores 7, 8, 13, 14 and 17, 18) were ER positive, to varying degrees, with cores 7 and 8 showing the weakest staining. The immunostaining results correlated with the mRNA levels: these levels are provided in the last column of the table, ESR1 (the gene designation for estrogen receptor), where the log of mRNA expression levels, relative to the mean, are provided. Cores 13, 14, 17 and 18 have the highest expression, with lower ER mRNA expression in samples 7 and 8. Three labs (122, 129, 151) showed false positive staining of ER negative cases. Two labs (148 and 199) showed a few positive cells at one edge of sample 16; we are uncertain of the significance of this finding but suspect that these may have been cells which originated from core 17 and were carried over during sectioning. Lack of sensitivity, with false negative results (particularly for the weakly staining cores 7 and 8) were seen for four labs (124, 141, 168, and 187), with an additional two labs (172 and 198) showing staining of only one of cores 7 or 8, which were duplicate samples from the same weakly ER positive cell line culture. Lab 134 showed very weak staining of cores 7 and 8 compared to the other laboratories participating in this run, indicating borderline sensitivity. Other issues noticed by the assessors included very dark nuclear counterstaining by labs 122, 141 and 199, which could potentially interfere with interpretation.

Lab /Core	101	102	103	105	106	107	109	111	112	113	114	115	116	117	118	119	122	123	124	125	126	127	128	129	132	134	135	138	139	141	143	144	145	146	147	148	149	150	151	152	153	155	156	157	159	160	161	162	163	164	165	167	168	170	172	175	177	178	179	180	183	184	186	187	189	190	191	192	194	196	198	199	ESR1
1	U	U	U	U	U	U	U	U	N	N	U	U	U	U	U	U	P	N	U	U	N	U	U	U	U	N	U	U	U	U	U	N	U	N	N	N	U	U	P	U	N	U	U	N	U	N	N	N	N	N	U	N	N	N	U	U	N	U	U	U	U	U	U	N	U	U	U	U	U	N	N	-6.9
2	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	P	N	N	N	U	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-6.9
3	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	U	N	N	N	N	N	U	U	U	N	N	P	N	N	N	N	N	N	N	N	N	N	N	U	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-0.38
4	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-0.38
5	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-3.7
6	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-3.7
7	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	N	P	P	P	P	P	P	P	P	P	P	N	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	N	P	N	P	P	P	P	P	P	P	N	P	P	P	P	P	P	P	N	P	P	0.7
8	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	N	P	P	P	P	P	P	P	P	P	P	N	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	N	P	P	P	P	P	P	P	P	P	N	P	P	P	P	P	P	N	P	P	0.7
9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-5.8
10	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-5.8
11	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-7.05
12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	P	N	N	N	N	N	N	N	U	N	N	N	N	U	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-7.05
13	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	U	P	P	P	P	P	P	P	U	U	U	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	U	U	N	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	3.16
14	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	N	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	3.16
15	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-4.3
16	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	-4.3
17	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	2.4
18	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	2.4

ER

Run 22 cIQc

- Postivie
- Negative
- Unsat

PR: Results for PR staining were superior to ER. The same cores that were ER positive were PR positive, but cores 7 and 8, which were weakly ER positive were more strongly positive for PR. The mRNA levels for PR correlated with immunoexpression, as for ER. Non-specific PR staining was only seen with labs 125 and 186 (with staining of a single PR negative case by each lab). Labs 165 and 199 showed positive staining of a few cells in a single core, the significance of which is uncertain (and may represent a contaminant, as noted in the discussion about ER staining). Impressively, no labs showed lack of PR staining sensitivity. Lab 125 had very dark nuclear counterstaining, that could potentially interfere with interpretation.

Lab /Cores	101	102	103	105	106	107	109	111	112	113	114	115	116	117	118	119	122	123	124	125	126	127	128	129	132	134	135	138	139	141	143	145	146	147	149	150	151	152	153	155	156	157	159	160	161	162	163	164	165	167	168	170	172	175	177	178	179	183	184	186	187	189	190	191	192	194	196	198	199	PGR
1	U	U	U	U	U	U	U	U	N	N	U	U	U	U	N	N	N	N	N	U	N	U	U	U	U	U	N	U	U	U	U	U	N	N	U	U	U	U	U	U	U	N	U	N	N	N	N	N	N	N	N	N	N	U	U	N	U	U	U	U	U	U	U	U	U	N	N	N	-11.7
2	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-11.7
3	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	U	U	N	N	U	N	N	N	N	N	N	N	N	N	N	N	U	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-1.4
4	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-1.4
5	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-8.07
6	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-8.07
7	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	2.65
8	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	2.65
9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-10
10	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-10
11	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	-9.8
12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	U	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	U	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	-9.8
13	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	U	P	P	P	P	P	U	U	P	P	P	P	P	P	P	P	P	P	P	P	P	U	U	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	-0.94
14	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	-0.94
15	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	N	-8.83
16	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	P	N	N	N	N	N	N	N	N	N	P	-8.83
17	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	U	P	P	P	P	P	P	P	P	P	P	P	P	P	P	2.65
18	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	U	P	P	P	P	P	P	P	P	P	P	P	P	P	P	2.65

PR

Positive

Negative

Unsat

Run 22 cIQc

HER2: Assessment of HER2 membranous staining in isolated cells was challenging, and represents a departure from what we do in clinical practice. As such, assessment of HER2 staining in these cores is not a good test of interpretive abilities. Nonetheless, performance of HER2 staining was excellent, with no false positive or false negative results (if 2+ staining results are considered indeterminate and neither a positive or negative result)! While there was some variability from lab to lab, the six cores (cores 5,6,7,8,15,16) from HER2 amplified/over-expressing lines were all considered 3+ or 2+ positive, while none of the HER2 non-amplified/overexpressing lines were 3+. Labe 113 showed high background staining, and cytoplasmic staining of tumor cells.

Lab /Cores	101	102	103	105	106	107	109	110	111	112	113	114	115	116	117	118	119	123	124	125	126	127	129	135	139	145	147	149	150	151	152	153	155	156	157	160	161	162	164	167	170	175	179	186	187	189	190	191	194	198	199	ERBB2
1	U	U	U	U	U	U	U	U	U	N	2	U	U	U	U	U	N	N	N	N	N	U	U	N	N	U	N	1	N	U	U	U	U	U	N	1	N	N	N	N	N	U	U	U	U	U	U	U	U	N	N	0.9
2	N	N	N	N	N	N	N	N	N	N	2	N	N	N	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	N	N	N	N	N	1	1	N	N	N	N	N	N	0.9
3	N	N	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	U	U	N	N	N	N	1	N	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	-3
4	N	N	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	1	N	N	1	N	N	N	N	N	N	N	N	-3
5	3	3	3	3	3	3	3	U	3	3	3	3	3	3	3	2	2	2	3	2	3	3	3	3	2	3	3	3	2	3	2	3	3	3	3	3	2	3	3	3	3	3	2	3	3	3	3	3	3	3	3	7.79
6	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	2	2	3	2	3	3	3	3	2	3	3	3	2	3	2	3	3	3	3	3	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3	7.79
7	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	7.29
8	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	7.29
9	N	N	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	N	N	N	1	N	N	N	2	N	N	1	N	N	N	N	N	1	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	1.49
10	N	1	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	N	N	N	1	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	1.49
11	N	N	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	N	N	N	N	2	N	N	N	N	N	U	N	N	N	N	N	N	N	N	N	1	N	N	N	1	N	N	N	N	N	1	N	0.4
12	N	N	N	N	N	N	N	N	N	N	1	N	N	N	N	N	N	N	N	N	N	N	N	U	N	N	U	U	N	1	N	N	N	N	N	N	N	N	N	1	N	N	N	1	1	N	N	N	N	1	N	0.4
13	N	N	1	1	N	N	1	N	N	N	2	N	1	N	1	N	N	N	N	N	N	N	1	U	N	N	U	U	N	1	N	N	N	1	N	2	N	N	1	1	N	N	1	1	1	N	N	1	1	1	1	1.4
14	N	N	1	1	N	1	1	N	N	N	2	N	N	N	N	N	N	1	N	N	N	N	2	N	N	N	1	1	N	1	N	N	1	1	N	1	N	N	N	1	1	U	1	1	1	N	N	N	1	1	N	1.4
15	3	3	3	3	2	3	3	3	3	3	3	3	3	3	3	3	3	2	2	3	3	3	3	3	2	3	3	3	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	7.29
16	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	2	3	2	3	3	3	3	3	3	2	3	3	3	2	3	3	3	3	3	3	3	3	3	3	3	3	2	2	3	3	3	3	3	3	3	3	7.29
17	N	2	2	1	1	2	1	1	1	1	2	1	U	N	U	N	1	1	1	1	1	1	2	2	1	1	2	2	1	2	1	N	1	1	1	2	1	1	1	2	1	N	2	2	2	1	1	U	1	2	2	2.69
18	N	2	1	1	1	1	1	N	1	1	2	1	1	1	U	N	1	1	N	1	1	1	2	2	1	N	2	2	1	U	1	N	1	2	1	2	1	1	1	2	1	N	2	2	2	1	1	1	2	1	2	2.69

HER2

Negative

1+

2+

3+

Unsat

Run 22 cIQc

Thank you for your participation in CIQC. We look forward to continuing to improve the service we are able to offer, working with you and the Canadian Association of Pathologists - Association canadienne des pathologistes. This is our first atttempt to use cell lines for breast biomarker proficiency testing and the results are encouraging, in that it does appear that they can identify suboptimal staining results.

submitted on behalf of CIQC, on May 26, 2012

Blake Gilks MD FRCPC

Protocols

Laboratories	101	102	103	105	106	107	109	110	111	112	113	114	115	116
Clone	SP3	SP3	4B5	4B5	4B5	4B5	4B5	SP3	4B5	4B5	Polyclonal	SP3	4B5	SP3
Dilution	1:50	1/500	PRE	Neat	Pre-dilute	pre-diluted RT, 24 min	RTU	1:300	PREDILUTE	READY TO USE	1/100	1/50	PREDILUTED	1/100
Supplier	NeoMarkers	Labvision	Ventana	Ventana	Ventana	Ventana	Ventana Medical	Thermo/ Fisher	VENTANA	VENATNA	DAKO	Thermo Fisher	VENTANA	Thermo Scientific
Antigen Retrieval	CC1	Dako FLEX High TRS	CC1	CC1 standard	Ventana CC1 (Tris-based pH 8.5)	Ultra CC1 64 min	CC1	Bull's Eye Decloaker	CC1 36 MINUTES	CC1	Microwave/ Citrate	CC1 32min	CC1	CC1 -court
Detection System	Opti-view	Envision+ Rabbit	VEntana as per kit	DABMAP-ventana	Ventana UltraView	Ultraview DAB	Ultraview Universal DAB	DAKO Rabbit Envision +	ULTRAVIEW	ultraVIEW	Iview	Optiview Ventana	iVIEW DAB	UltraView DAB Ventana
Enhancement	no	CuSO4	none	heat	None	none	Copper	CUSO4	COPPER	COPPER	Copper Sulphate	oView Copper	COOPER	no
Chromagen	DAB	DAB+	Ventana as per kit	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB
Protocols	HER2	Run 22 cIQc												

Laboratories	117	118	119	123	124	125	126	127	129	135	139	145	147
Clone	sp3	4B5	C-ERB2	4B5	4B5	4B5	SP3	4B5	Cerb b2 A0485	polyclonal Dako A0485	4B5	SP3	Polyclonal
Dilution	1:200	RTU	1/1000	pre-dilute	Prediluted	predilute	1:300	PREDILUTE	1:600	1:700	ready use	1/600 from concentrate	1:300
Supplier	neomarkers	Ventana	DAKO	Ventana Medical Systems	Ventana	Roche	Thermo	VENTANA	DAKO	Dako	Ventana	CELL MARQUE	Dako
Antigen Retrieval	CC1	sCC1	HIER/CC1	EDTA HIER	CC1 4 min	CC1 mild	ph10.0 steam	ULTRA CC1	BOND ER1 LOW pH	citrate buffer PH6	30 min.	30 mins CC1	ER1 (Citrate, pH6)
Detection System	ULTRA VIEW	DABmap	ULTRA-VIEW	polymer	Kit DAB View	Roche ultraView Universal DAB	Envision Plus	Benchmark Ultraview	BOND REFINE DETECTION KIT	polymer	Iviewdab	XT ULTRAVIEW DAB v3	Leica Refine Polymer
Enhancement	CUSO4	Copper	---	copper sulphate	no	Copper	None	N/A	NO	n/a	no	VENTANA	N/A
Chromagen	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB

Laboratories	149	150	151	152	153	155	156	157	160	161	162	164
Clone	A0485	SP-3	MDA-175	4B5	SP3	anti Her-2-neu (4B5)	4B5	4B 5	A0485	Rabbit anti-human HER2 protein	4B5	4B5
Dilution	1:500	1:100	1:250	Pre-diluted	1/100	none	pre-diluted	PRE DILUTED	1/700	RTU	Ready to use	predilute
Supplier	Dako	Neomarkers	DAKO	Ventana	Thermo Fisher(neomarker)	Ventana	Ventana	VENTANA	Dako	DAKO autostainer plus LINK	Ventana	Ventana
Antigen Retrieval	PT Link low pH 98 C 20 min	CC1, heat	PH6.0 20 MIN	CC1 (standard)	CC1 Court	CC1	CC1	CC1 60 MIN.	EDTA pH8	Herceptest epitope retrieval solution	CC1 Mild	CC1
Detection System	Envision Flex 20	ultraview	BOND REFINE POLYMER	iVIEW	Ultraview DAB	Ultraview dab	ibiew dab	Benchmark Ultraview	Ventana Ultraview	Herceptest visualisation reagent	UltraView	UltraView
Enhancement	none	copper	NONE	Copper sulfate	Ultraview Cooper	Iview Copper	-	YES	No	no		copper
Chromagen	DAB	DAB	DAB	DAB	DAB	Dab	Dab	YES	DAB	DAB	UltraView DAB	DAB

Laboratories	167	170	175	179	186	187	189	190	191	194	198	199
Clone	A0485	Her 2 protein	4B5	CB11	Polyclonal	Cerb-B2	4B5	SP3	4B5	4B5	SP3	AO485
Dilution	1/1700	ready to use	1:1	1:250	1:200	1:750	Predilute	RABBIT	RTU	Predilute	1/100	1:800
Supplier	Dako	Dako	Ventana	Leica	Dako	Dako	Ventana Medical Systems	1:50	Roche	Ventana	Fisher-Thermo Scientific	DAKO
Antigen Retrieval	Yes (CC1)	citrate buffer0.1 mol/L	Heat retreval	Citrato pH6,0+EDTA pH9,0(1:1)	HIER 20' EDTA buffer	Ph 9.0 Envision Flex	CC1	THERMO SCIENTIFIC	CC2 mild	CC1	Citrate-pH 6.0	HIER 20 min
Detection System	Ultra View DAB Ventana	Hercept test dako	DAB	Novolink	Bond refine detection kit	Envision Flex+	UltraView DAB	CCI 30 MIN	ultraview (Roche)	Avidin/Biotin	Polymer-Biogenex	Leica DAB
Enhancement	Yes (copper)	no	Blocker A, Blocker B	Hematoxilin	n/a	None	Copper	VENTANA	none	Copper	Copper Sulphate	No
Chromagen	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB

Laboratories	101	102	103	105	106	107	109	111	112	113	114	115	116	117	118	119
Clone	SP1	SP1	SP1	SP1	6F11	SP1	SP1	SP1	SP1	SP1	SP1	SP1	SP1	SP1	SP1	SP1
Dilution	1:50	1/50	Pre	1:50	1:75	pre-diluted 37degrees Celcius, 16 min	RTU	PREDILUTE	READY TO USE	Pre-Dilute	1/50	PREDILUTED	RTU	prediluted	RTU	pre diluted
Supplier	NeoMarkers	Dako	Ventana	Thermo scientific	Vector	Ventana	Ventana Medical	VENTANA	VENTANA	Ventana	Thermo Fisher	VENTANA	Ventana	Ventana	Ventana	VENTANA
Antigen Retrieval	CC1	Dako Flex High TRS	CC1 Standard	CC1 standard	0.1M Tris-HCl, pH 9.0	Ultra CC1 36 min	CC1	CC1 36 MINUTES	CC1	CC2	CC1 32min	CC1	CC1- standard	CC1	sCC1	HIER/CC1
Detection System	Opti-view	Envision+ Rabbit	Ventana as per kit	Ultramap anti-Rb HRP ventana	Elite Avidin/Biotin	Ultraview DAB	UltraView Universal DAB	ULTRAVIEW	ultraView	Iview	OptiView Ventana	iVIEW DAB	UltraView DAB Ventana	UltraView DAB	DABmap	ULTRA-VIEW
Enhancement	no	CuSO4	None	none	None	none	Copper	COPPER	COPPER	Copper sulphate	oView Copper	COOPER	no	CuSO4	Copper	---
Chromagen	DAB	DAB+	Ventana as per kit	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB

Laboratories	122	123	124	125	126	127	128	129	132	134	135	138	139	141	143	144
Clone	6F11	SP1	SP1	SP1	SP1	SP1	ER (SP1)	6F11	6F11	SP 1	6F11	SP1	SP1	6F11	SP1	SP1
Dilution	RTU	pre-dilute	1/100	predilute	1:600	PREDILUTE	PREDILUTED	1:125	1:80	predilute	1:100	RTU	ready use	pre-dilute	NO	neat
Supplier	Leica Microsystems	Ventana Medical Systems	Cell marque	Roche	Thermo	VENTANA	VETANNA	Nova Castra	vector	Ventana/ Roche	Leica	Dako	Ventana	Leica	CONFIRM VENTANA	Ventana
Antigen Retrieval	ER2 PH 9.0/20 MIN	EDTA buffer HIER	CC1 30 min	ER2-20	pH6.0 PT module	ULTRA CC1	CC1 MILD 30min.	BOND ER2 High pH	high pH- flex target ret	citrate buffer	Citate buffer PH9	High pH	30 min.	pH6 Citrate buffer	CC1 STANDART (60')	CC1 mild, 30 min
Detection System	POLYMER REFINE	polymer	Kit DAB view	Bond Refine Detection	Quanto detection system	Benchmark Ultraview	UNIVERSAL DAB KIT	BOND REFINE DETECTION KIT	Envision Flex	I View	polymer	HRP Flex	iviewdab	LSAB2	IVIEW DAB DETECTION KIT	Ultraview
Enhancement	BOND DAB ENHANCER	copper sulphate	no	Bond DAB Enhancer	None	N/A	COPPER	NO	none	NO	n/a	mouse Linker	no	Copper Sulphate	NO	copper
Chromagen	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB

Laboratories	145	146	147	148	149	150	151	152	153	155	156	157	159	160	161
Clone	SP1	SP1	6F11	SP1	SP1	SP-1	6F11	SP1	SP1	Er (SP1)	SP1	SP-1	EP1	SP1	EP1
Dilution	1/10 from pre-diluted	RTU	1:200	RTU	RTU	r/u	1:80	Pre-diluted	ready to use	none	pre-diluted	PRE-DILUTED	prediluted	pre-diluted	RTU
Supplier	VENTANA	Dako	NCL	Ventana	Dako 1R151	ventana	NCL	Ventana	Ventana	Ventana	Ventana	VENTANA	DAKO	Ventana	DAKO autostainer plus Link
Antigen Retrieval	30 mins CC1	FLEX TRS High	ER2 (EDTA, pH9)	Ultra CC1 36	PT Link high pH 98 C 20 min	CC1, heat	ph9.0 20 min	CC1 (mild)	CC1 court	CC1	CC1	CC1 30 MIN.	High pH	EDTA pH8	High EDTA Buffer TRIS
Detection System	XT ULTRA VIEW DAB v3	EnVision FLEX Peroxydase/HRP	Leica Refine Polymer	Ultraview DAB	Envision Flex 20	ultraview	BOND REFINE /POLYMER	iVIEW	Ultraview DAB	Ultraview dab	iview dab	BENXHMARK ULTRAVIEW	FLEX	Ventana Ultraview	Envision FLEX
Enhancement	VENTANA	None	N/A	n/a	None	copper	NONE	Copper sulfate	Ultraview cooper	Iviewcopper	-	YES	no	No	no
Chromagen	DAB	Substrate Working Solution (DAB)	DAB	DAB	DAB	DAB	DAB	DAB	DAB	Dab	Dab	YES	DAB	DAB	DAB
							Protocols	ER	cIQc	Run 22					

Laboratories	162	163	164	165	167	168	170	172	175	177	178	179	180	183	184
Clone	SP1	SP1	SP1	SP1	SP1	SP1	sp1	SP1	SP1	6F11	SP1	6F11	SP1	SP1	ER: ID5 & ER-2-123
Dilution	1:100	prediluted	predilute	NIL	PrÃ©-dilution par la Cie	RTU	ready to use	pre-diluted by dako	1:1	1:50	PREDILUTE	1:150	prediluted	predilute	RTU
Supplier	Thermo Scientific	benchmark ventana	Ventana	VENTANA	Ventana	Dako	Dako	dako	Ventana	Novocastra	Ventana	Leica	Ventana	Ventana	Dako K4071
Antigen Retrieval	CC1 mild	HIER	CC1	CC1	Yes (CC1)	High pH	tris/Edta buffer ph9	97C 20 min pH9	Heat retreval	CC1	CC1 MILD	Citrato pH6,0	CC1 mild	CC!	citrate buffer, low pH
Detection System	UltraView	peroxydase	UltraView	ULTRAVIEW	Ultra View DAB Ventana	Envision Flex +	EnVision Flex	envision flex +	DAB	Ventana Ultraview	Ultraview DAB	Novolink	BMK iView DAB	Ultaview	EnVision +
Enhancement	UltraView Amplifier	Copper	copper	ULTRAVIEW	Yes (copper)	None	no	no	I-View Copper	Yes	none	Hematoxilin	no	none	none
Chromagen	UltraView DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB +

Laboratories	101	102	103	105	106	107	109	110	111	112	114	115	116	117	118	119	122	123	124	125	126	127	128	129	132	134	135	138	139	140	141	145	146	147	148	150	151	152	153	155	156	157	158	160	161	162	163	164	165	167	168	170	172	175	177	178	179	183	184	186	187	188
Clone	15	15	100	PgR635	1:294	PgR 1:294	PgR1:294	100	100	Polyclonal	15	100	clone 15	100	100	15	15	15	100	100	635	100	PR(E2)	15	15	1: E2	15	PgR 635	100	PgR 636	100	100	SP1	15	PgR636	100	1A6	100	100	Pr (1E2)	E2	E 2	PgR636	100	PgR636	E2	100	100	100	100	PgR636	PgR36	pgr 636	100	Pgr 636	100	SP42	100	PgR 1:294	PR88	PgR 636	100
Dilution	1:100	1:125	Pre	1:50	1:1250	1:50.37 serious, 32 min	1:50	PREDILUTE	READY TO USE	1:40	1:25	PREDILUTED	1:100	prediluted	RTU	pre-diluted	RTU	1:50	Predilated	0.4 ml predilute	1:500	PREDILUTE	PREDILUTED	1:400	1:200	Predilute	1:400	RTU	ready use	pre-dilute	NO	1:4 from pre-diluted	RTU	1:800	RTU	ntu	1:200	Pre-diluted	Ready to use	none	pre-diluted	PRE-DILUTED	predilutedd	pre-diluted	RTU	Ready to use	predilutedd	predilute	NIL	Pre-RO-dilution par la Cie	RTU	ready to use	pre-diluted by dako	1:1	1:100	PRE-DILUTE	1:100	predilute	RTU	1:100	1:50	Predilute
Supplier	Novocastra	Leica	Ventana	Dako	Dako	Dako	Dakocy-tomation	VENTANA	VENTANA	DAKO	Novocastra	VENTANA	Leica	Ventana	Ventana	VENTANA	Leica Microsystems	Vector	Ventana	Roche	Dako	VENTANA	VETANNA	NOVA CASTRA	vector	Ventana/ Roche	Leica	Dako	Ventana	Dako	CONFIRM VENTANA	VENTANA	Dako	NCL	Dako	ventana	NCL	Ventana	Ventana	Ventana	Ventana	VENTANA	DAKO	Ventana	DAKO autostainer plus link	Ventana	ventana benchmark	Ventana	VENTANA	Ventana	Dako	Dako	dako	Ventana	Dako	Ventana	Spring	ventana	Dako K4071	Biogenex	Dako	Ventana Medical Systems
Antigen Retrieval	CC1	Dako Flex High TRS	CC1 mild	CC1 standard	0.1M Tris-HCl pH 9.0	Ultra CC1 64 min	CC	CC1 36 MINUTES	CC1	Pressure cooker/Citrate	CC1 32min	CC1-VENTANA	CC1 -standard	CC1	pCC1	HIER/CC1	ERE1 PH 9.0/20 MIN	EDTA HIER	CC1 30 min	ERC-30	pH6.0 PT module	ULTRA CC1	CC1 MILD 20min.	BOND ERZ High pH	high pH- flex target ret	citrate buffer	citrate-buffer PH6	high pH	30 min.	pH6 Citrate buffer	CC1 STANDART (BT)	30 mins CC1	FLEX TRS High	ERZ (EDTA, pH9)	PT Link high pH 98 C 20 min	CC1, heat	PH6.0 20 MIN	CC1 (mild)	CC1 Court	CC1	CC1	CC1.30 MIN.	High pH	EDTA pH9	High EDTA buffer TRS	CC1 Mild	HIER	CC1	CC1	Hes (CC1)	High pH	tris/Edta buffer pH9	STC 20min pH6	Heat retrieval	CC1	CC1 MILD	Citrate pH6, 0-EDTA pH9 (00:1)	CC1	citrate buffer, low pH	HIER 20' EDTA buffer	pH 6.0 Citric Acid	CC1
Detection System	Dab-view	Envision+ Mouse	Ventana as per kit	Ultramap anti-Ms HRP ventana	Elite Avidin/ Biotin	Ultraview DAB	Ultraview Universal DAB	ULTRAVIEW	VIEW	LSAB Plus	Optiview Ventana	VIEW DAB	ultraview DAB Ventana	Ultraview DAB	DAB+reg	ULTRA-VIEW	POLYMER REFINE	polymer	K3 DAB view	Bond Polymer Refine	Quanto detection system	BENCHMARK ULTRA VIEW	UNIVERSAL DCT KIT	BOND REFINE DETECTION KIT	Envision Flex	View	polymer	HRP-Flex	viewdab	LSAB2	VIEW DAB DETECTION KIT	KIT ULTRAVIEW DAB v3	Envision FLEX Peroxidase/HRP	Leica Refine Polymer	Envision Flex+ 20	ultraview	BOND-REFINE POLYMER	VIEW	Ultraview DAB	Ultraview Dab	view dab	Benchmark Ultraview	FLEX	Ventana Ultraview	Envision FLEX	Ultraview	peroxydase	Ultraview	ULTRAVIEW	Ultra View DAB Ventana	Envision Flex +	Envision-Flex	envision flex +	DAB	Ventana ultraview	Ultraview DAB	Novolink	ultraview	Envision +	Bond refine detection kit	Envision Universal Polymer	Ultraview DAB
Enhancement	no	CuSO4	none	none	None	Ventana Amplification Kit	Copper	COPPER	COPPER	Copper Sulphate	ioView Copper	COPPER	yes	CuSO4	Copper	–	BOND DAB ENHANCER	copper sulphate	no	Bond DAB Enhancer	none	NIA	COPPER	NO	none	none	n/a	none	no	Copper Sulphate	ENDOGENOUS BIOTIN KIT	VENTANA	None	NIA	none	copper	NONE	Copper sulfate	Ultraview copper	view Copper		YES	no	No	mouse linker		copper	copper	ULTRAVIEW	Yes (copper)	Mouse Linker	no	no	Blocker A, Blocker B	yes	none	Hema-zolvilin	none	none	n/a	None	Copper
Chromagen	DAB	DAB+	Ventana as per kit	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	Substrate Working Solution (DAB)	DAB	DAB	DAB	DAB	DAB	DAB	Dab	Dab	YES	DAB	DAB	DAB	Ultraview DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB	DAB+	DAB	DAB	DAB
					Protocols	PR	Pan 22	KDC																																																						