Breast cancer: Antibody selection, protocol optimzation controls and EQA

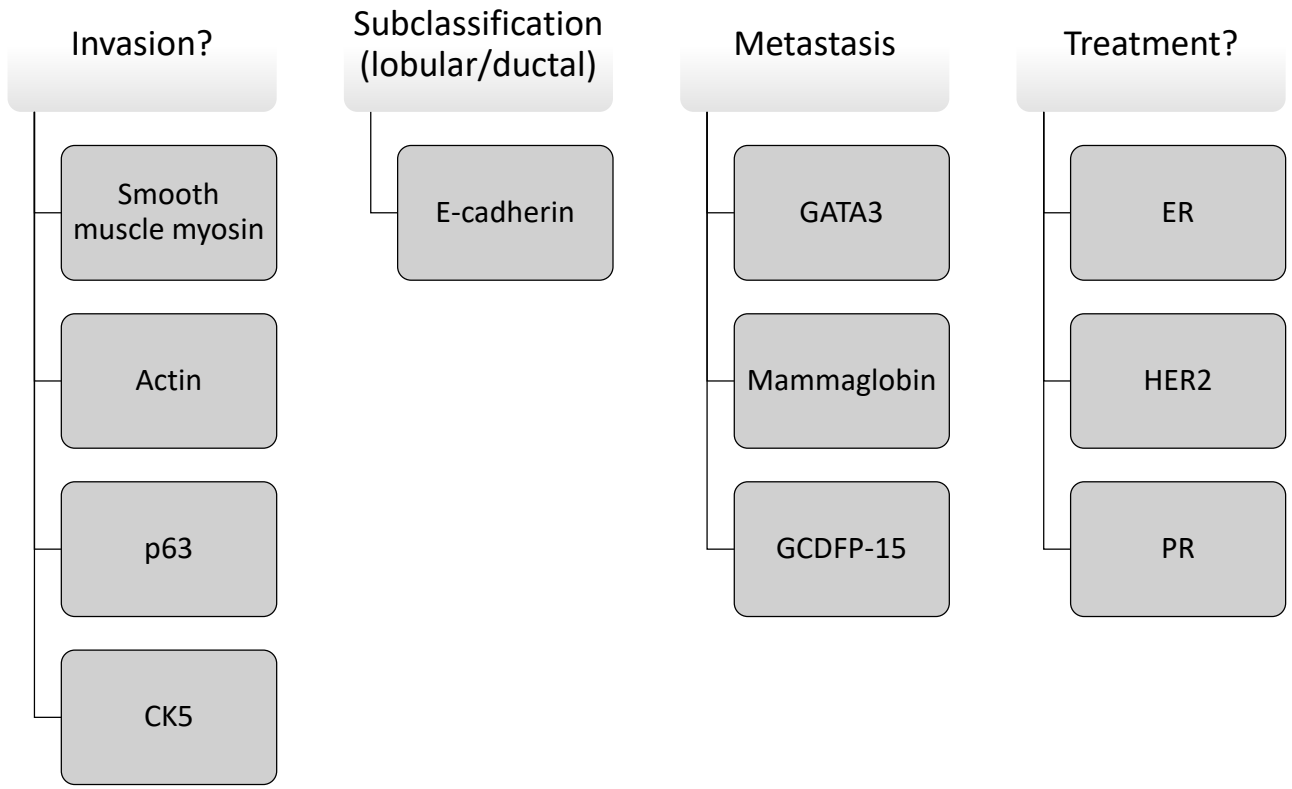
Workshop in Diagnostic Immunohistochemistry
Oud St. Jan/ Old St. John – Brugge (Bruges),
Belgium June 13th – 15nd 2018

Rasmus Røge, MD, NordiQC scheme organizer

With compliments to Søren Nielsen

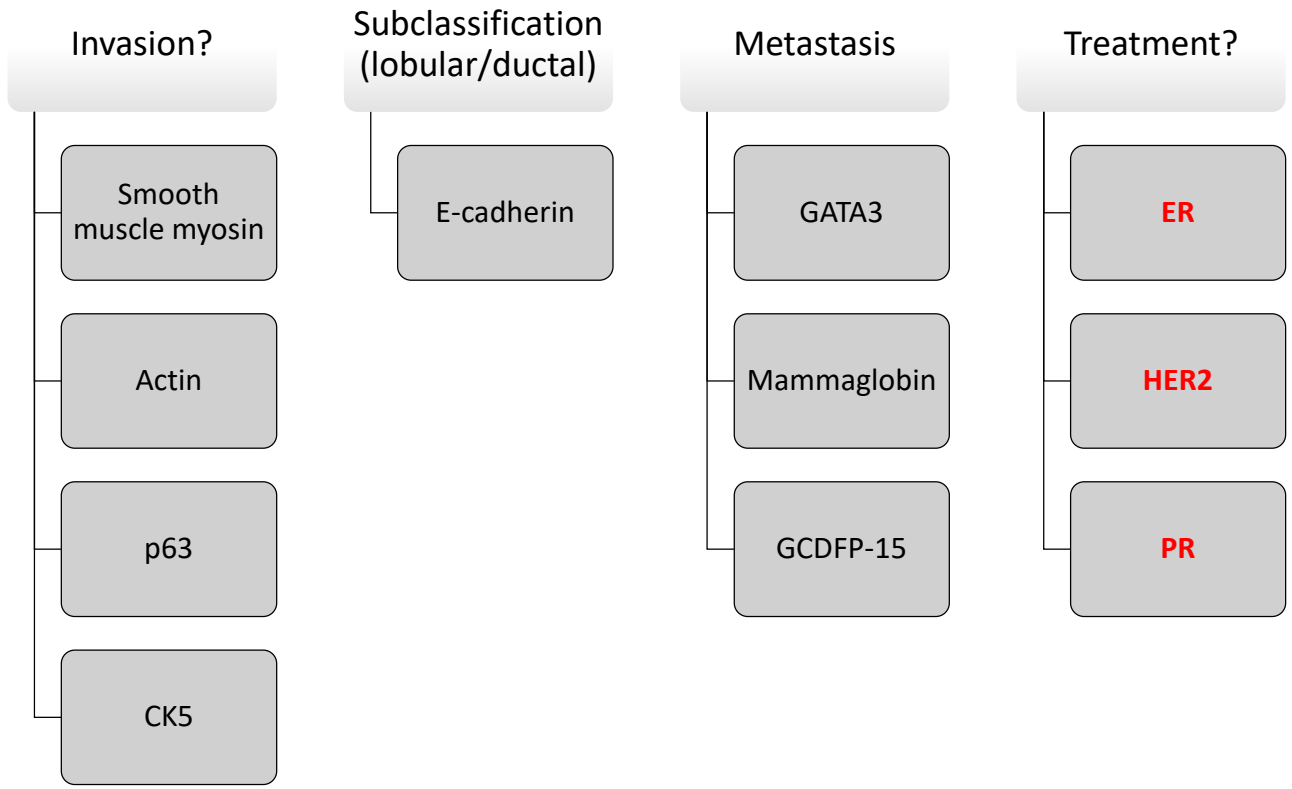
NordiQC

IHC markers in Breast Cancer

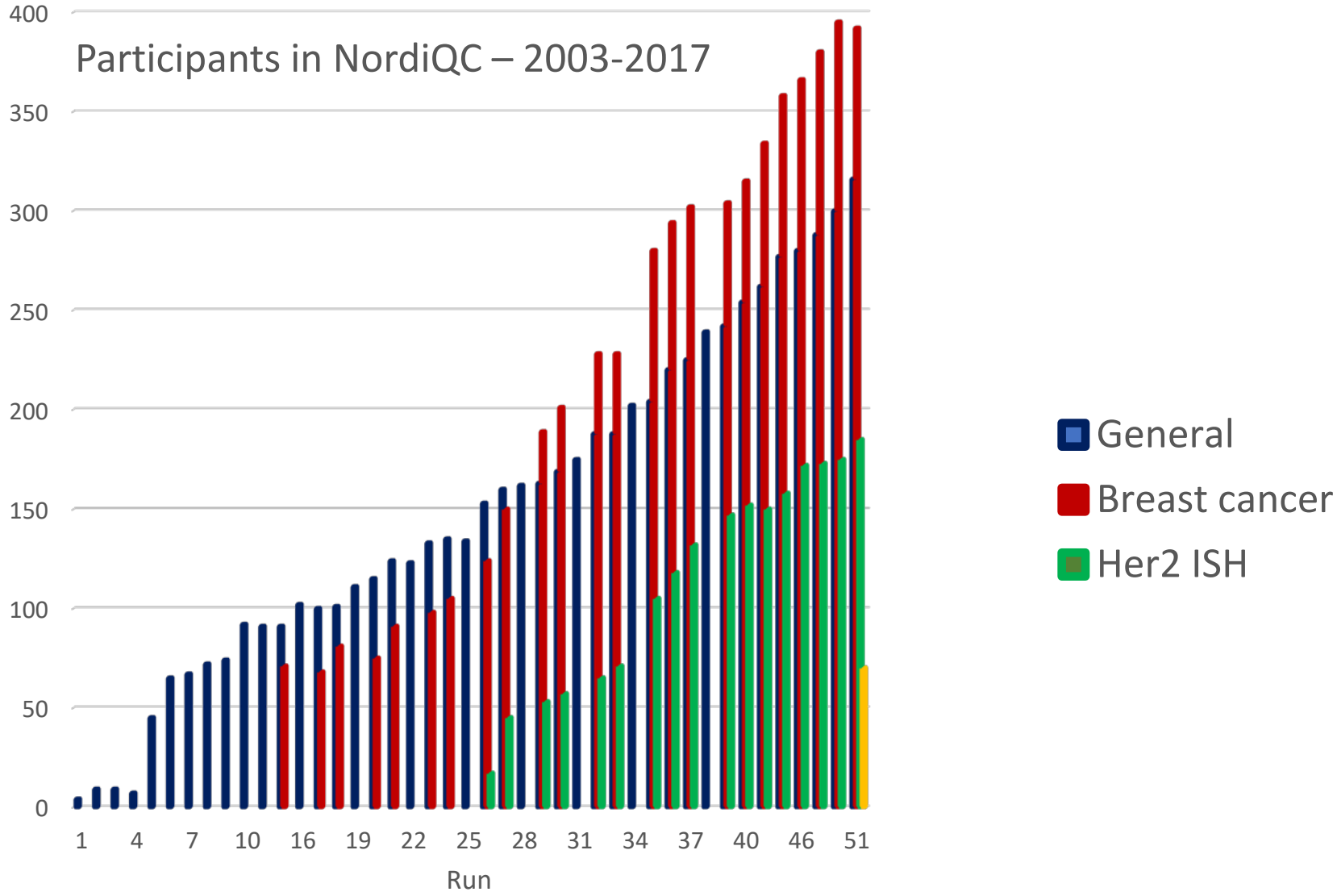


NordiQC

IHC markers in Breast Cancer

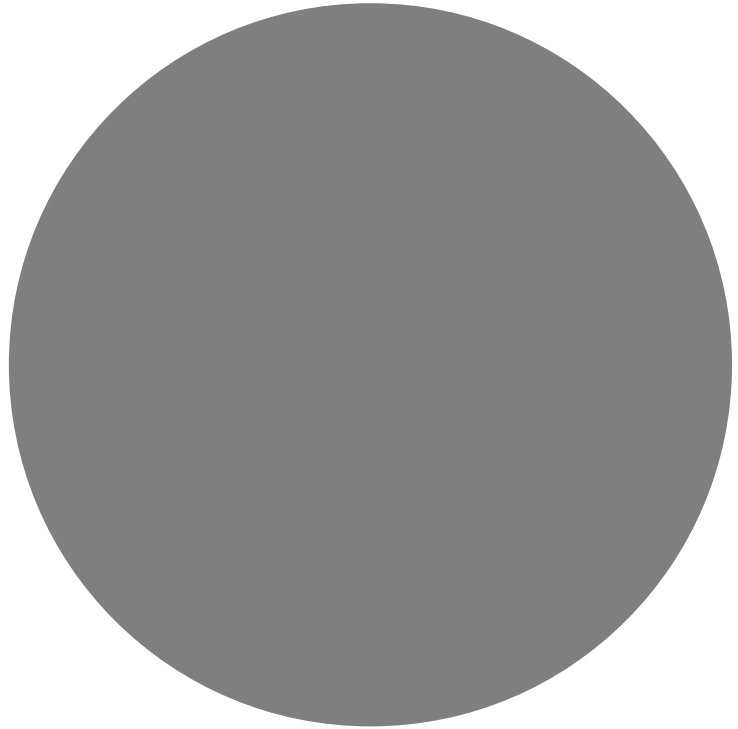


NordiQC



2018: General – 359, Breast cancer module – 460, HER2-ISH – 231, Companion module – 187

Estrogen receptor (ER)



Data obtained in run B25, 2018

NordiQC

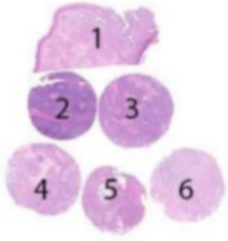
Assessment B25 2018

Estrogen receptor (ER)

Material

The slide to be stained for ER comprised:

No.	Tissue	ER-positivity*	ER-intensity*
1.	Uterine cervix	80- 90%	Moderate to strong
2.	Tonsil	< 2-5%	Weak to strong
3.	Breast carcinoma	0%	Negative
4.	Breast carcinoma	90- 100%	Moderate to strong
5.	Breast carcinoma	60-80%	Weak to moderate
6.	Breast carcinoma	90-100%	Weak to moderate

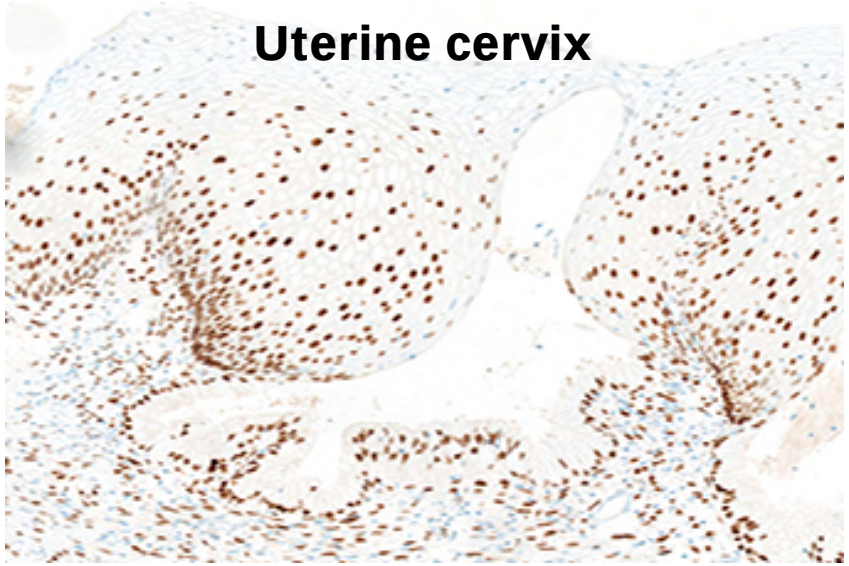


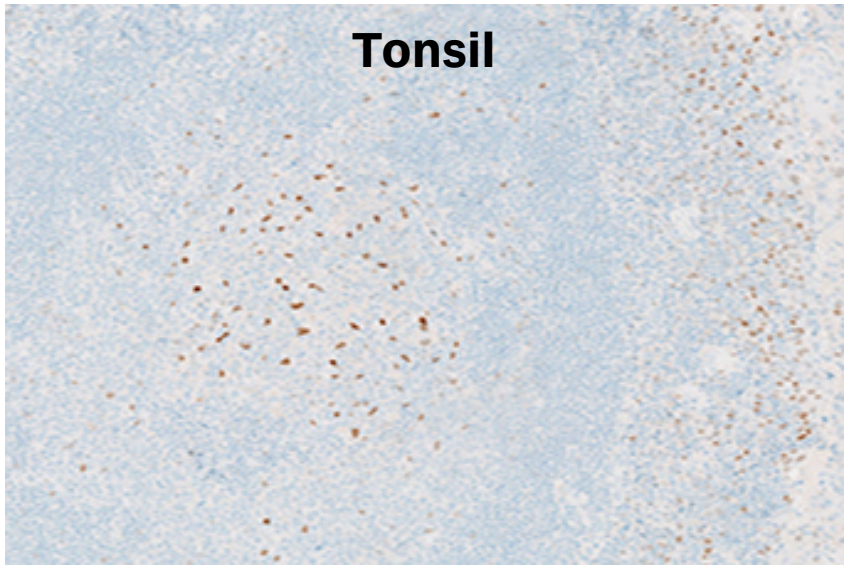
*ER-status and staining pattern as characterized by the NordiQC reference laboratories using the rmAb clones EP1 and SP1.

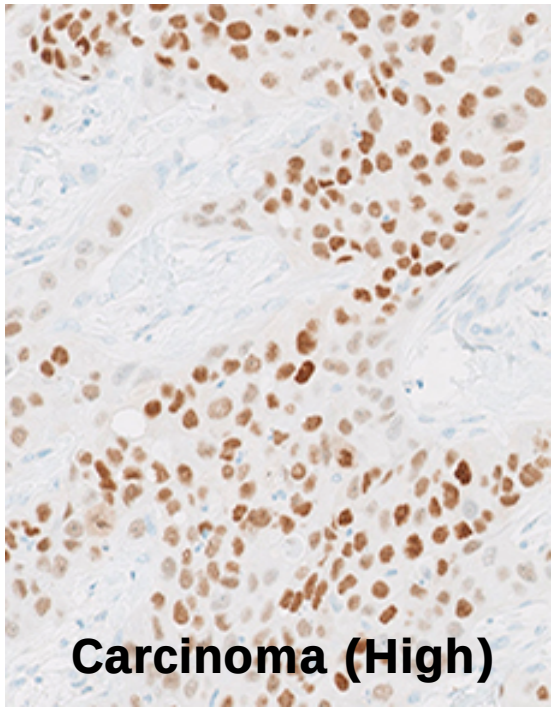
Main focus of assessment:

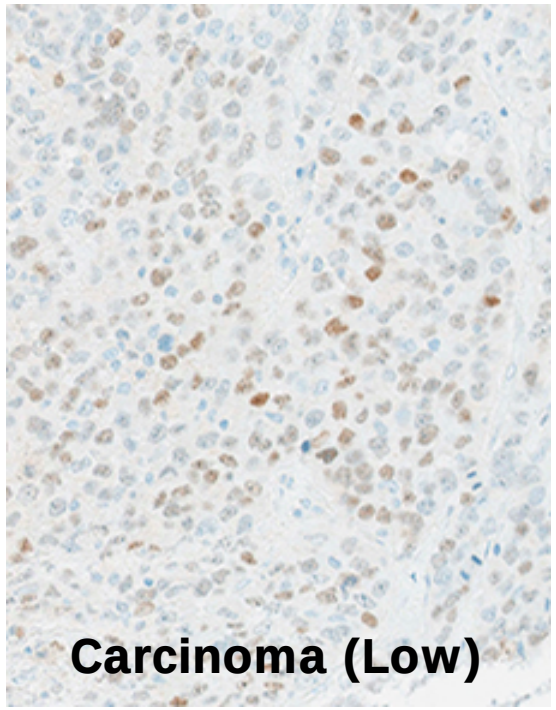
- Appropriate technical quality (signal-to-noise, good morphology etc.)
- Appropriate analytical sensitivity and specificity – indicated by concordance of ER status and proportion of positive cells in the included tumours to references

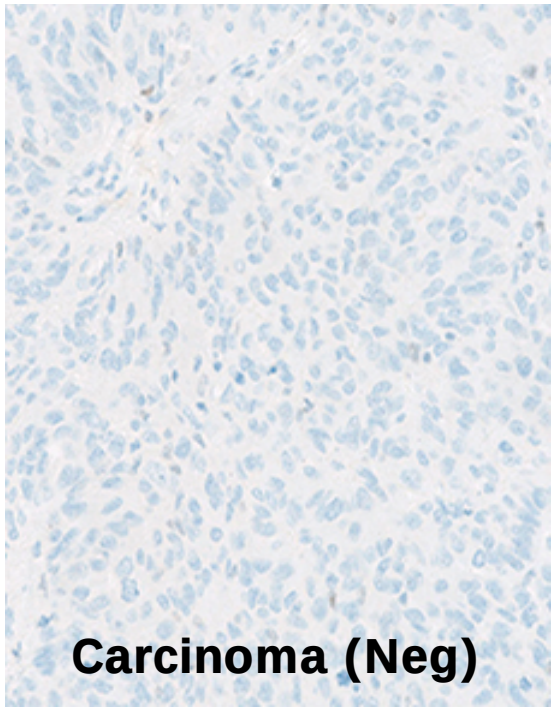
Breast cancer module – assessment setup (B25)


Uterine cervix


Tonsil


Carcinoma (High)


Carcinoma (Low)

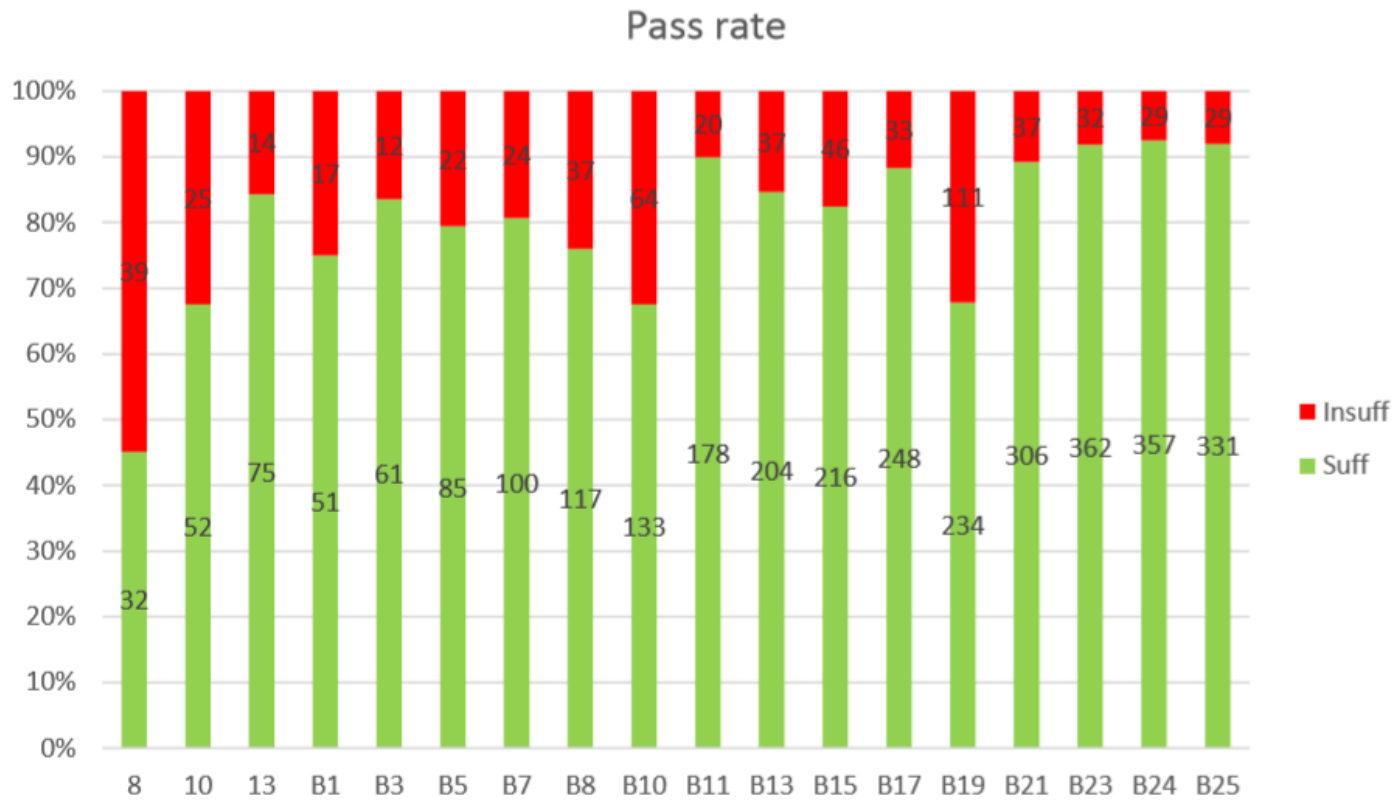

Carcinoma (Neg)

NordiQC

ER: Overall performance

Performance history
This was the eighteenth NordiQC assessment of ER. The proportion of sufficient results was similar compared to the latest run (see Graph 1).

Graph 1. **Participant numbers and pass rates for ER during 18 runs**



ER: Protocol parameters

Pass rate influenced by protocol harmonization and availability of fully automated IHC systems

	2003 B8	2017 B23
Ready-To-Use format	21%	81%
HIER by in-house buffer	88%	5%
HIER by high pH	70%	94%
Polymer/multimer kit	56%	97%
Fully automated system	6%	78%

NordiQC

ER: Development in Ab clones

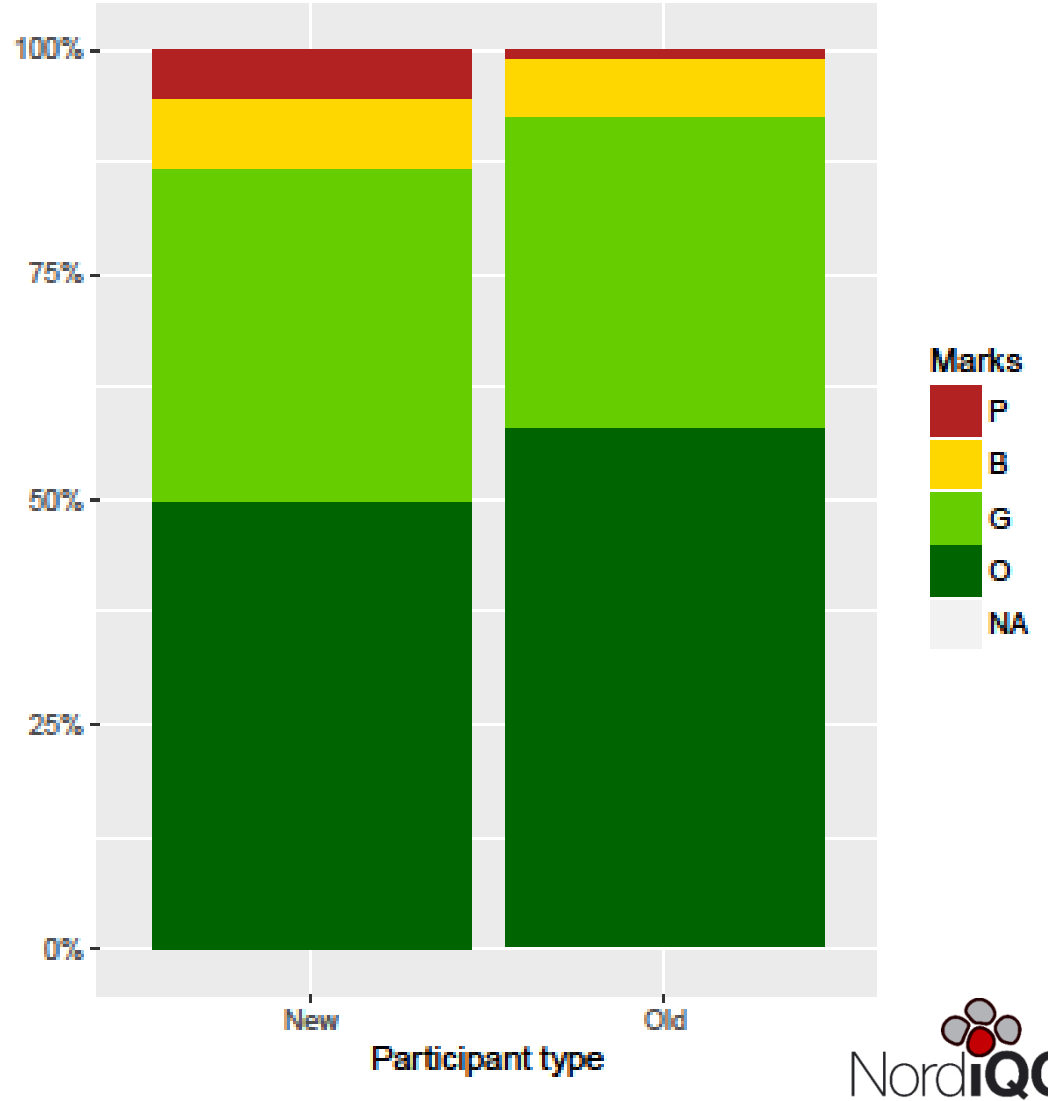
EP1: a novel rabbit monoclonal antibody for detection of oestrogen receptor α

Sunil Badve,[1] I Tudor Vladislav,[1] Betsy Spaulding,[2] Anna Strickland,[2]
Sylvia Hernandez,[1] Lisa Bird-Turner,[1] Cecelia Dodson,[1] Bjorn Elleby,[2] Therese Phillips[2]

NordiQC

ER: Pass rate influenced by participation

	New participants	Old participants
Run B10, 2004	57% (n=61)	71% (n=134)
Run B15, 2010	70% (n=54)	86% (n=208)
Run B19, 2015	51% (n=86)	73% (n=259)
Run B25, 2017	87% (n=38)	93% (n=326)

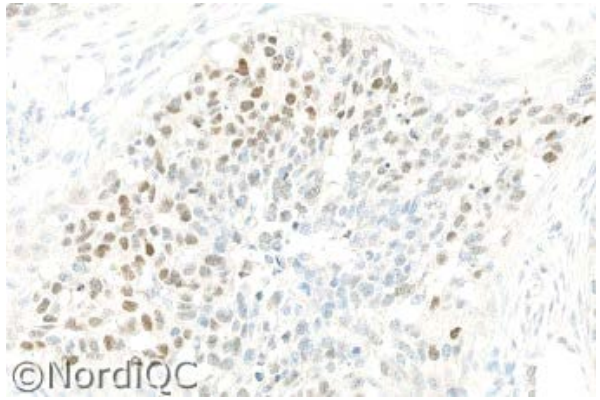


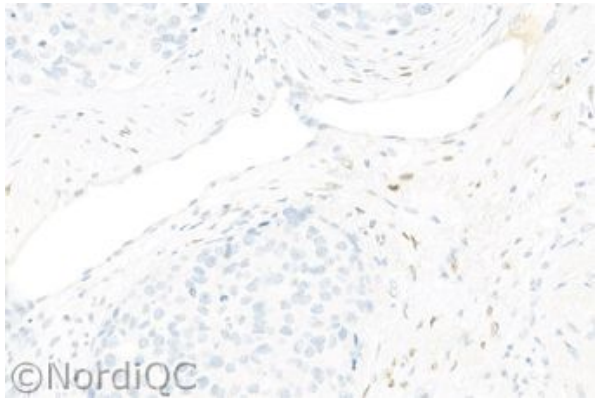
ER: Typical challenges

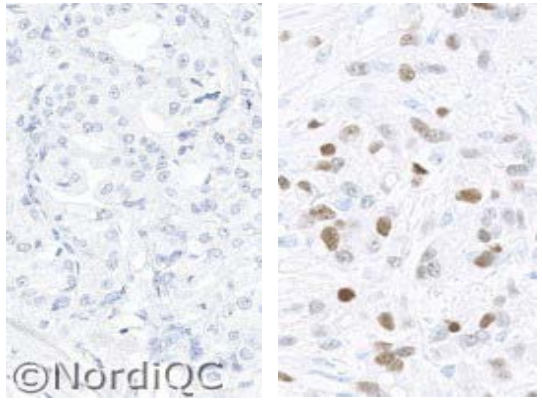
85% Weak / False negative

10% False positive

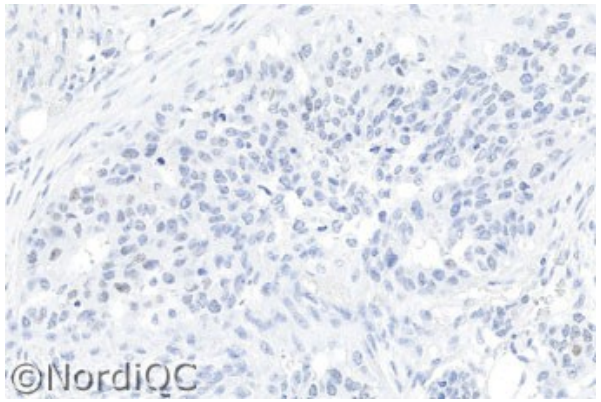
5% Impaired morphology, etc

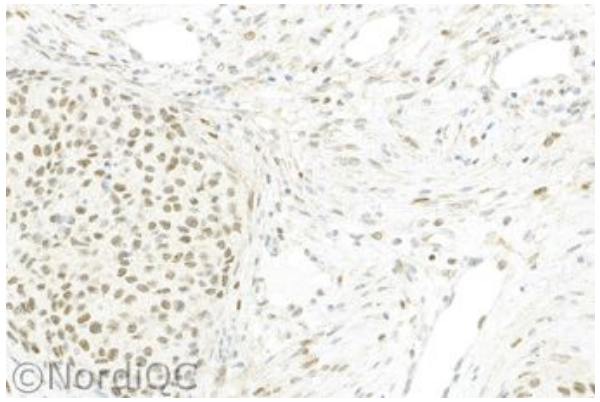


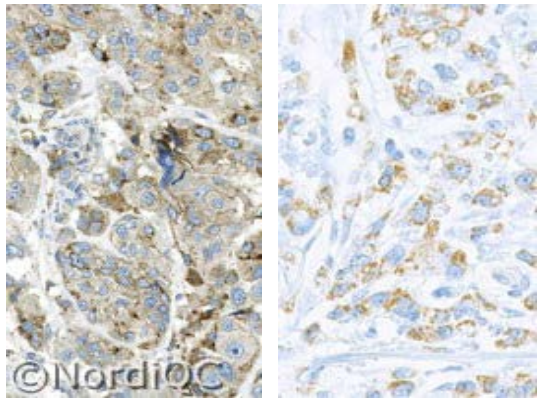




Sufficient







Insufficient

Too low titre (EP1, SP1 conc.)
Insufficient HIER,
Clone 1D5

Clone 6F11 by HIER at high pH, 3-step pol.
(not observed on VMS)

Clone 1D5 at high titre,
Biotin-based kits,
HIER in pressure cooker

NordiQC

ER: Selection of primary Ab and format

Table 1. **Antibodies and assessment marks for ER, B25**

Concentrated antibodies	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	Suff. OPS[2]
mAb clone **6F11**	22 1	Leica/Novocastra Celnovte	10	8	4	1	78%	87%
rmAb clone **EP1**	12 2 1	Dako/Agilent Cell Marque BioGenex	7	6	2	0	87%	91%
rmAb clone **SP1**	22 4 3 1 1 1	Thermo Scientific Cell Marque Spring Bioscience Immunologic BioCare Zytomed	22	6	2	2	88%	93%
rmAb clone **S21-V**	1	DB Biotech	0	0	0	1	-	-
mAb clone **1D5**	1	Dako/Agilent	0	1	0	0	-	-
Ready-To-Use antibodies								
mAb clone **1D5 IR/IS657**	1	Dako/Agilent	0	0	1	0	-	-
mAb clones **1D5 + ER-2-123 SK310**	2	Dako/Agilent	0	1	1	0	-	-
mAb clones **1D5 + ER-2-123 K4071**	1	Dako/Agilent	0	1	0	0	-	-
mAb clone **6F11 PA0009/PA0151**	10	Leica	5	3	2	0	80%	100%
rmAb **EP1 8361-C010**	1	Sakura Finetek	1	0	0	0	-	-
rmAb **EP1 IR/IS084**	45	Dako/Agilent	17	24	3	1	91%	94%
rmAb **EP1 GA084**	24	Dako/Agilent	14	8	2	0	92%	94%
rmAb clone **SP1 790-4324/5**	196	Ventana/Roche	123	66	7	0	96%	96%
rmAb clone **SP1 249R-1**	4	Cell Marque	2	2	0	0	-	-
rmAb clone **SP1 KIT-0012**	1	Maixin	1	0	0	0	-	-
rmAb clone **SP1 RMPD001**	1	Diagnostic Biosystems	0	0	1	0	-	-
rmAb clone **SP1 ILM30142-R25**	1	Immunologic	1	0	0	0	-	-
rmAb clone **SP1 MAD-000306QD**	1	Master Diagnostica	0	1	0	0	-	-
rmAb clone **SP1 RM-9101-R7**	1	Thermo Scientific	1	0	0	0	-	-
Total	361		204	127	25	5	-	
Proportion			57%	35%	7%	1%	92%	

1) Proportion of sufficient stains (optimal or good).
2) Proportion of sufficient stains with optimal protocol settings only, see below.

Concentrated format:
Overall protocol parameters

HIER alk. pH
2- & 3-step kits

Carefully calibration of primary Ab

NordiQC

ER: Selection of primary Ab and format

Table 3. **Comparison of pass rates for vendor recommended and laboratory modified RTU protocols**

RTU systems	**Vendor recommended protocol settings***		**Laboratory modified protocol settings****	
	Sufficient	Optimal	Sufficient	Optimal
Dako AS48 rmAb EP1 **IR084/IS084**	14/15 (93%)	7/15 (47%)	19/20 (95%)	7/20 (35%)
Dako Omnis rmAb EP1 **GA084**	12/13 (92%)	8/13 (62%)	7/8 (88%)	5/7 (63%)
Leica Bond mAb 6F11 **PA009/PA0151**	1/3	0/3	7/7 (100%)	5/7 (71%)
VMS Ultra/XT/GX rmAb SP1 **790-4324/4325**	35/36 (97%)	23/36 (64%)	154/160 (96%)	100/160 (62%)

* Protocol settings recommended by vendor – Retrieval method and duration, Ab incubation times, detection kit, IHC stainer/equipment.
** Significant modifications: retrieval method, retrieval duration and Ab incubation time altered >25%, detection kit. Only protocols performed on the specified vendor IHC stainer are included.

NordiQC

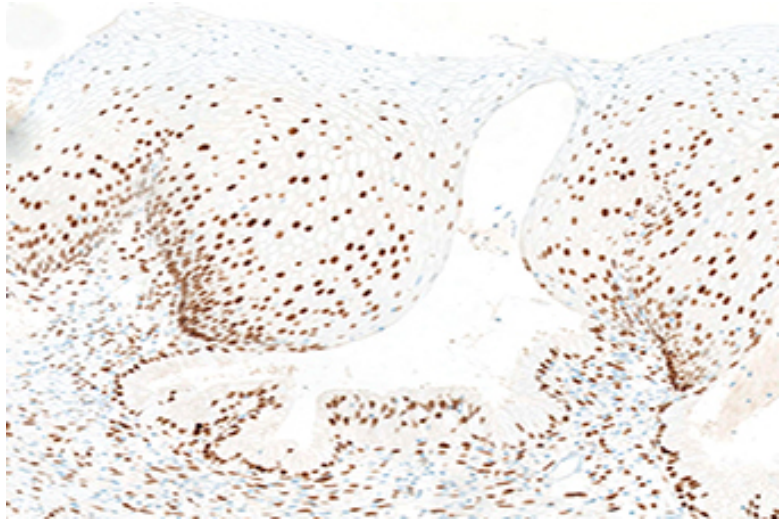
ER: Basic protocol for optimal staining

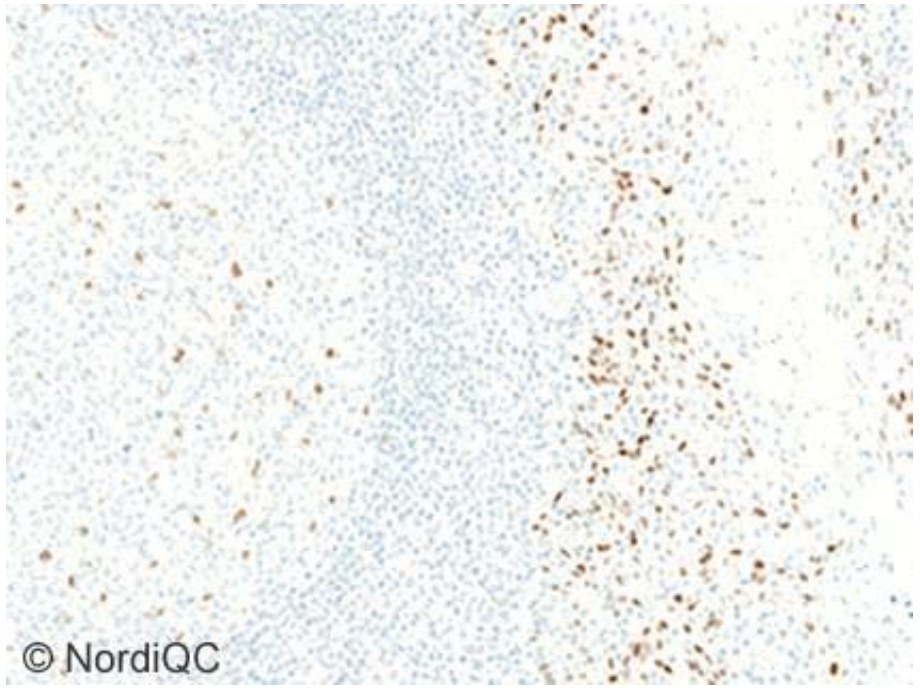
	Retrieval	Titre	Detection	RTU	Detection
mAb 1D5	HIER High	1:25-50	2- & 3-step	Dako	2- & 3-step
mAb 6F11*	HIER Ci, High	1:50-200	2- & 3-step	Leica	3-step
rmAb EP1	HIER High	1:25–30	2- & 3-step	Dako	2- & 3-step
rmAb SP1	HIER High	1:30-100	2- & 3-step	Ventana	2- & 3-step

** Efficient HIER, high conc., 3-step pol. & low stringent washing can give aberrant nuclear staining*
Not seen on Ventana stainer, rarely on Autostainer and most commonly on Bond stainer.

NordiQC

ER: Controls





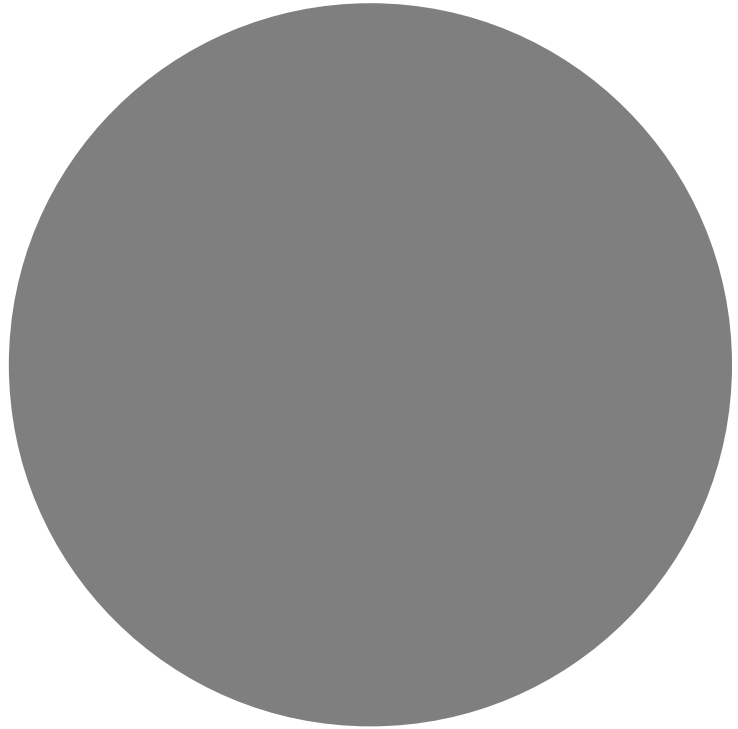
Controls

In concordance with previous NordiQC runs, uterine cervix was found to be an appropriate positive tissue control for ER staining: In optimal protocols, virtually all epithelial cells throughout the layers of the squamous epithelium and in the glands showed a moderate to strong and distinct nuclear staining reaction. In the stromal compartment, moderate to strong nuclear staining reaction was seen in most cells except endothelial and lymphatic cells.

Tonsil was found to be highly recommendable as a tool to monitor the analytical sensitivity for the IHC demonstration of ER and was in fact superior to uterine cervix. It was observed, that dispersed germinal centre cells (most likely macrophages) and squamous epithelial cells were distinctively demonstrated in virtually all protocols providing an optimal result.

Progesteron receptor (PR)

Data obtained in run B24, 2018



NordiQC

Assessment Run B24 2017

Progesterone receptor (PR)

Material

The slide to be stained for PR comprised the following tissues:

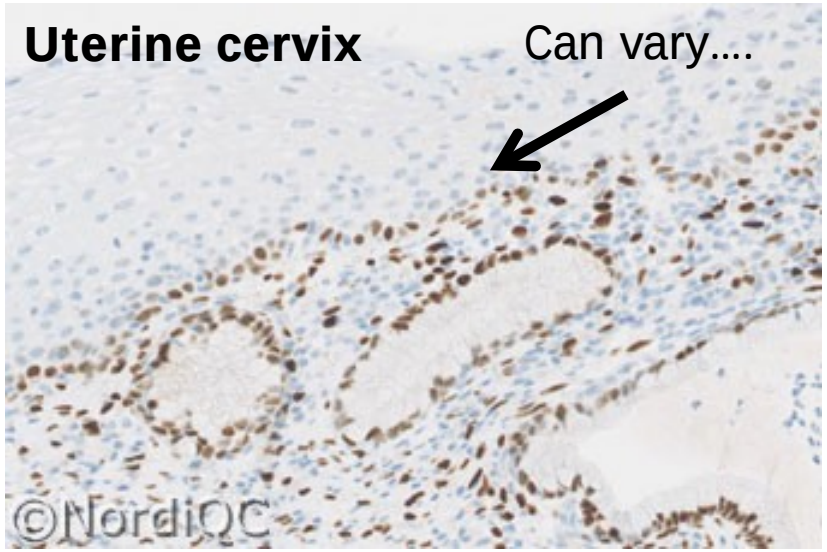
No.	Tissue	PR-positivity*	PR-intensity*
1.	Uterine cervix	80-90%	Moderate to strong
2.	Tonsil	0%	Negative
3.	Breast carcinoma	0%	Negative
4.	Breast carcinoma	50-80%	Weak to moderate
5.	Breast carcinoma	40-60%	Weak to moderate
6.	Breast carcinoma	90 - 100%	Moderate to strong

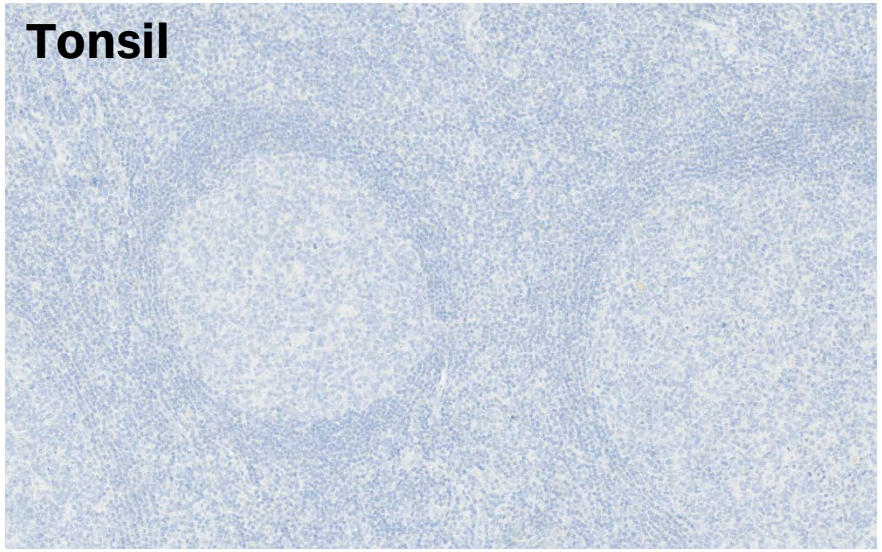
*PR-positivity and intensity as characterized by NordiQC reference laboratories using the mAb clone 16

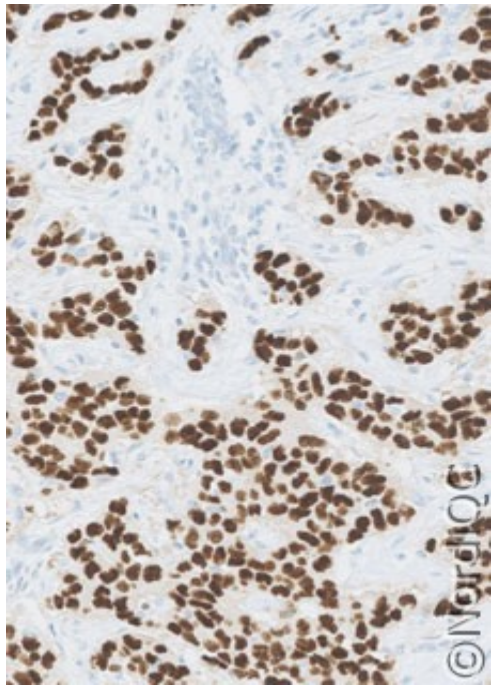
Main focus of assessment:

- Appropriate technical quality (signal-to-noise, good morphology etc.)
- Appropriate analytical sensitivity and specificity – indicated by concordance of PR status and proportion of positive cells in the included tumours to references

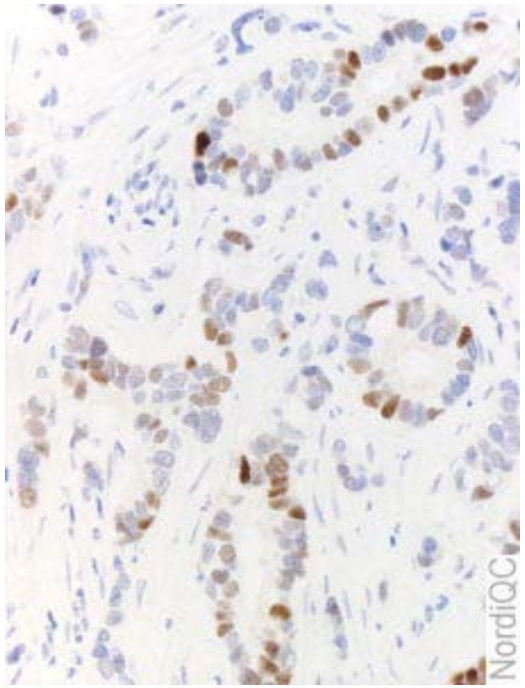
Breast cancer module – assessment setup (B24)



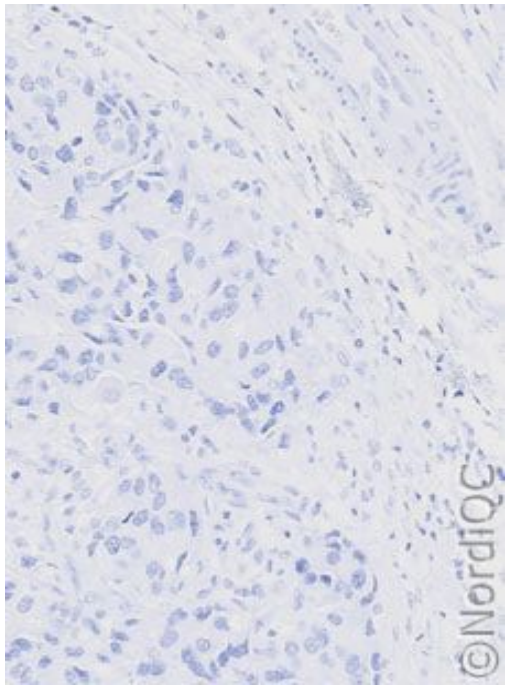




Carcinoma (High)



Carcinoma (Low)

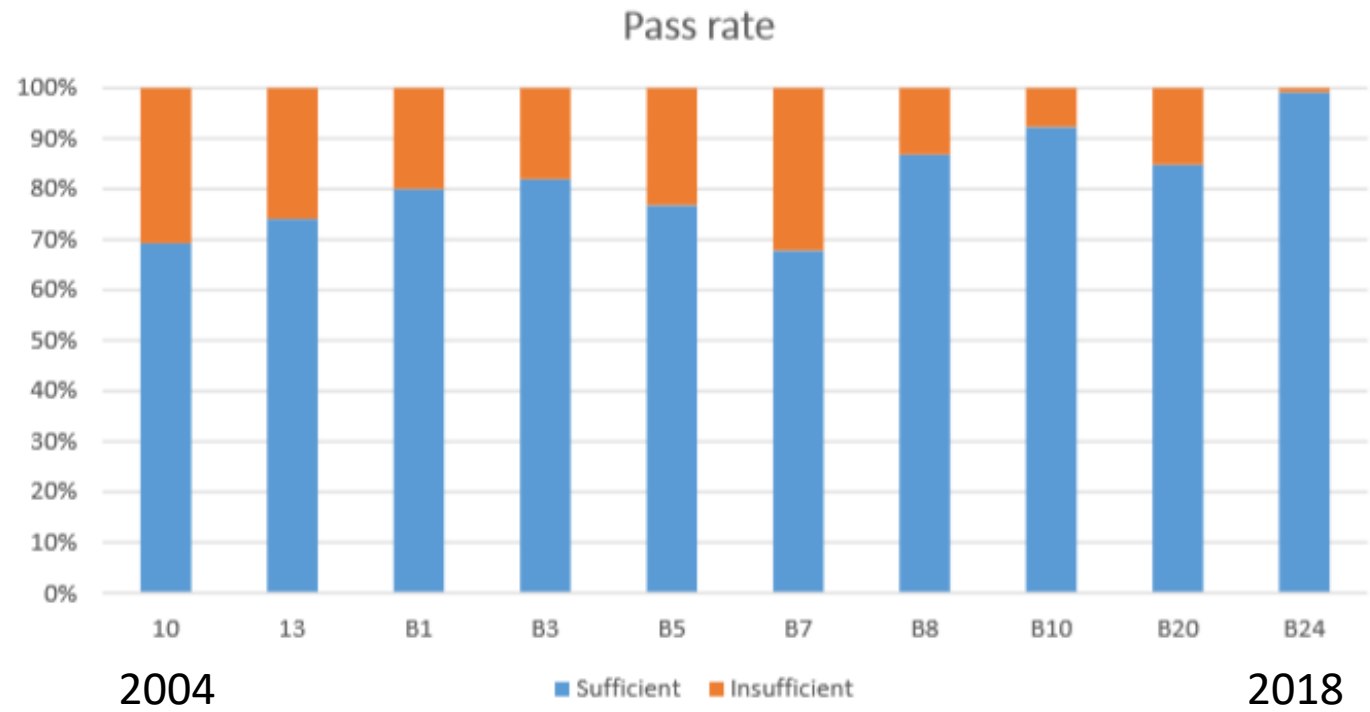


Carcinoma (Neg)

PR: Overall performance

Performance history
This was the tenth NordiQC assessment of PR. A significant higher proportion of sufficient results was seen in B24 compared to the previous runs, as shown in Graph 1:

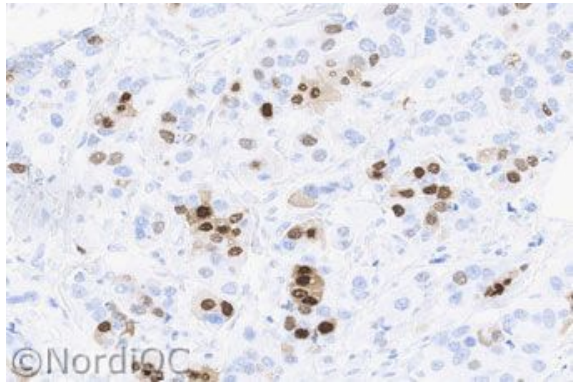
Graph. **Pass rate in the NordiQC assessments for PR**



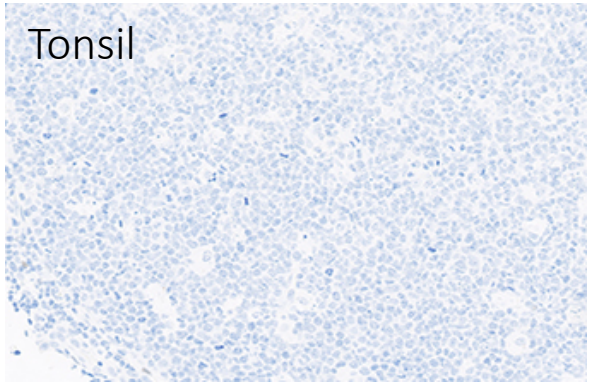
2004 2018

PR: Typical challenges

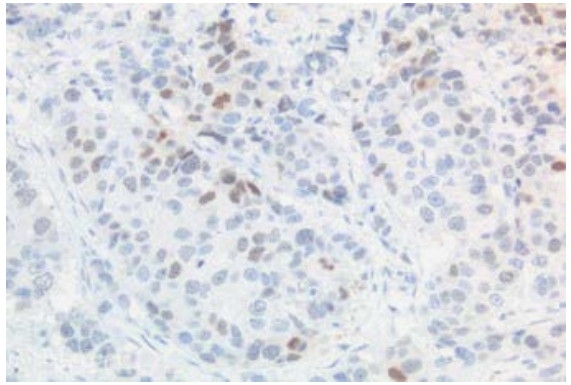
75% Weak / False negative



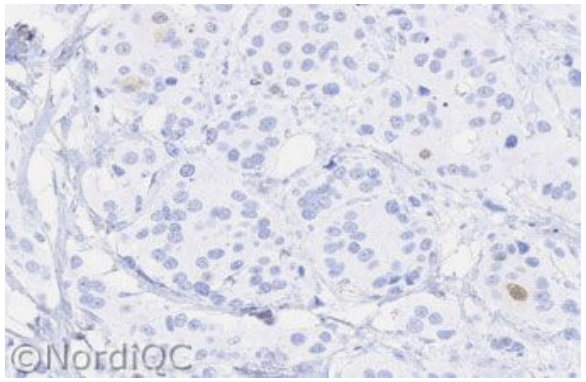
20% False positive

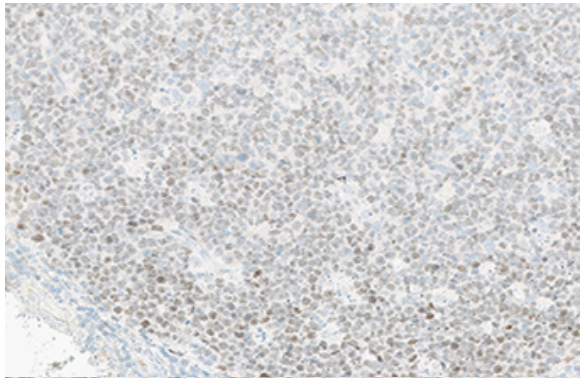


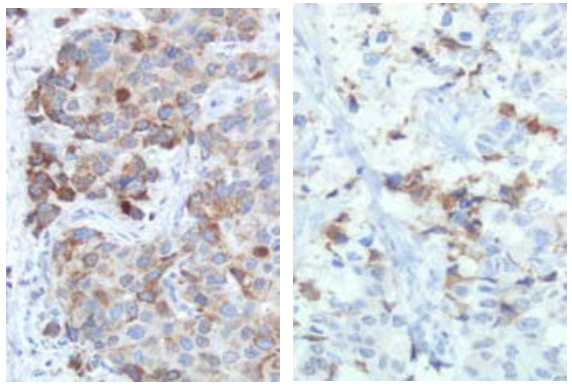
5% Impaired morphology, etc



Sufficient







Insufficient

Too low titre (16, PgR636)
Insufficient HIER

Clone SP2 and 1E2.
1E2 mainly by off-label protocol (ext. sensitivity)

Clone 1A6,
Biotin-based kits,
HIER in pressure cooker

NordiQC

PR: Selection of primary Ab and format

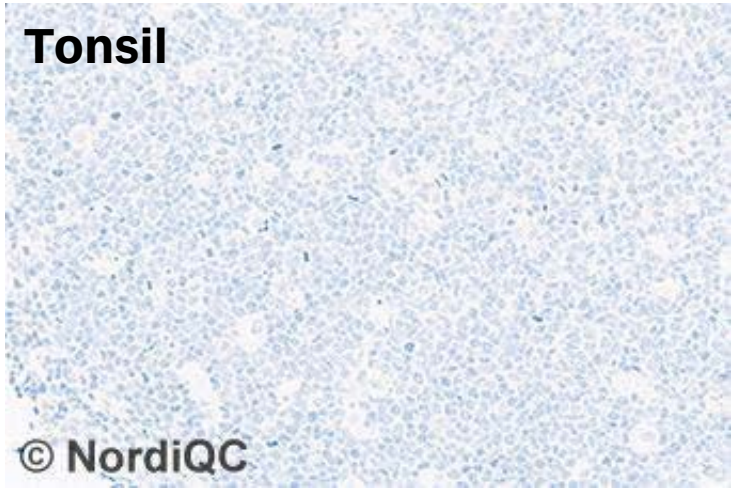
Table 1. **Antibodies and assessment marks for PR, run B24**

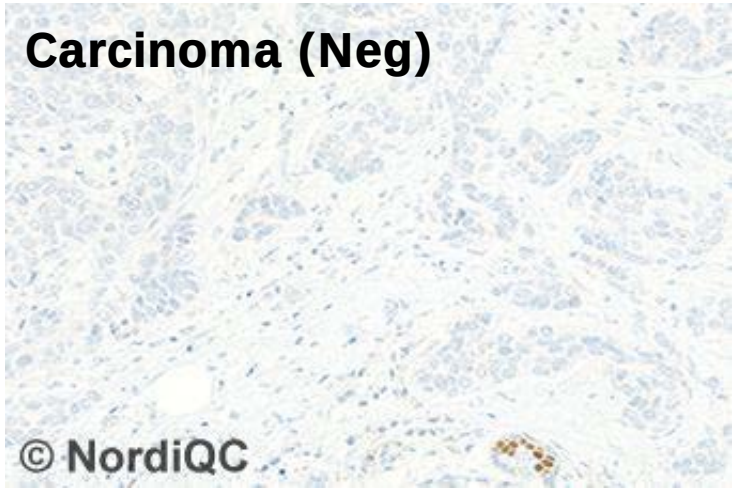
Concentrated antibodies	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	Suff. OPS[2]
mAb clone **16**	35 2	Leica/Novocastra Biocare	28	9	0	0	100%	100%
mAb clone cocktail **16 + SAN27**	2	Leica/Novocastra	1	1	0	0	-	-
mAb clone **1A6**	2	Leica/Novocastra	2	0	0	0	-	-
mAb clone **PgR 636**	41	Dako Agilent	29	12	0	0	100%	100%
mAb clone **PgR 1294**	16	Dako Agilent	14	2	0	0	100%	100%
rmAb clone **SP2**	1 1 1	Thermo Scientific BioSystems Spring Biosystems	2	1	0	0	-	-
rmAb clone **SP42**	1 1	Zytomed Cell Marque	1	1	0	0	-	-
rmAb clone **Y85**	1	Cell Marque	1	0	0	0	-	-
Ready-To-Use antibodies								
mAb clone **16** **PA0312**	17	Leica/Novocastra	13	4	0	0	100%	100%
mAb clone **16** **MAD-000670QD**	1	Master Diagnostica	1	0	0	0	-	-
mAb clone **16** **CPM-0360**	1	Celnovte	1	0	0	0	-	-
mAb **PgR 636** **IR/IS068**	43	Dako Agilent	34	9	0	0	100%	100%
mAb **PgR 1294** **GA090**	21	Dako Agilent	17	4	0	0	100%	100%
mAb clone **PgR 1294** **K4071/SK310**	2	Dako Agilent	2	0	0	0	-	-
rmAb clone **1E2** **790-2223/4296**	193	Ventana	146	44	3	0	98%	98%
rmAb clone **SP2** **Kit-0013**	1	Maixin	1	0	0	0	-	-
rmAb clone **EP2** **AN711-5M**	1	BioGenex	1	0	0	0	-	-
rmAb **SP42** **BRB038**	1	Zytomed	1	0	0	0	-	-
Total	385		295	87	3	0		
Proportion			77%	22%	1%	-	99%	

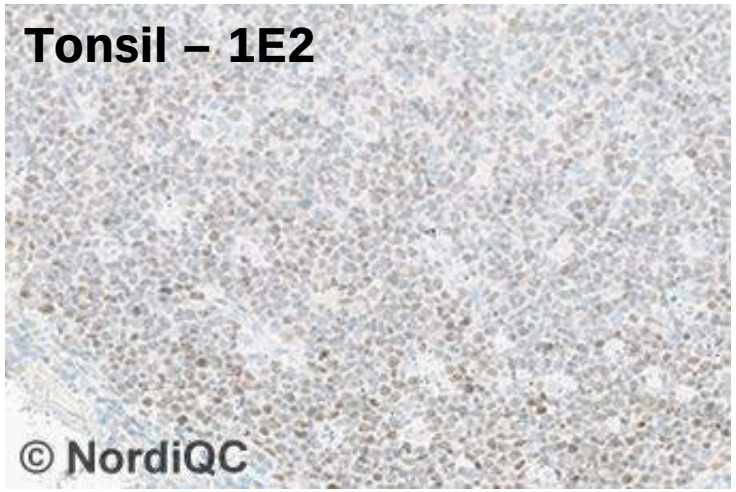
1) Proportion of sufficient stains (optimal or good).
2) Proportion of sufficient stains with optimal protocol settings only, see below.

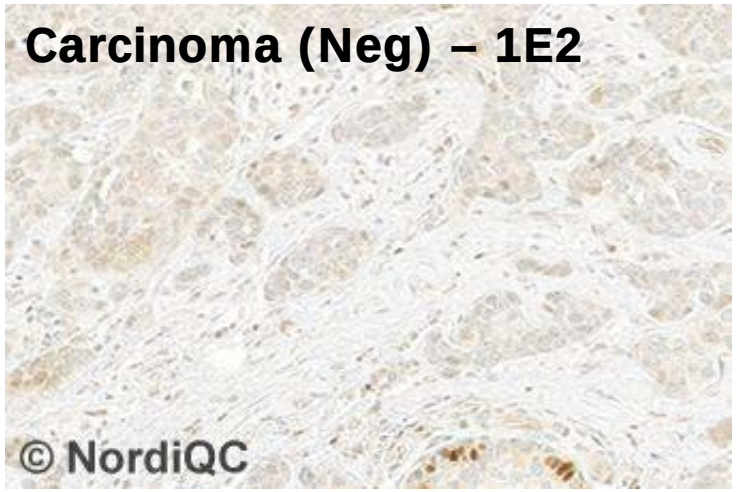
NordiQC

PR: 1E2 RTU False-positive staining (B18-24)









Typically related to reduced HIER time and/or increased incubation time of primary Ab

NordiQC

PR: Basic protocol for optimal staining

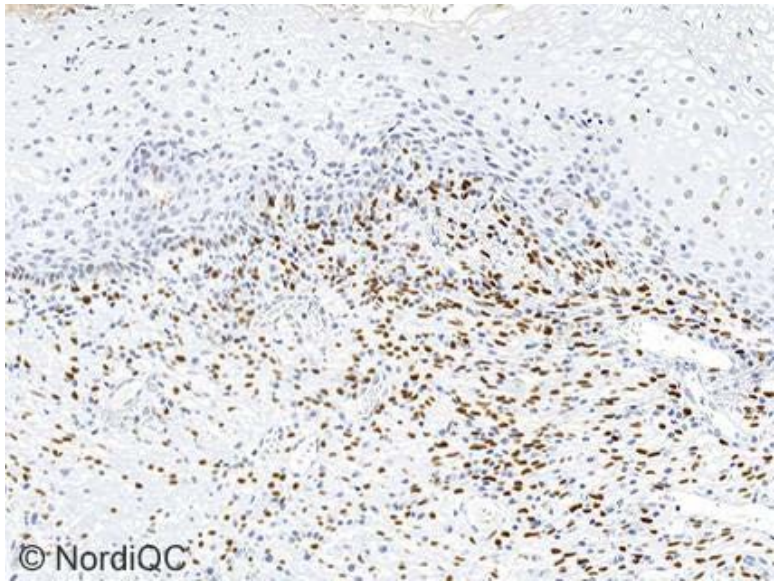
	Retrieval	Titre	Detection	RTU	Detection
mAb 16	HIER High	1:75-800	2- & 3-step	Leica	3-step
mAb PGR636*	HIER (High)	1:100-800	2- & 3-step	Dako	3-step
mAb PGR1294	HIER (High)	1:250–5.000	2- & 3-step	Dako	2-step
rmAb 1E2**	HIER High	-	-	Ventana	2-step

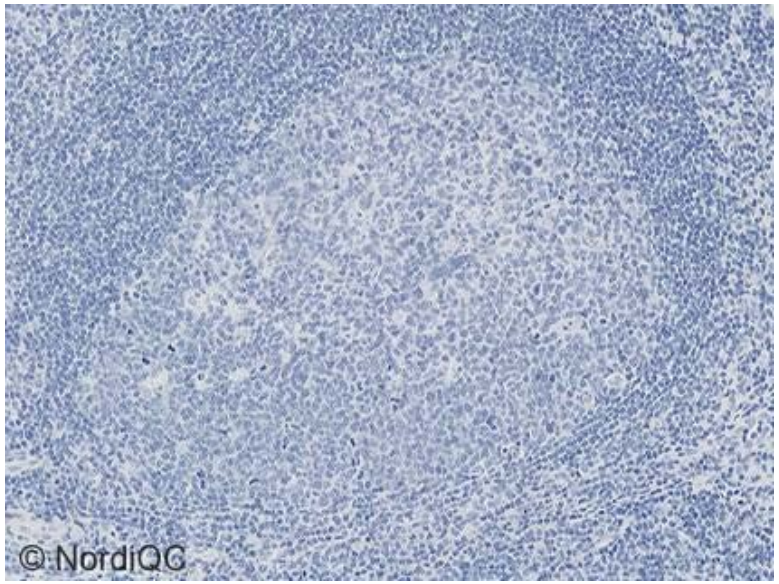
* *mAb clone PGR636 has shown to be less successful on Ventana BenchMark Ultra*

** *rmAb clone 1E2, RTU might provide aberrant false pos. result by 3-step protocols, reduced HIER and prolonged Ab incubation time compared to Ventana guidelines*

NordiQC

PR: Controls





Controls

As observed in the previous NordiQC assessments of PR, uterine cervix is an appropriate positive tissue control for evaluation of the sensitivity of PR staining: With an optimal protocol almost all columnar epithelial cells, the majority of basal squamous epithelial cells and most of the stromal cells must show a strong and distinct nuclear staining with only a minimal cytoplasmic reaction. No staining must be seen in endothelial cells and lymphocytes. However, it must be taken into consideration that the PR expression level is reduced in the uterine cervix of post-menopausal women and thus especially demonstration of PR in squamous epithelial cells can be compromised.

Tonsil is recommendable as negative tissue control, in which no nuclear staining should be seen.

HER-2 IHC

Data obtained in run B25, 2018

Assessment Run B25 2018

HER2 IHC

Material

The slide to be stained for HER2 comprised the following 5 materials:

	IHC: HER2 Score* (0, 1+, 2+, 3+)	FISH: HER2 gene/chr 17 ratio**
1. Breast carcinoma, no. 1	0-1+	1.2 – 1.4 (unamplified)
2. Breast carcinoma, no. 2	3+	> 6.0 (clusters) (amplified)
3. Breast carcinoma, no. 3	0-1+	1.1 – 1.4 (unamplified)
4. Breast carcinoma, no. 4	2+	5.3 – 5.8 (amplified)
5. Breast carcinoma, no. 5	2+	0.9 – 1.1 (unamplified)

* HER2 immunohistochemical score (see table below) as achieved by using the two FDA approved kits and antibodies, HercepTest™ (Dako) and PATHWAY® (Ventana), in NordiQC reference laboratories.

** HER2 gene/chromosome 17 ratios achieved using Zyto*Light* ® SPEC HER2/CEN 17 Dual Color FISH (Zytovision)

Main focus of assessment:

- Appropriate technical quality (signal-to-noise, good morphology etc.)
- Appropriate analytical sensitivity and specificity – indicated by concordance of HER2 status to IHC reference slides and FISH status in all the included tumours.

Breast cancer module – assessment setup (B25)

HER2 IHC: Results B25

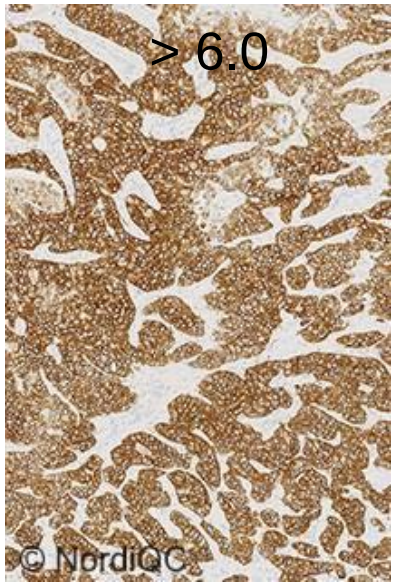
Table 1. Assessment marks for **IHC assays and antibodies run B25, HER2 IHC**

FDA approved HER2 assays	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	Suff. OPS[2]
PATHWAY® rmAb clone **4B5, 790-2991**	195	Ventana/Roche	181	14	0	0	100%	100%
PATHWAY® rmAb clone **4B5, 790-2991**[4]	2	Ventana/Roche	2	0	0	0	-	-
CONFIRM™, rmAb clone **4B5, 790-4493**	19	Ventana/Roche	18	1	0	0	100%	100%
CONFIRM™, rmAb clone **4B5, 790-4493**[4]	1	Ventana/Roche	1	0	0	0	-	-
HercepTest™ **SK001**	33	Dako/Agilent	28	5	0	0	100%	100%
HercepTest™ **SK001**[5]	5	Dako/Agilent	3	1	1	0	80%	-
HercepTest™ **K5204**	1	Dako/Agilent	1	0	0	0	-	-
Oracle™ mAb clone **CB11, TA9145**	6	Leica	4	2	0	0	100%	100%
Antibodies[3] for laboratory developed HER2 assays, conc. antibody	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	Suff. OPS[2]
rmAb clone **BSR44**	1	Nordic Biosite	1	0	0	0	-	-
mAb clone **CB11**	7 1	Leica/Novocastra Biogenex	0	2	4	2	25%	-
rmAB clone **EP1045Y**	2	ThermoFisher Scientific	1	1	0	0	-	-
pAb clone **A0485**	38	Dako/Agilent	25	9	0	4	89%	89%
rmAb clone **RM228**	1	RevMAB Bioscience	1	0	0	0	-	-
rmAb clone **SP3**	14 4 3 1 1	ThermoFisher Scientific Zytomed Cell Marque Immunologic Springer Bioscience	7	16	0	0	100%	100%
rmAb clone **A24-V**	1	DB Biotech	0	0	1	0	-	-
Antibodies for laboratory developed HER2 assays, RTU	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	Suff. OPS[2]
rmAb clone **EP3, CCR-0843**	1	Celnovte	1	0	0	0	-	-
rmAb clone **EP3, RMPD049R**	1	Diagnostic Biosystems	1	0	0	0	-	-
rmAb clone **EP3, AN726**	1	Biogenex	0	0	1	0	-	-
rmAb clone **GR011, 8362-C010**	1	Sakura Finetek USA Inc	1	0	0	0	-	-
Ab clone **MXR001, RMA-0701**	1	Maixin	0	0	0	1	-	-
rmAb clone **SP3, MAD-000308QD**	1	Master Diagnostica	0	1	0	0	-	-
Total	342		276	52	7	7	-	-
Proportion			81%	15%	2%	2%	96%	-

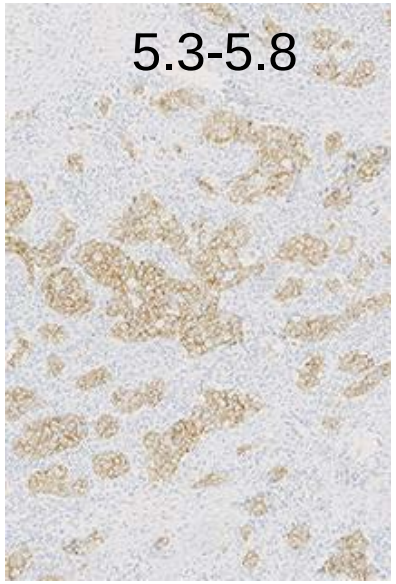
1) Proportion of sufficient stains (optimal or good),
2) Proportion of sufficient stains with optimal protocol settings only, see below.
3) mAb: mouse monoclonal antibody, rmAb: rabbit monoclonal antibody, pAb: polyclonal antibody.
4) RTU system developed for the Roche/Ventana's fully automated systems (BenchMark) but used by laboratories on different platforms (e.g. Leica Bond)
5) RTU system developed for the Agilent/Dako`s semi-automated systems (Autostainer Link48) but used by laboratories on different platforms (Leica Bond and Dako Omnis)

NordiQC

False negative

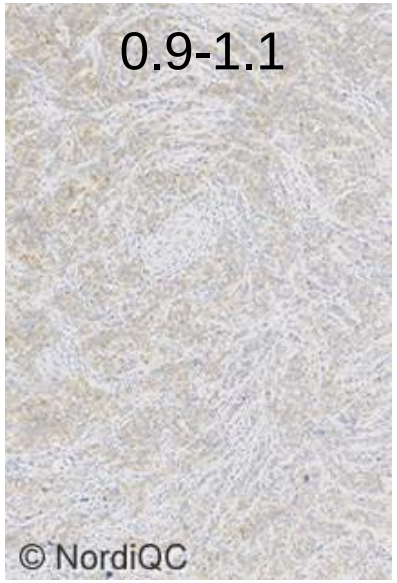


Amplified, 3+



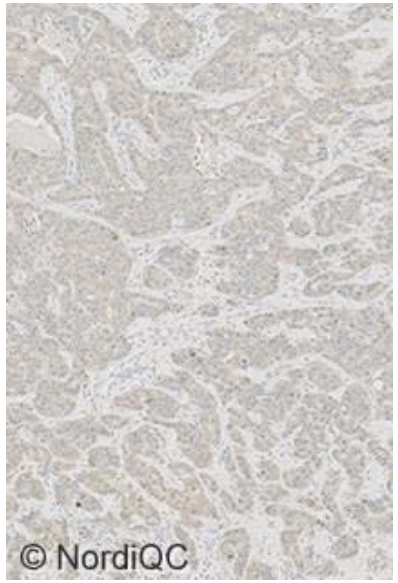
Amplified, 2+

Optimal



Unamplified, 2+

Unamplified, 0



Amplified, 1+

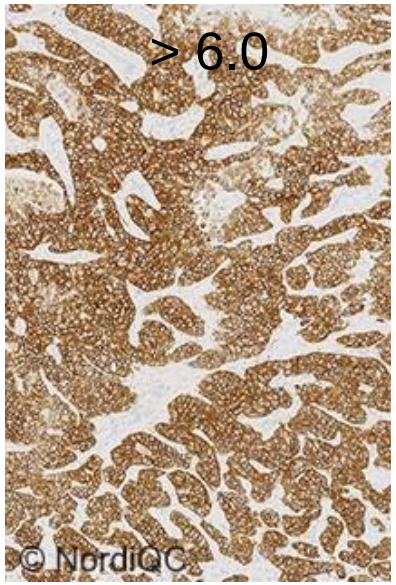

Amplified, 0

Poor

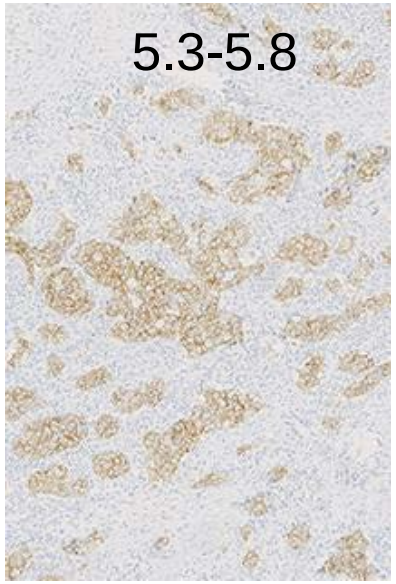
Unamplified, 0


Unamplified, 0

NordiQC

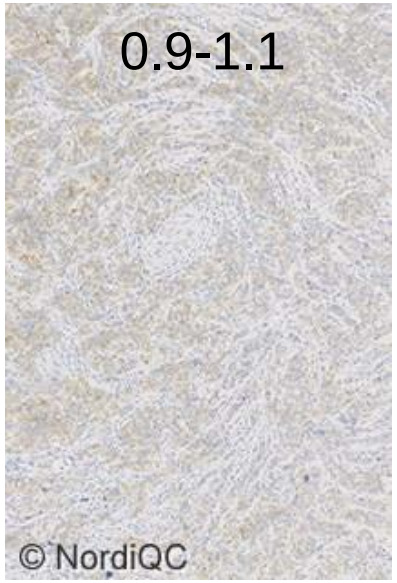


Amplified, 3+



Amplified, 2+

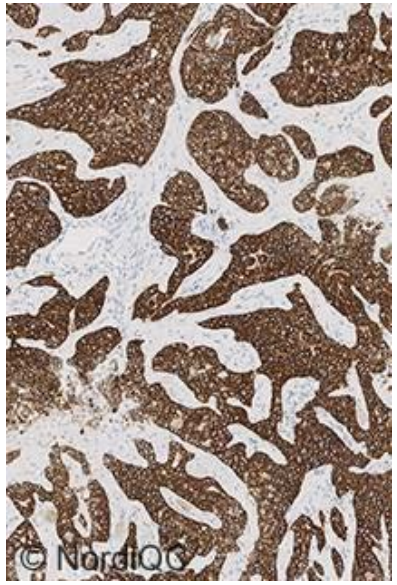
Optimal



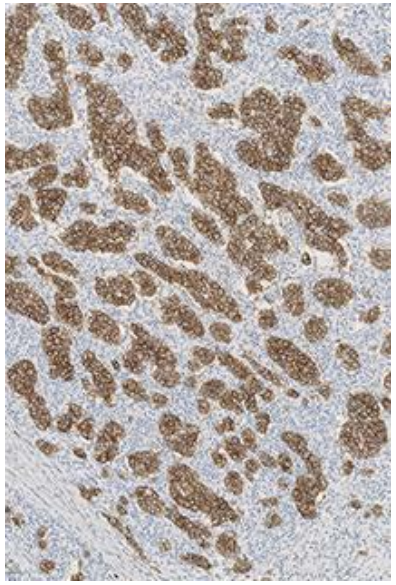
Unamplified, 2+

Unamplified, 0

False positive

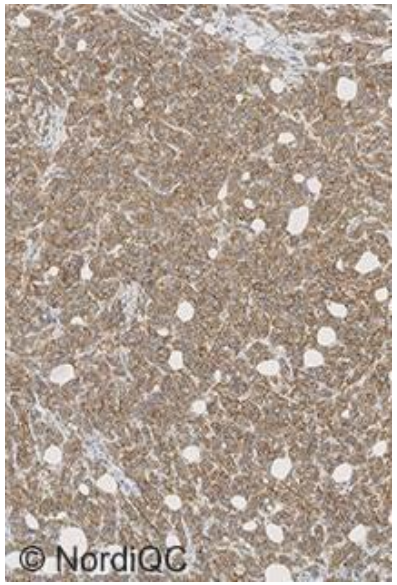


Amplified, 3+



Amplified, 3+

Poor



Unamplified, 3+

Unamplified, 1+

NordiQC

Typical causes for insufficient results in the NordiQC HER2 IHC breast module

FDA / CE-IVD HER2 IHC kits

- PATHWAY®, Ventana: Too short HIER (<24 min) and/or too short incubation of primary Ab (<12 min)
- HercepTest™, Dako: Too short HIER (<40 min) and/or too short incubation of primary & secondary Ab (<30 min)
- Oracle™, Leica: No single or combination of causes have been identified

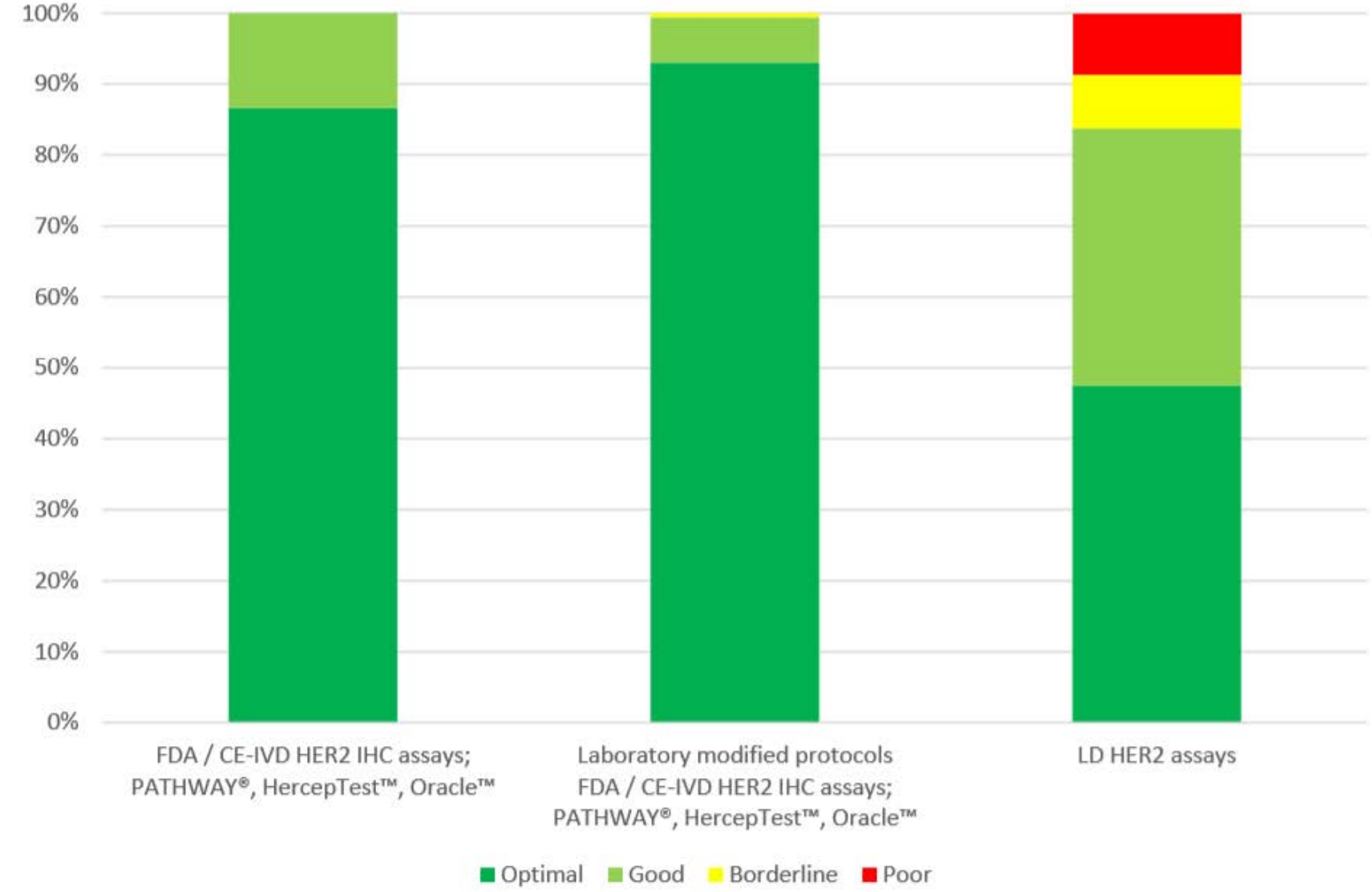
Laboratory developed assays

- Inappropriate titre of primary Ab
- Less successful primary Ab
- Insufficient HIER

NordiQC

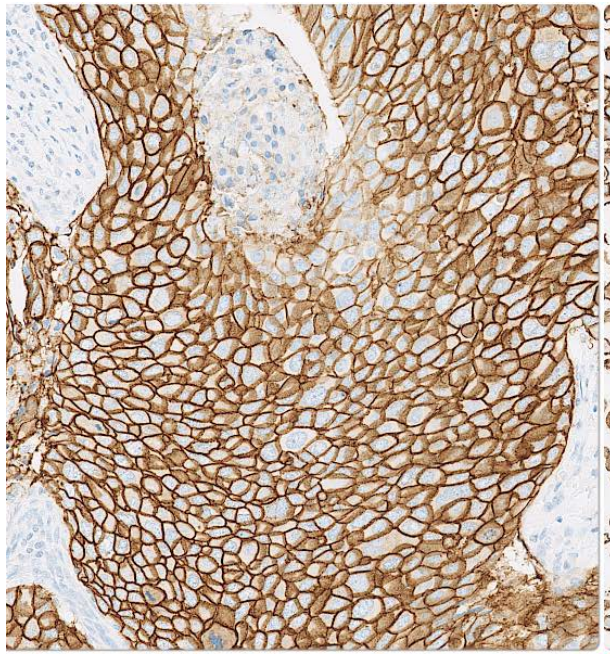
HER2 IHC: FDA-/CD-IVD versus LD assays

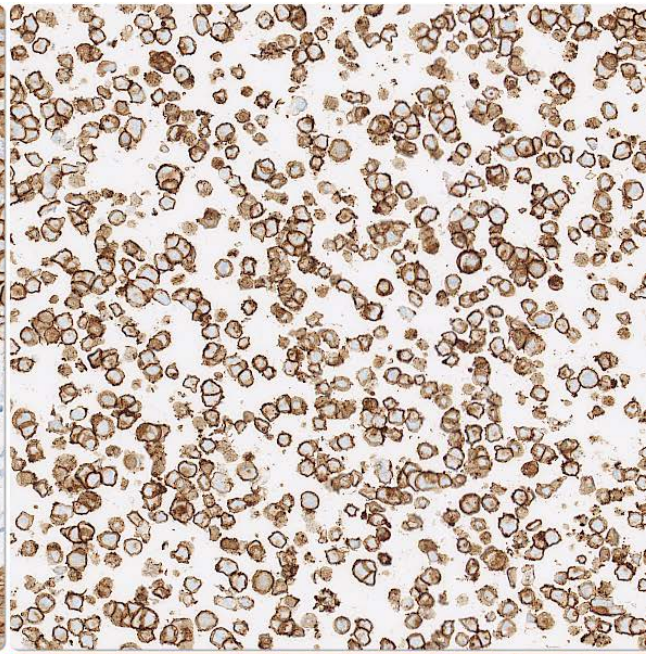
Graph 2. **Proportion of assessment marks using FDA-/CD-IVD and LD assays**



HER2 IHC: Controls

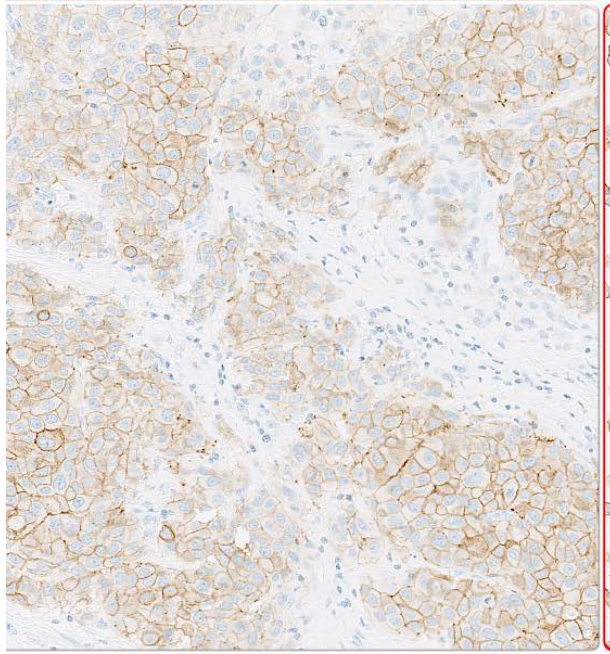
Histology: 3+ tumour

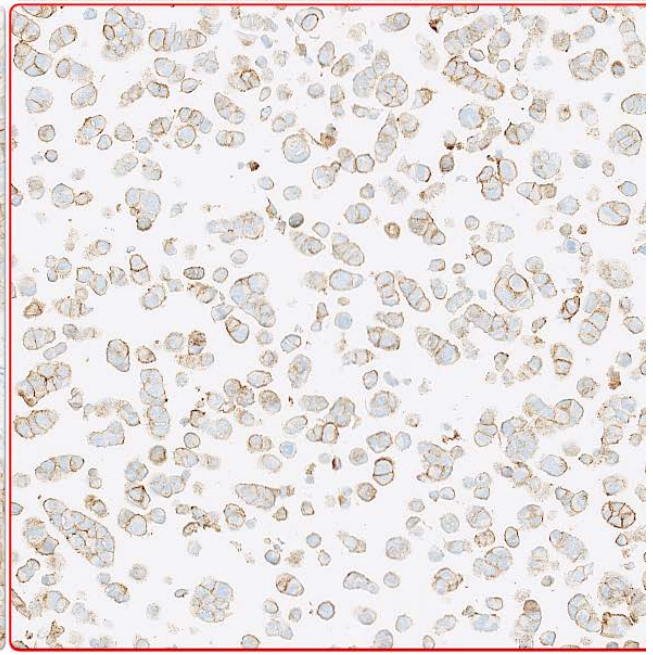




Cell lines: 3+

<u>2+ tumour</u>



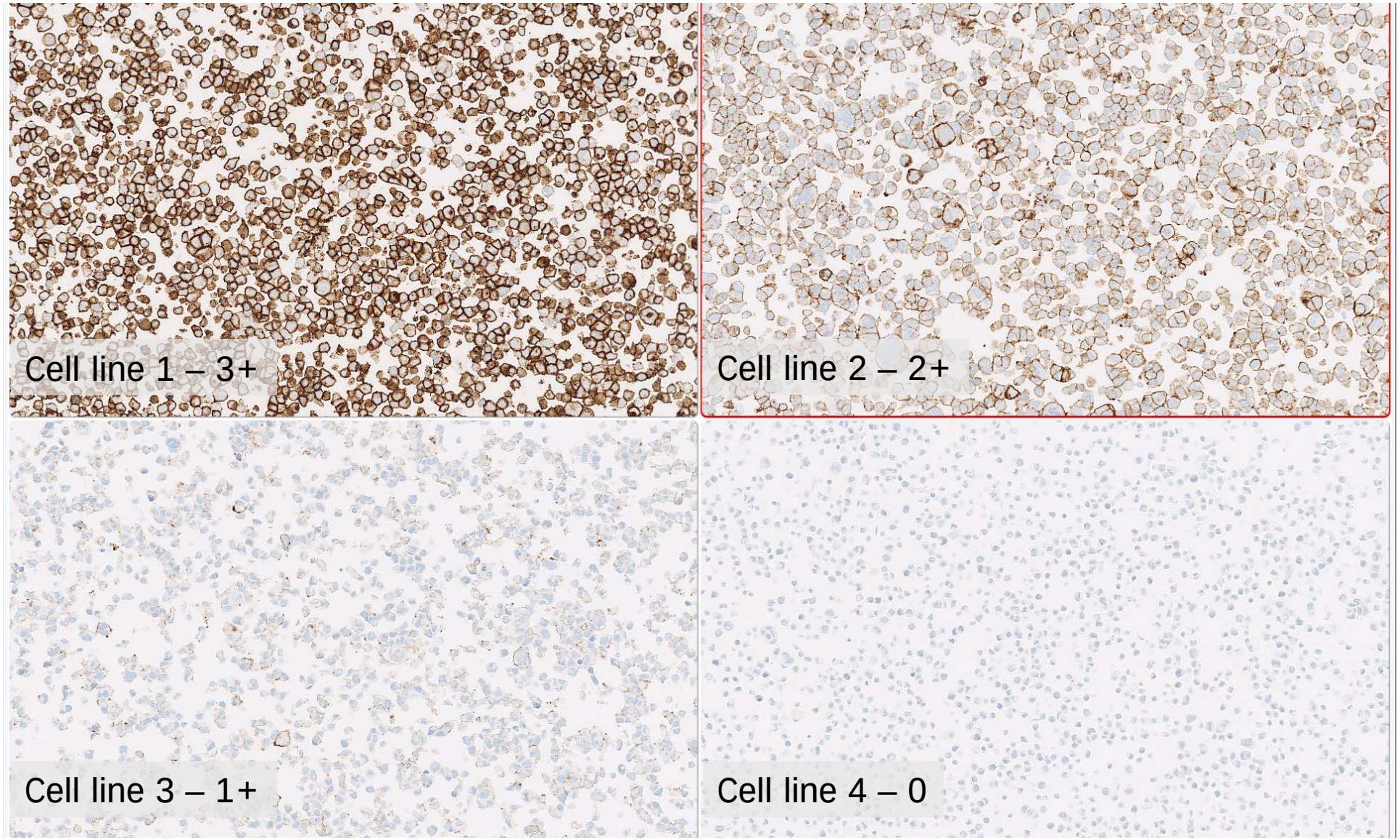


<u>2+</u>

Applicable for DIA & ref data comparing run-to-run

NordiQC

Histocyte cell lines HER2 stained with: PATHWAY IHC



HER-2 ISH

Data obtained in run H13, 2018

HER2 BRISH, Technical assessment

The main criteria for assessing a BRISH HER2 analysis as technically **optimal** were the ability to interpret the signals and thus evaluate the HER2/chr17 ratios in all **four** tissues.

Staining was assessed as **good**, if the HER2/chr17 ratios could be evaluated in all **four** tissues, but the interpretation was slightly compromised e.g. due to excessive retrieval, weak or excessive counterstaining or focal negative areas.

Staining was assessed as **borderline** if one of the tissues could not be evaluated properly e.g. due to weak signals, large negative areas with no signals (> 25% of the core) or a low signal-to-noise ratio due to excessive background staining.

Staining was assessed as **poor** if two or more of the tissue cores could not be evaluated properly e.g. due to weak signals, large negative areas with no signals (> 25% of the core) or a low signal-to-noise ratio due to excessive background staining.

HER2 BRISH and FISH interpretation

For both BRISH and FISH, participating laboratories were asked to submit a scoring sheet with their interpretation of the HER2/chr17 ratio. Results were compared to NordiQC FISH data from reference laboratories to analyze scoring consensus.

Consensus scores from the NordiQC FISH reference laboratories

- Breast ductal carcinomas, no. 1: non-amplified
- Breast ductal carcinomas, no. 2: non-amplified or equivocal
- Breast ductal carcinoma no. 4 and 5: amplified
- Breast ductal carcinoma no. 3: *not assessed*

NordiQC

Assessment Run H13 2018

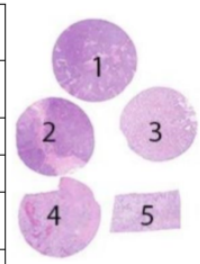
HER2 (BRISH or FISH)

Material

Table 1. **Content of the multi-block used for the NordiQC HER2 ISH assessment, run H13**

	HER2 IHC*	Dual - SISH**	FISH***	FISH***
	IHC score	HER2/chr17 ratio¤	HER2/chr17 ratio¤	HER2 copies
1. Breast carcinoma	0	0.8	0.8 – 1.0	< 4
2. Breast carcinoma	2+	1.1	1.0 – 1.2	≥ 4 and < 6
3. Breast carcinoma	*Core no. 3 was not assessed in run H13, due to suboptimal tissue quality.*			
4. Breast carcinoma	2+	2.3	2.8 – 3.3	> 6
5. Breast carcinoma	3+	8.0	6.5 – 8.5	> 6

* PATHWAY® (Ventana/Roche), data from two reference labs.
** Inform HER2 Dual ISH kit (Ventana/Roche), range of data from one reference lab.
*** HER2 FISH (Zytovision), range of data from one reference lab.
¤HER2/chr17: HER2 gene/chromosome 17 ratio



HER2 ISH module – assessment setup (H13)

NordiQC

HER2 ISH: BRISH results H13

Participation

Number of laboratories registered for HER2 BRISH	141
Number of laboratories returning slides	127 (90%)
Number of laboratories returning scoring sheet	118 (93%)
Number of laboratories registered for HER2 FISH	59
Number of laboratories returning scoring sheet	55 (93%)

Results BRISH, technical assessment

In total, 127 laboratories participated in this assessment. 90 laboratories (71%) achieved a sufficient mark (optimal or good). Results are summarized in Table 2.

Table 2**. HER2 BRISH systems and assessment marks for BRISH HER2 run H13.**

Two colour HER2 systems	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	Suff. OPS[2]
INFORM™ HER2 Dual ISH **800-4422**	93	Ventana/Roche	32	28	24	9	65%	69%
INFORM™ HER2 Dual ISH + IHC **800-4422 + HER2 IHC**	17	Ventana/Roche	14	3	0	0	100%	100%
Zyto*Dot*® 2C **C-3022 / C-3032**	8	ZytoVision	4	1	3	0	63%	71%
One colour HER2 systems								
INFORM™ HER2 SISH **780-4332**	6	Ventana/Roche	1	4	1	0	83%	-
Zyto*Dot*® **C-3003**	3	ZytoVision	3	0	0	0	100%	100%
Total	127		54	36	28	9		-
Proportion			43%	28%	22%	7%	71%	

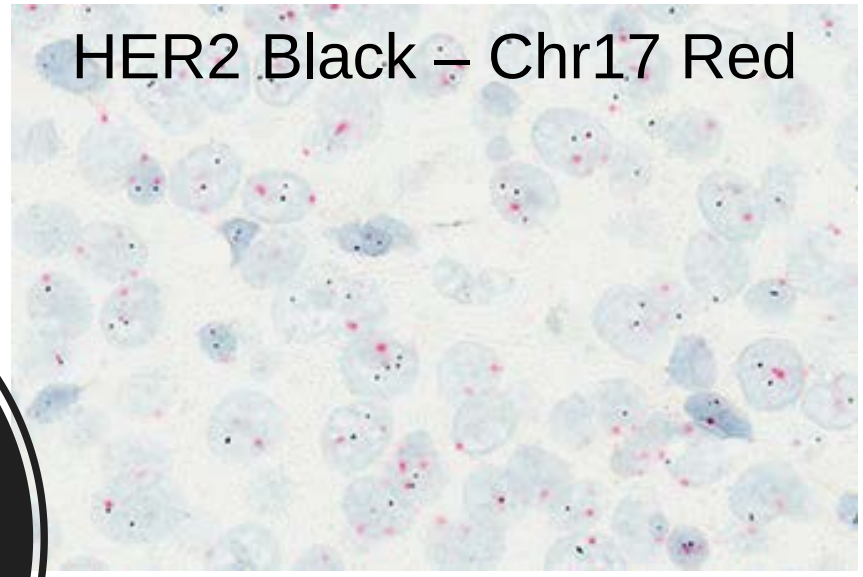
1) Proportion of sufficient stains.
2) Proportion of sufficient stains with optimal protocol settings only, see below.

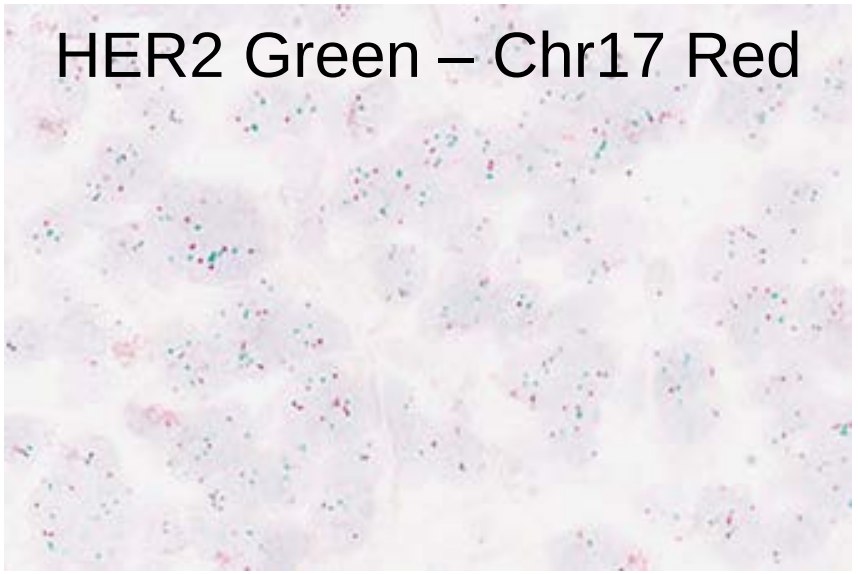
NordiQC

HER2 ISH: Optimal results

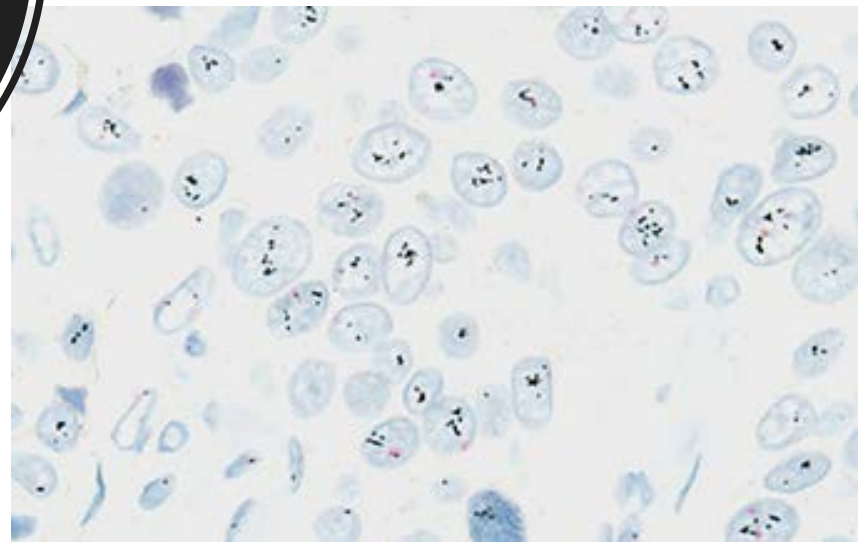
INFORM™ HER2 Dual ISH, Ventana

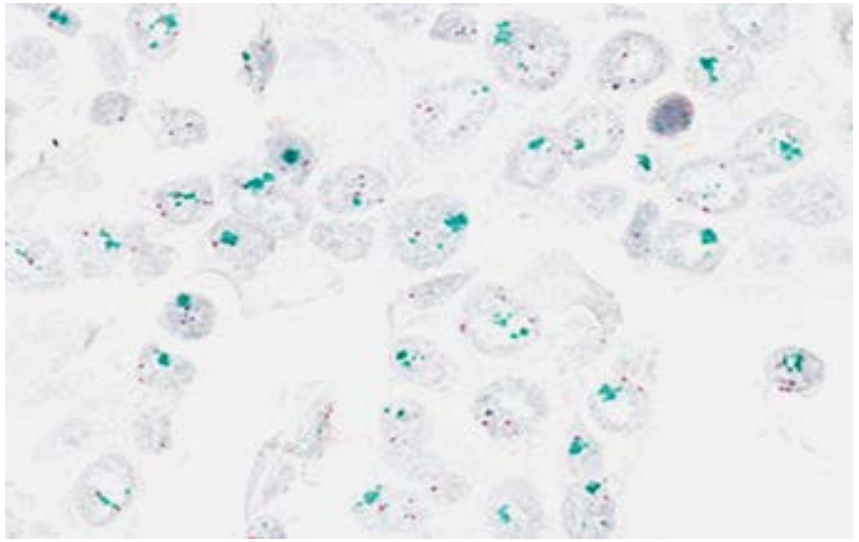
ZytoDot® 2C, ZytoVision





Unamplified





Amplified

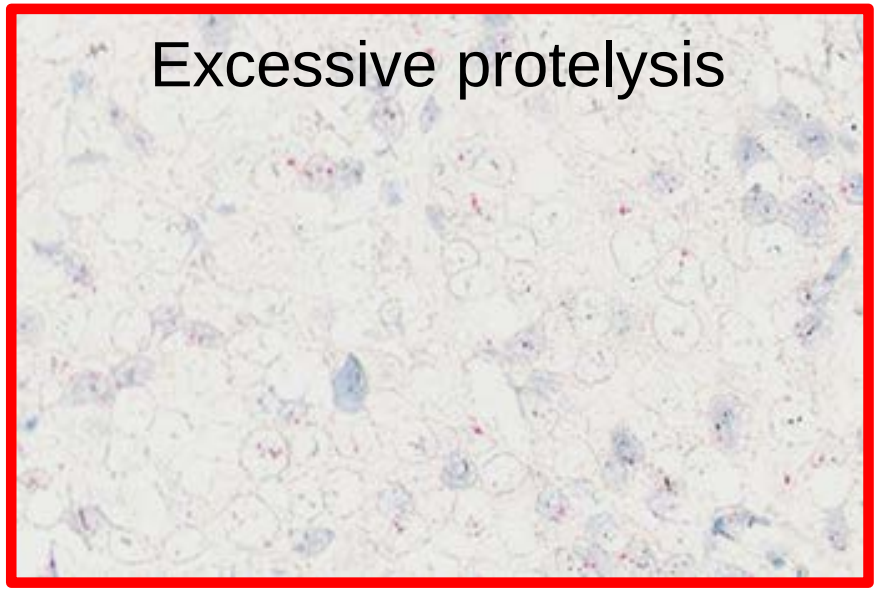
NordiQC

HER2 ISH: Technically insufficients results

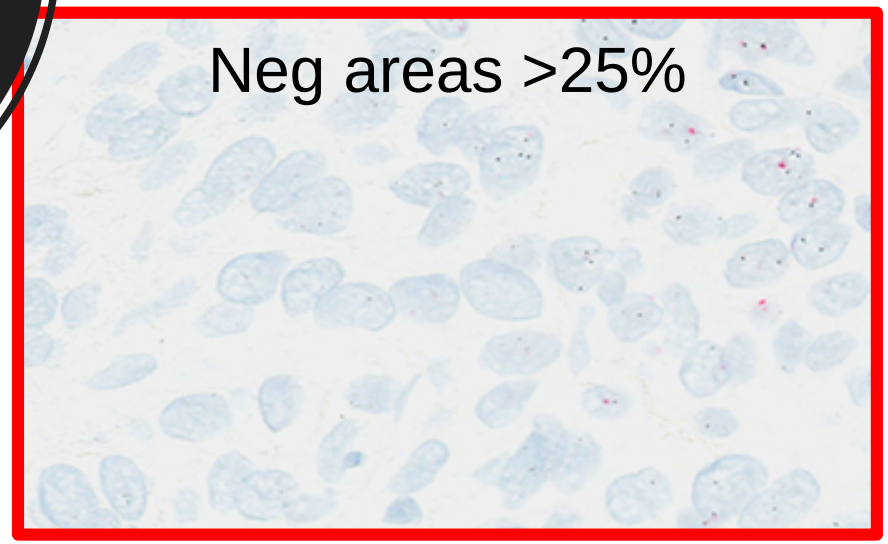
INFORM™ HER2 Dual ISH, Ventana

HER2 Black – Chr17 Red

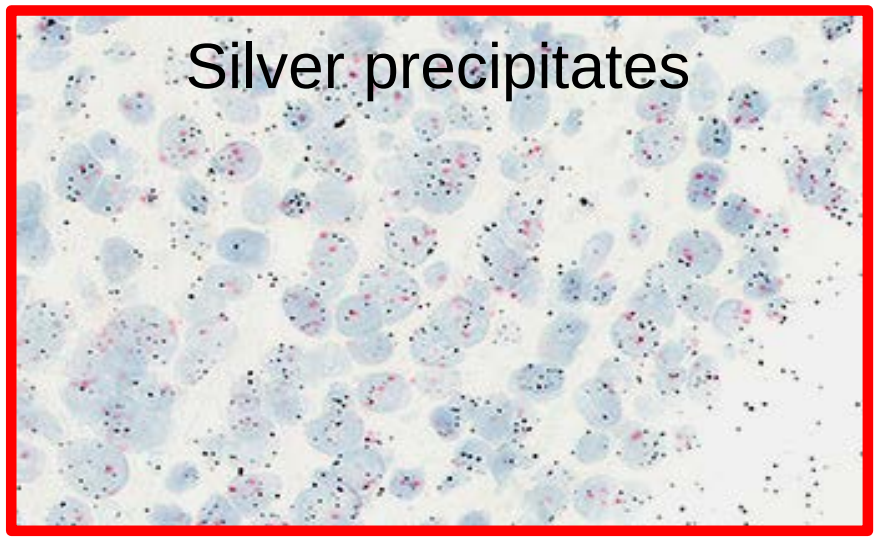
Excessive protelysis



Neg areas >25%



Silver precipitates



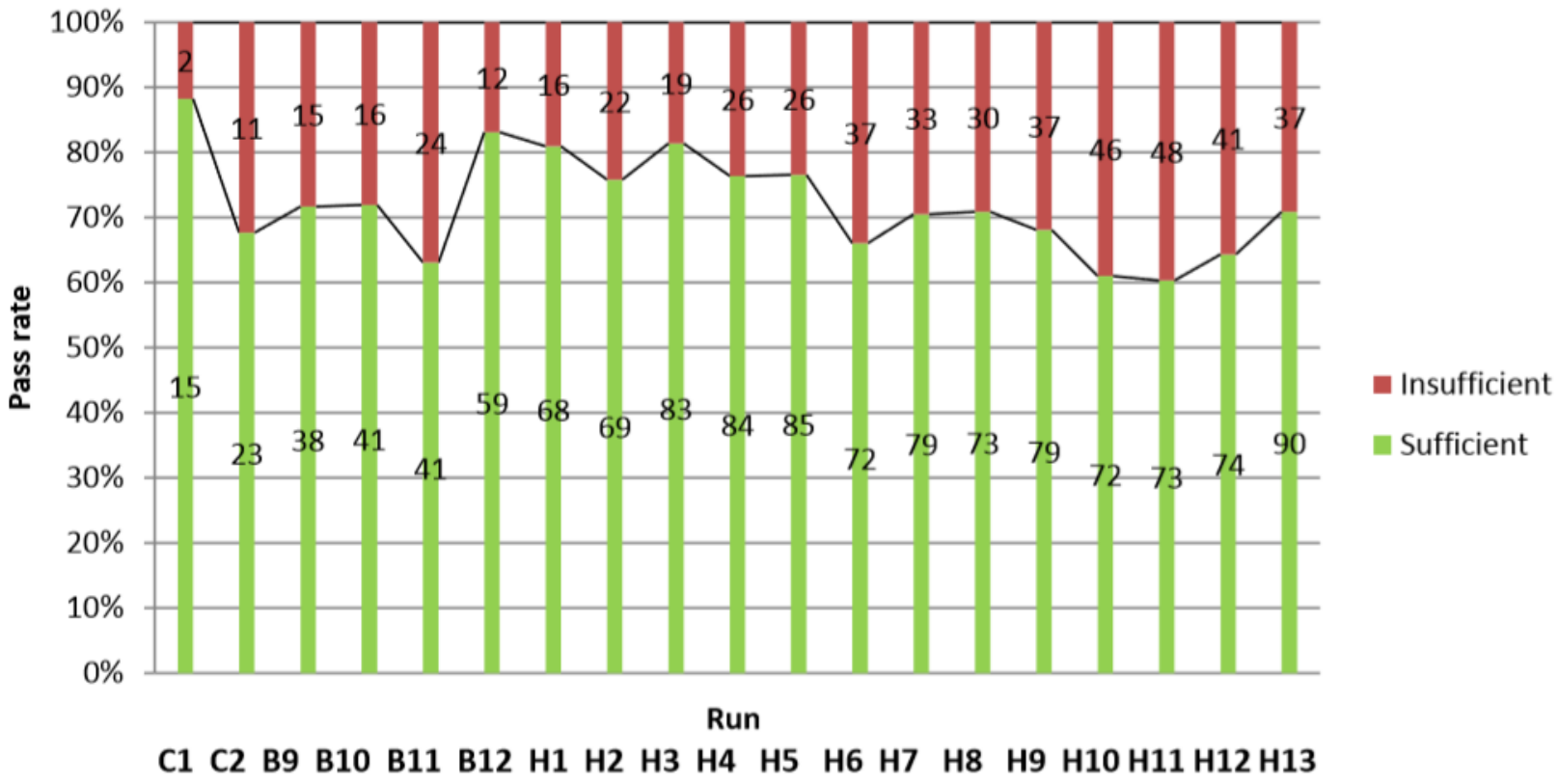
NordiQC

Tycial causes for insufficient BRISH HER2 results

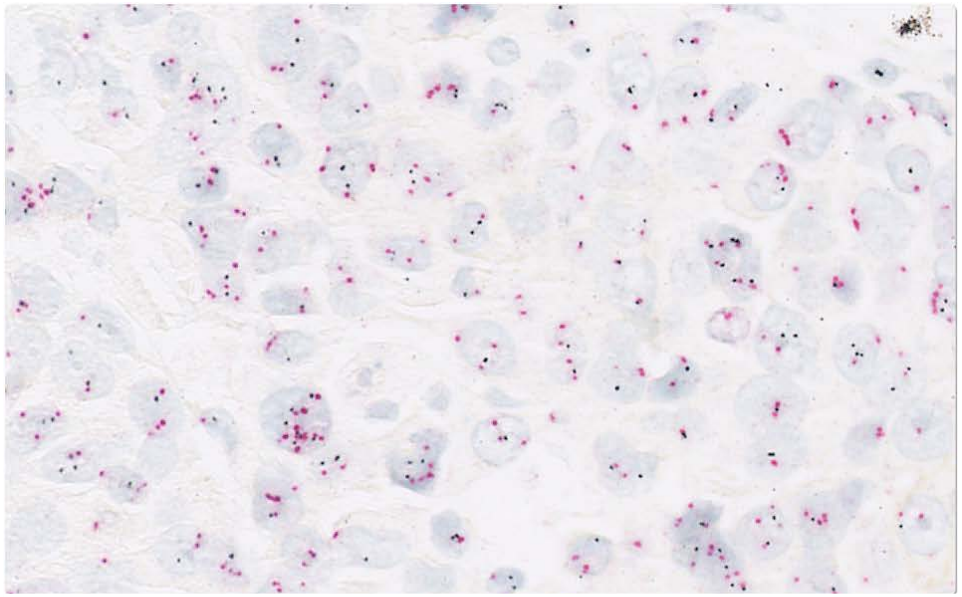
- INFORM™ HER2 Dual ISH, Ventana
  - Excessive proteolysis (> 16 min)
  - HIER in CC1
- DuoCISH™ pharmDx™, Dako
  - Insufficient proteolysis
  - Inappropriate handling of chromogen
- ZytoDot® 2C, ZytoVision
  - Excessive proteolysis
- **However, in most insufficient results no single cause (or combination) could be identified**

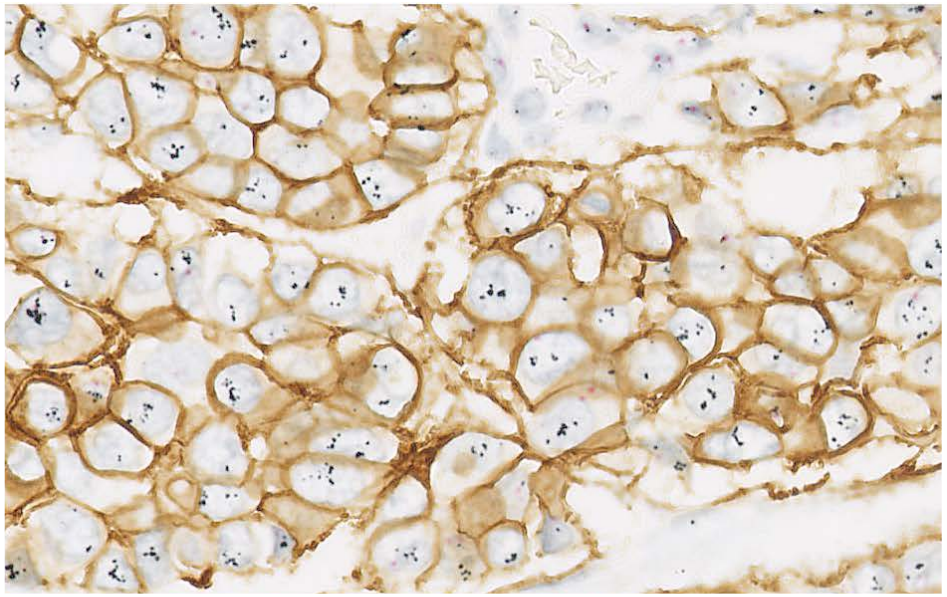
Development of pass rate in the NordiQC HER2 ISH module

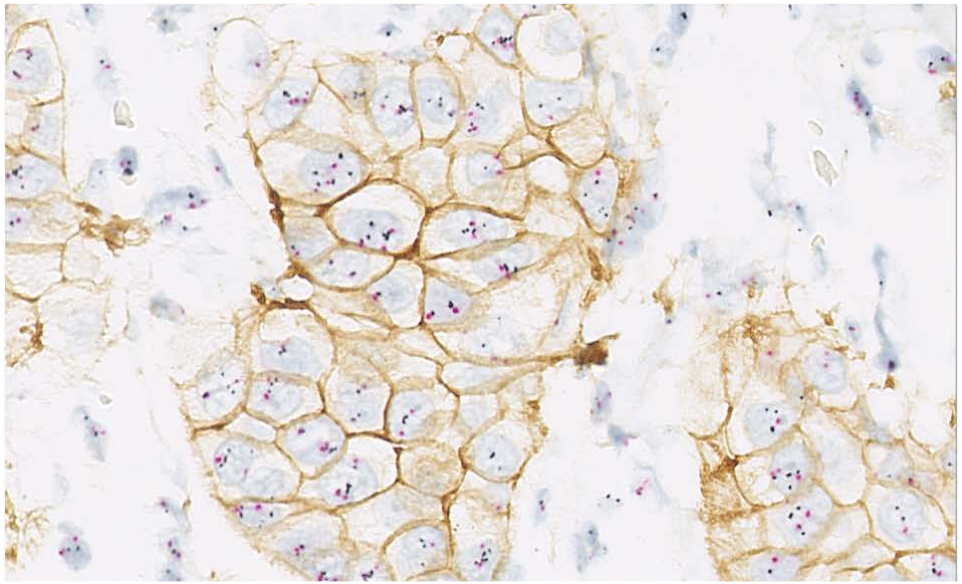
Graph 1. **Proportion of sufficient results for HER2 BRISH in the NordiQC assessment**

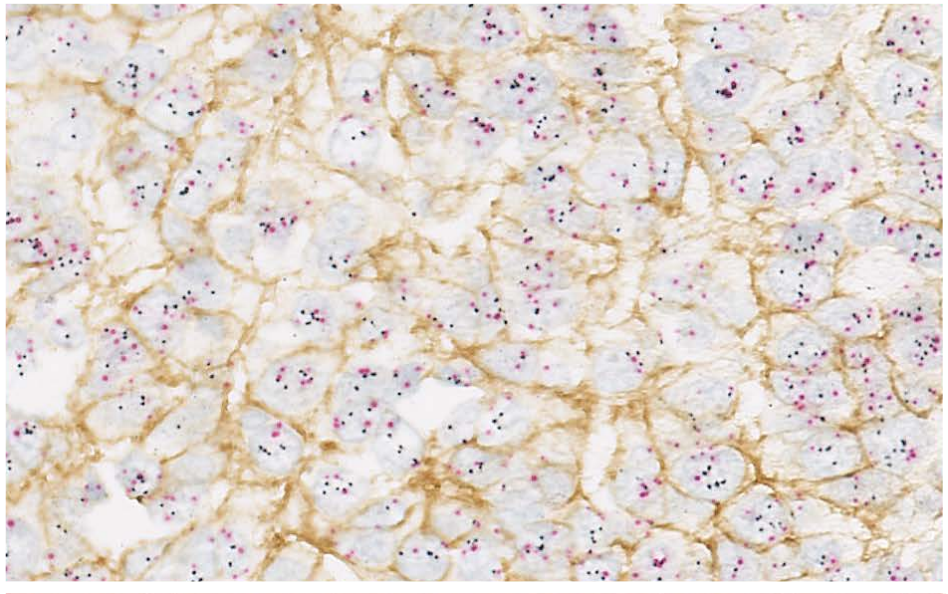


HER2 Gene-Protein-Assay (Roche): HER2 IHC + DDISH (800-4422)









<u>Pass rates</u>

H9: 86% (n=7)

H10: 75% (n=12)

H11: 50% (n=14)

H12: 94% (n=17)

H13: 100% (n=17)

NordiQC

Conclusions

Pass rates for ER, PR and HER2 IHC have improved due to robust clones and high quality IHC systems.

CE-IVD labelled RTU assays / systems show superior performance compared to laboratory developed assays.

HER2 BRISH (DDISH/SISH/CISH) results have not been improved significantly.

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