Assessment Run 51 2017
PAX8

Material
The slide to be stained for PAX8 comprised:

1. Fallopian tube, 2. Tonsil, 3. Kidney, 4. Renal clear cell carcinoma,
5. Lung adenocarcinoma, 6. Ovarian serous adenocarcinoma.

All tissues were fixed in 10% neutral buffered formalin.

Criteria for assessing a PAX8 staining as optimal included:

- An at least weak to moderate, distinct nuclear staining reaction of the majority of ciliated epithelial cells and a strong nuclear staining of intercalated secretory epithelial cells in the Fallopian tube.
- An at least weak to moderate, distinct nuclear staining reaction in the majority of epithelial cells of the proximal, distal/collecting renal tubules, loops of Henle and the parietal epithelial cells of Bowman's capsule in the kidney.
- A strong, nuclear staining reaction of virtually all neoplastic cells of the ovarian serous carcinoma.
- A moderate to strong, nuclear staining reaction of the majority of neoplastic cells in the renal clear cell carcinoma.
- Strong, nuclear staining reaction of virtually all mantle zone B-cells, germinal center B-cells and interfollicular peripheral B-cells in tonsils were expected and accepted for antibodies raised against the N-terminal part of PAX8 (1). This applied for all polyclonal Abs and mAbs clones MRQ-50, PAX8/1492 and DBM15.48
- No nuclear staining reaction of B-cells was expected for antibodies raised against the C-terminal part of PAX8. This applied for mAb clone BC12 and rmAbs clones EP298 and ZR-1. According to the datasheet the rmAb clone SP348 is raised against a synthetic peptide derived from the N-terminus of human PAX8 protein. In spite of that, no reaction with B-cells was seen with this clone.
- No staining reaction in the tumor cells in the lung adenocarcinoma

In cells with strong specific nuclear staining reaction, weak cytoplasmic staining was accepted.

Participation

Number of laboratories registered for PAX8, run 51	232
Number of laboratories returning slides	213 (92%)

Results
213 laboratories participated in this assessment. 120 laboratories (56%) achieved a sufficient mark (optimal or good). Abs used and assessment marks are summarized in Table 1 (see page 2)

The most frequent causes of insufficient staining were:
- Less successful performance of the mAb MRQ-50 on the Ventana BenchMark platform.
- Use of detection systems with a low sensitivity
- Too short efficient HIER time
- Too low concentration of the primary Ab
- Too high concentration of the primary Ab

Performance history
This was the third NordiQC assessment of PAX8. A decrease in pass rate was seen compared to run 42 in 2014 (see Table 2). The reason for this is uncertain, but many new laboratories participated in run 51 compared to the previous run and the majority of these new laboratories used the mAb clone MRQ-50 on the Ventana BenchMark platform, which seems to be a challenging combination.

Table 2. **Proportion of sufficient results for PAX8 in the three NordiQC runs performed**

	Run 34 2012	Run 42 2014	Run 51 2017
Participants, n=	35	125	213
Sufficient results	63 %	70 %	56 %

Conclusion
Optimal staining results could be obtained with the mAbs clones **MRQ-50**, **BC12** and **PAX8/1492**, the rmAb clones **EP298**, **SP348** and **ZR-1** and the pAb **10336-1-AP**, **363A** and **CP379**. With the exception of mAb clone BC12, the highest proportion of optimal results was obtained performing HIER in an alkaline buffer for at least 20 min. (or at least 32 min. for Ventana BenchMark users) and use of a sensitive and specific 3-step polymer/multimer based detection system. The concentration of the primary antibody must be carefully calibrated. The most widely used PAX8 antibody, mAb clone **MRQ-50,** had – both as a laboratory develop (LD) assay and as a Ready to Use assay - an alarmingly low pass rate on the Ventana BenchMark platform, whereas it performed with a satisfactory high pass rate on both the Leica Bond and Dako Autostainer platforms. The pAb **10336-1-AP** provided sufficient results on all main IHC systems, but optimal results were only seen on the Ventana BenchMark and Dako Autostainer platforms. The recently introduced rmAbs clones **EP298**, **SP348** and **ZR-1** gave encouraging results especially on the Ventana Benchmark and Dako Omnis systems. In addition to relative high pass rates these clones showed – similar to mAb clone BC12 - no cross reactivity with PAX5 in B-cells (1), resulting in an improved signal to noise ratio.
Kidney and fallopian tube are both recommendable positive tissue controls for PAX8. In kidney, an at least weak to moderate, distinct nuclear staining reaction in epithelial cells of the proximal and distal/collecting renal tubules and parietal epithelial cells of Bowman's capsule must be seen. In fallopian tube, an at least weak to moderate, distinct nuclear staining reaction of the majority of ciliated epithelial cells and a strong nuclear staining of intercalated secretory epithelial cells must be seen.

Table 1. **Antibodies and assessment marks for PAX8, run 51**

Concentrated antibodies	n	Vendor	Optimal	Good	Borderline	Poor	Suff.[1]	Suff. OPS[2]
mAb clone **BC12**	11 1	Biocare Zytomed Systems	1	4	0	7	42%	100%
mAb clone **DBM15.48**	1	Diagnostic Biosystems	0	1	0	0	-	-
mAb clone **MRQ-50**	63 1	Cell Marque Menarini Diagnostics	17	24	13	10	64%	69%
mAb clone **PAX8R1**	2	abcam	0	0	2	0	-	-
rmAb clone **EP298**	4 2 1	Cell Marque Epitomics BIO SB	3	3	0	1	86%	100%
rmAb clone **SP348**	1	Spring Biosciences	1	0	0	0	-	-
rmAb clone **ZR-1**	3 1 1	Zeta Corporation Abcam Nordic Biosite	2	2	1	0	80%	100%
pAb, **10336-1-AP**	29	Protein Tech	8	10	9	2	62%	83%
pAb, **363A-15**	1	Cell Marque	1	0	0	0	-	-
pAb, **CP379**	3	Biocare	1	1	1	0	-	-
pAb, **MP-379**	1	Menapath	0	1	0	0	-	-
Unknown Ab,	1		1	0	0	0	-	-
Ready-To-Use antibodies								
mAb clone **MRQ-50 760-4618**	11	Ventana/Cell Marque	0	4	5	2	36%	-
mAb clone **MRQ-50 363M**	68	Cell Marque	3	25	27	13	41%	55%
mAb clone **PAX8/1492 MAD-000753QD/V**	2	Master Diagnostica	2	0	0	0	-	-
rmAb **ZR-1 ZA0558**	1	ZSGB-BIO	0	1	0	0	-	-
rmAb clone **EP298 8502-C010**	1	Sakura Finetek	1	0	0	0	-	-
pAb **363A-18**	1	Cell Marque	1	0	0	0	-	-
pAb **RAB-0657**	1	maixin	0	1	0	0	-	-
pAb **RBG047**	1	Zytomed	0	1	0	0	-	-
Total	213		42	78	58	35	-	
Proportion			20%	36%	27%	17%	56%	

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

Detailed analysis of PAX8, Run 51
The following protocol parameters were central to optimal staining:

Concentrated Antibodies
mAb clone **MRQ-50**: Protocols with optimal results were all based on heat induced epitope retrieval (HIER) using either Bond Epitope Retrieval Solution 2 (BERS2, Leica) (8/12) *, Target Retrieval Solution (TRS) pH 9 (3-in-1) (Dako) (6/16), Target Retrieval Solution pH 9 (1/1), Citrate buffer pH 6.7 (1/1), or Cell Conditioning 1 (CC1, Ventana) (1/23) as retrieval buffer. The mAb was typically diluted in the range of 1:25-1:200 depending on the total sensitivity of the protocol employed. Using these protocol settings, 35 of 51 (69%) laboratories produced a sufficient staining result (optimal or good).
*(number of optimal results/number of laboratories using this buffer)

mAb clone **BC12**: One protocol with an optimal result was based on HIER in citrate pH 6 using a pressure cooker. The mAb was diluted 1:40 and incubated for 30 min. at room temperature and visualized with a 3-step polymer conjugate system (UltraVision Quanto, ThermoFisher). Using similar protocol settings, 3 of 3 (100%) laboratories produced a sufficient staining result.

rmAb clone **EP298**: Protocols with optimal results were all based on HIER using TRS High pH (3/5) (Dako). The mAb was diluted in the range of 1:50-1:150 depending on the total sensitivity of the protocol employed. Using these protocol settings, 5 of 5 (100%) laboratories produced a sufficient staining result (optimal or good).

rmAb clone **SP348**: One lab used the rmAb clone SP348 and an optimal result was achieved. The protocol was based on HIER in TRS High pH (Dako). The rmAb was diluted 1:200 and incubated for 30 min. at 32°C and visualized with a 3-step polymer conjugate system (EnVision Flex+, Dako/Agilent).

rmAb clone **ZR-1**: Protocols with optimal results were all based on HIER using either TRS High pH (Dako) (1/1) or CC1 (Ventana) (1/2). The mAb was diluted in the range of 1:25-1:50 depending on the total sensitivity of the protocol employed. Using these protocol settings, 2 of 2 (100%) laboratories produced a sufficient staining result (both optimal).

pAb **10336-1-AP**: Protocols with optimal results were all based on HIER using either, CC1 (Ventana/Roche) (5/15) or TRS pH 9 (3-in-1) (Dako/Agilent) (3/5) as retrieval buffer. The pAb was typically diluted in the range of 1:200-1:1,000 depending on the total sensitivity of the protocol employed. Using these protocol settings, 15 of 18 (83%) laboratories produced a sufficient staining result (optimal or good).

pAb, **363A-15**: One lab used the pAb 363A and an optimal result was achieved. The protocol was based on HIER in CC1 (Ventana). The pAb was diluted 1:25 and incubated for 32 min. at 36°C and visualized with a 3-step multimer conjugate system (OptiView, Ventana).

pAb, **CP379**: One protocol with an optimal result was based on HIER in BERS2 (Leica). The pAb was diluted 1:500 and incubated for 25 min. at room temperature and visualized with a 3-step multimer conjugate system (Bond Refine, Leica).

Table 3. **Proportion of optimal results for PAX8 for the most commonly used antibodies as concentrate on the 4 main IHC systems***

Concentrated antibodies	**Dako Autostainer Link / Classic**		**Dako Omnis**		**Ventana BenchMark GX / XT / Ultra**		**Leica Bond III / Max**	
	TRS pH 9.0	TRS pH 6.1	TRS pH 9.0	TRS pH 6.1	CC1 pH 8.5	CC2 pH 6.0	ER2 pH 9.0	ER1 pH 6.0
mAb **MRQ-50**	6/15** (40%)	-	0/3	0/1	1/22 (5%)	0/2	8/12 (67%)	0/2
mAb **BC12**	0/1	-	-	0/1	0/2	-	0/4	-
pAb **10336-1-AP**	3/5 (60%)	-	0/4	0/1	5/15 (33%)	0/1	0/3	-

* Antibody concentration applied as listed above, HIER buffers and detection kits used as provided by the vendors of the respective systems.
** (number of optimal results/number of laboratories using this buffer)

Ready-To-Use antibodies and corresponding systems
mAb clone **MRQ-50,** product no. **363M-18**, Cell Marque, BenchMark GX/XT/Ultra:
One protocol with an optimal result was based on 56 min. HIER using Cell Conditioning 1 (CC1, Ventana), 32 min. incubation of the primary Ab and OptiView with amplification (Ventana 760-700) as detection system. Using similar protocol settings, 6 of 11 (55%) laboratories produced a sufficient staining result (optimal or good).

mAb clone **PAX8/1492**, product no. **MAD-000753QD/V**, Master Diagnostica: MD-Stainer:
The protocol with an optimal result was based on 20 min. HIER using Tris-EDTA / EGTA pH 9, 35 min. incubation of the primary Ab and Master Polymer Plus (Master Diagnostica) as detection system.

rmAb clone **EP298,** product no. **8502-C010**, Sakura Finetek, Genie:
The protocol with an optimal result was based on 45 min. HIER using Sakura Finetek Tissue-Tek Genie High pH Antigen Retrieval Buffer, 30 min. incubation of the primary Ab and Tissue-Tek PRO DAB Detection Kit (8826-K250) as detection system.

pAb **363A-18,** product no. **363A-18**, Cell Marque, BenchMark GX/XT/Ultra:
The protocol with an optimal result was based on 32 min. HIER using CC1 (Ventana), 8 min. incubation of the primary Ab and OptiView with amplification (Ventana 760-700) as detection system.

Table 4 summarizes the proportion of sufficient and optimal marks for the most commonly used RTU systems. The performance was evaluated both as "true" plug-and-play systems performed strictly accordingly to the vendor recommendations and by laboratory modified systems changing basal protocol settings. Only protocols performed on the specific IHC stainer device are included.

Table 4. **Proportion of sufficient and optimal results for PAX8 for the most commonly used RTU IHC systems**

RTU systems	**Recommendedprotocol settings***		**Laboratory modified protocol settings****	
	Sufficient	Optimal	Sufficient	Optimal
VMS Ultra/XT mAb MRQ-50 **760-4618**	0% (0/1)	0% (0/1)	40% (4/10)	0% (0/10)
VMS Ultra/XT mAb MRQ-50 **363M-18**	25% (1/4)	0% (0/4)	36% (20/56)	2% (1/56)

* 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 integrated.

Comments
In this assessment and in concordance with the previous NordiQC PAX8 assessments, the prevalent feature of an insufficient result was a too weak or false negative staining reaction of cells expected to be demonstrated. This pattern was seen in 88% of the insufficient results (82 of 93 laboratories). The remaining 12% of insufficient results were characterized by a poor signal-to-noise ratio and false positive staining reaction compromising interpretation.
The majority of the participating laboratories were able to demonstrate PAX8 in high-level antigen expressing cell, such as secretory epithelia cells of the fallopian tube and neoplastic cells of the ovarian serous carcinoma, whereas demonstration of PAX8 in low-level antigen expressing cells as the neoplastic cells of the renal clear cell carcinoma, epithelial cells of collecting ducts, parietal cells lining the Bowman capsules of the kidney and in particular ciliated epithelial cells of the fallopian tube and epithelial cells of the proximal tubules in the kidney were more challenging and only seen with appropriate protocol settings (see Fig. 1 to Fig. 4). Cases of insufficient staining due to false positive cytoplasmic and/or aberrant nuclear reaction of cells not expressing PAX8 were also seen. This pattern was typically caused by a too high concentration of the primary Ab or the use of a less successful primary antibody (see Fig. 6b). As in previous assessments, cross reactivity to PAX5 – resulting in nuclear staining in B-cells – was accepted. Within the last few years, a number of well performing rmAbs without this cross reactivity has been introduced to the market. This makes it increasingly difficult to vindicate the use of PAX8 antibodies cross reacting with PAX5 (see Fig. 5a, Fig. 5b and Fig. 6a).

60% (127 of 213) of the laboratories used Abs as concentrated format within laboratory developed (LD) assays for PAX8. The mAb clone MRQ-50 and the pAb 10336-1-AP were the most widely used antibodies (see Table 1). Both antibodies could be used to obtain an optimal staining result, but in general the pass rate for both antibodies was not impressive. For LD assays the pass rate for mAb clone MRQ-50 and pAb 10336-1-AP was 64% (41 of 64) and 62% (18 of 29), respectively. Data focusing on the 3 main IHC systems (see Table 3) showed that the proportion of optimal results using the mAb clone MRQ-50 as a concentrate was significantly lower on the Ventana system compared to the Dako Autostainer and Leica Bond systems. On the Ventana system, only 5% (1 of 22) were evaluated as optimal. On the Dako Autostainer and Leica Bond systems, the proportion of optimal results was 40% (6 of 15) and 67% (8 of 12), respectively (see Table 3). The reasons for this difference are unclear, but similar findings were observed on the Dako Omnis system, suggesting that mAb clone MRQ-50, on fully automated systems with integrated high temperature washing (32°C on the Omnis and 36°C on the BenchMark), is more difficult to optimize than on "room temperature systems" (e.g. Dako Autostainer and Leica Bond). Possibly, efficient washing at elevated temperatures (32°C to 36°C) could reverse binding of antibodies to their epitopes, especially if the antibody affinity is relatively low. Whether this is the case with the mAb

clone MRQ-50 is so far uncertain. The MRQ-50 protocols applied on Dako Autostainer and Leica Bond achieving optimal marks were all based on HIER at high pH and a 3-step polymer detection system. With the pAb 10336-1-AP, optimal staining results could be obtained on both the Dako Autostainer (3 of 5) and Ventana Benchmark (5 of 15) systems, whereas no optimal staining results were seen on the Dako Omnis (0 of 5) and Leica Bond (0 of 3) systems.
Considering, the overall low pass rate and low proportion of optimal scores obtained by the most widely used concentrated antibodies, mAbs clone BC12 and MRQ-50 and pAb 10336-1-AP, it is important to focus on some encouraging results obtained by the 3 rabbit monoclonal Abs that recently has been introduced commercially. The clones EP298, SP348 and ZR-1 were all capable of producing optimal staining results within a LD assay for PAX8. Furthermore, all optimal staining results were seen on either the Dako Omnis system or Ventana BenchMark system, the two systems that seem to be a serious challenge for the mAb clone MRQ-50. An additional important bonus with the rmAb clones EP298, SP348 and ZR-1 is that none of them do cross react with PAX5, leaving all B-cells unstained and subsequently improving the signal to noise ratio (see Fig. 5a, Fig. 5b and Fig. 6a) and reducing the risk of clinical misdiagnosis.

40% (86 of 213) of the laboratories used Abs in Ready-To-Use (RTU) formats. This was a minor increase compared to the previous PAX8 assessment in 2014, where 38% of the laboratories used the RTU format. The most widely used RTU systems for PAX8 were the mAb clone MRQ-50 based **760-4616** from Ventana/Cell Marque and the mAb clone MRQ-50 based **363M-18** from Cell Marque both intended for use on the Ventana BenchMark system. Both RTU products had an alarmingly low pass rate of 36% (4 of 11) and 35% (21 of 60), respectively. However, these data are in line with the observation for the MRQ-50 based LD assays and supports the claim that the mAb clone MRQ-50 is very difficult to optimize on the Ventana BenchMark system. In total, 71 laboratories (see Table 4) used one of the two RTUs. Only 5 laboratories followed the recommended protocol settings, and 20% (1 of 5) achieved a sufficient staining result (none were optimal). The remaining 66 laboratories modified the protocol settings and 36% (24 of 66) achieved a sufficient staining result with 2% (1 of 66) optimal. In comparison, the MRQ-50 based 363M RTU was used by 8 laboratories using various non-Ventana systems and the pass rate was 88% (7 of 8) with 25% (2 of 8) optimal. Analyzing the data for the RTU products on the Ventana system did not reveal which modifications to the RTU protocol that would guaranty optimal or even sufficient staining results. The only lab that obtained optimal staining results used the OptiView detections system with tyramide signal amplification, in combination with prolonged incubation time of the primary Ab (32 min.) and a prolonged HIER pretreatment in CC1 (56 min.). This indicates that a highly sensitive detection system in combination with a careful recalibration of incubation time in primary Ab and HIER pretreatment might improve the general pass rate for the MRQ-50 RTUs on the Ventana system. In support of this was the fact that 13 laboratories using the OptiView detection system with signal amplification had a pass rate of 62% compared to only 33% for OptiView without amplification, 44% for UltraView with amplification and 20% for UltraView without amplification.

Controls
Kidney and fallopian tube are both recommended as positive tissue controls for PAX8. In kidney, optimally calibrated protocols must show an at least weak to moderate, distinct nuclear staining reaction in the epithelial cells of the proximal and distal renal tubules, loops of Henle, collecting ducts, and the parietal epithelial cells of Bowman's capsule. A weak cytoplasmic staining reaction in the same cells can be expected. In fallopian tube, the protocol must be calibrated to provide an at least weak to moderate, distinct nuclear staining of the majority of the ciliated epithelial cells and a strong nuclear staining of the intercalated secretory epithelial cells. A weak cytoplasmic staining in the intercalated secretory epithelial cells can be expected and must be accepted.

1: Moretti L, Medeiros LJ, Kunkalla K, Williams MD, Singh RR, Vega F. N-terminal PAX8 polyclonal antibody shows cross-reactivity with N-terminal region of PAX5 and is responsible for reports of PAX8 positivity in malignant lymphomas. Mod. Pathol. 2012 Feb;25(2):231-6. doi: 10.1038/modpathol.2011.162. Epub 2011 Oct 28. PubMed PMID: 22037256.

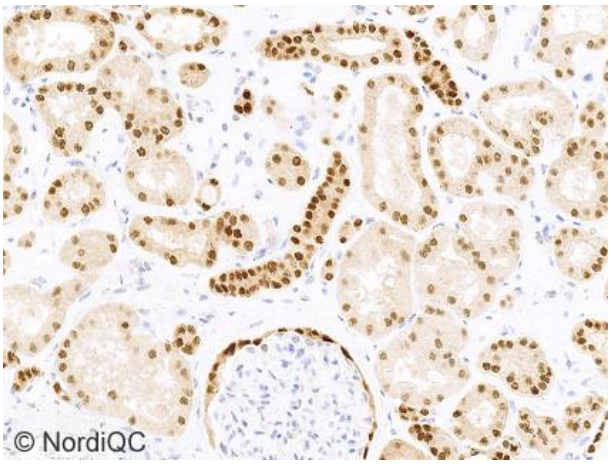

Fig. 1a
Optimal PAX8 staining of the kidney using the rmAb clone EP298 (Epitomics) within a laboratory developed assay optimally calibrated, using HIER in an alkaline buffer and a 3-step polymer system (Dako/Agilent) and performed on the Dako Omnis stainer. A moderate to strong, distinct nuclear staining of the epithelial cells lining the Bowman capsule and of the distal/collecting tubular cells in the kidney is seen. A weak to moderate nuclear staining is seen in the majority of proximal tubular cells. A weak cytoplasmic background staining is seen and accepted in both the epithelial cells lining the Bowman capsule and the tubular cells (same protocol used in Figs. 1a - 4a) Compare with Fig. 1b.

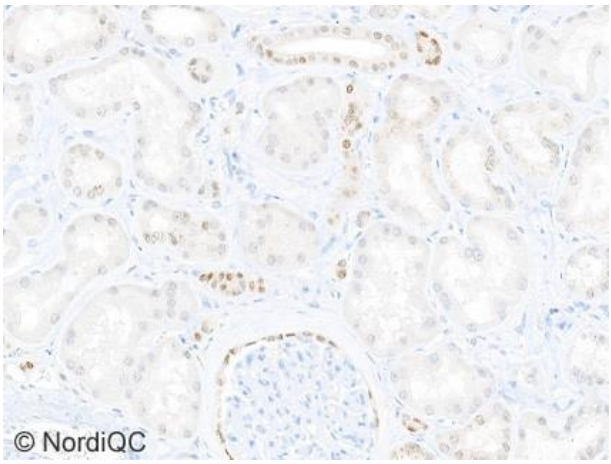

Fig. 1b
Insufficient PAX8 staining of the kidney using the mAb clone MRQ-50 (Cell Marque) within a laboratory developed assay providing a too low analytical sensitivity. A too low titre of the primary antibody and the use of a less sensitive 2-step multimer based system, UltraView on the Ventana BenchMark system, were the main causes for the insufficient result. Only a weak nuclear staining of the epithelial cells lining the Bowman capsule and of the distal/collecting tubular cells is seen. The proximal tubular cells are virtually negative. Compare with Fig. 1a. - same field. Also compare with Figs. 2b-4b – same protocol.

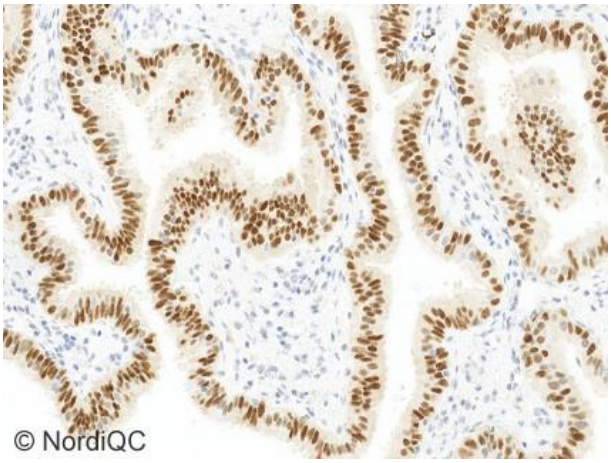

Fig. 2a
Optimal PAX8 staining of the fallopian tube using the same protocol as in Fig. 1a. A weak to moderate, distinct nuclear staining of the majority of the ciliated epithelial cells and a strong nuclear staining of the intercalated secretory epithelial cells is seen. A weak cytoplasmic background staining is seen and accepted in the epithelial cells. Compare with Fig. 2b.

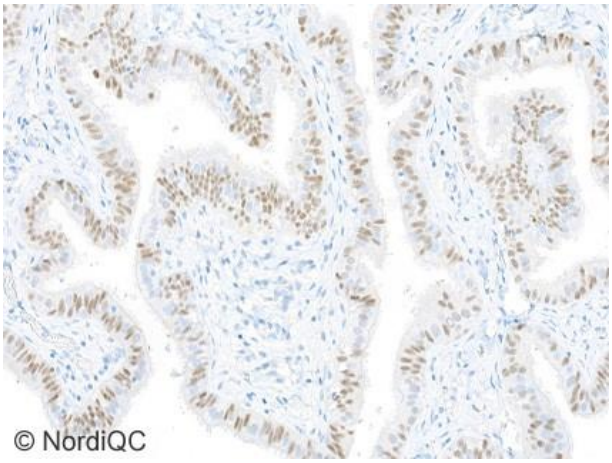

Fig. 2b
Insufficient PAX8 staining of the fallopian tube using the same protocol as in Fig. 1b. A moderate nuclear staining of the intercalated secretory epithelial cells is seen whereas the ciliated epithelial cells are virtually negative. Compare with Fig. 2a – same field.

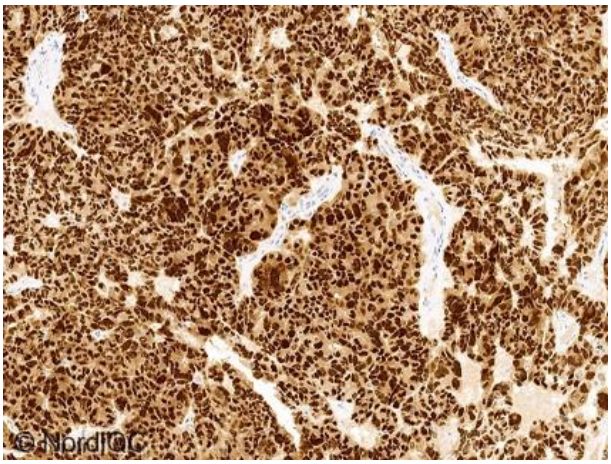

Fig. 3a
Optimal PAX8 staining of the ovarian serous carcinoma using the same protocol as in Figs. 1a and 2a. A very strong, nuclear staining is seen in virtually all the neoplastic cells. Compare with Fig. 3b.

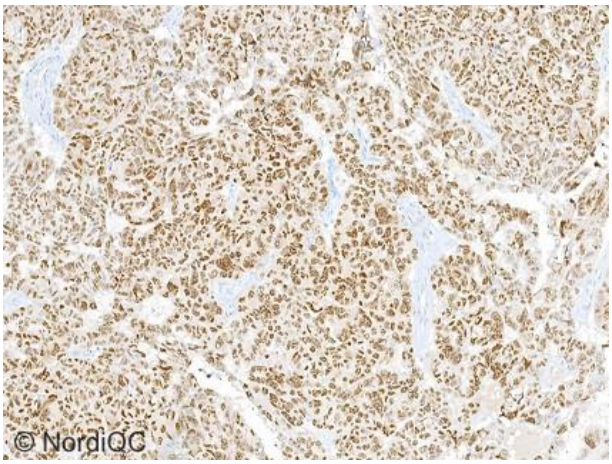

Fig. 3b
Insufficient PAX8 staining of the ovarian serous carcinoma using the same protocol as in Figs. 1b and 2b. The neoplastic cells display only a weak to moderate nuclear staining reaction. Compare with Fig. 3a – same field.

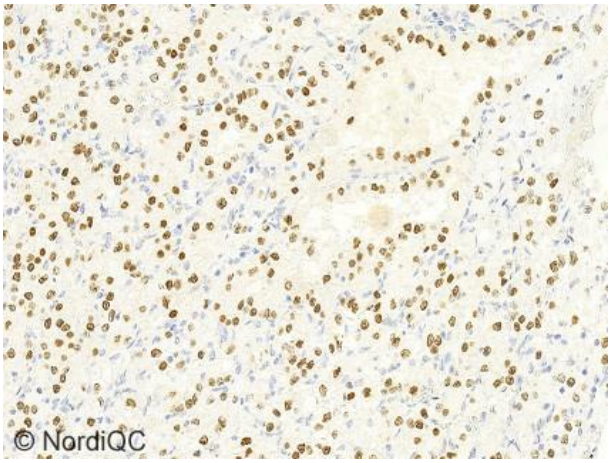

Fig. 4a
Optimal PAX8 staining in the renal clear cell carcinoma using the same protocol as in Figs. 1a-3a. Virtually all the neoplastic cells show a moderate to strong nuclear staining reaction. No background staining is seen. Compare with Fig 4b.

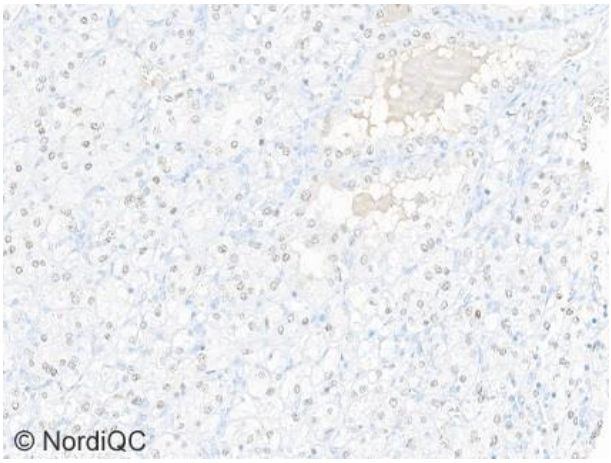

Fig. 4b
Insufficient PAX8 staining in the renal clear cell carcinoma using the same protocol as in Figs. 1b-3b. Only faint nuclear staining is seen and only in a minor fraction of the neoplastic cells. Compare with Fig. 4a – same field.

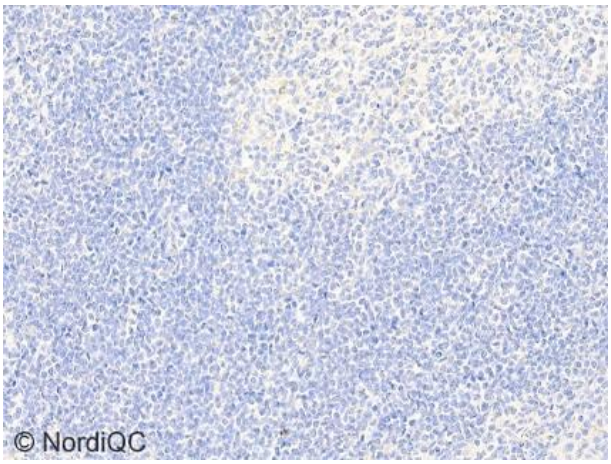

Fig.5a
PAX8 staining without PAX5 cross reactivity. PAX8 staining in tonsil using the same protocol as in Figs. 1a-4a. The rmAb clone EP298 do not cross react with PAX5, leaving the B-cells unstained. Compare with Fig. 5b.

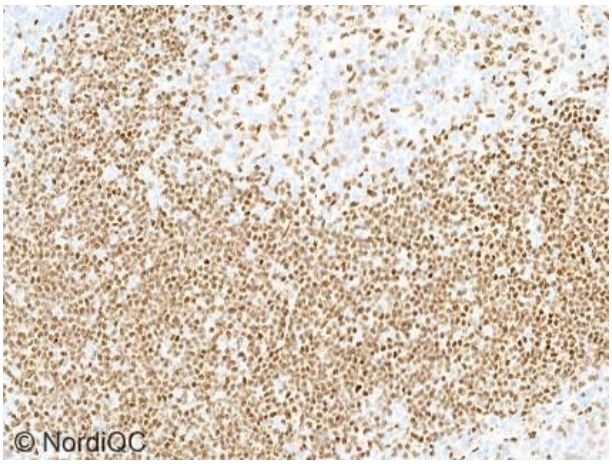

Fig. 5b
PAX8 staining with PAX5 cross reactivity. PAX8 staining in tonsil using the same protocol as in Figs. 1b-4b. The mAb clone MRQ-50 cross reacts with PAX5 resulting in nuclear staining in virtually all B-cells. Compare with Fig. 5a - same field.

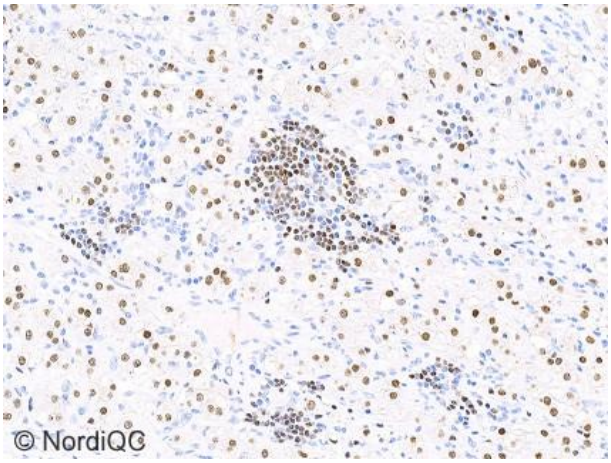

Fig. 6a
PAX8 staining with PAX5 cross reactivity. PAX8 staining in the renal clear cell carcinoma using the mAb clone MRQ-50 (Cell Marque) within a laboratory developed assay optimally calibrated on the Leica Bond platform. The mAb clone MRQ-50 cross reacts with PAX5 resulting in strong nuclear staining in virtually all infiltrating B-cells in the tumour.

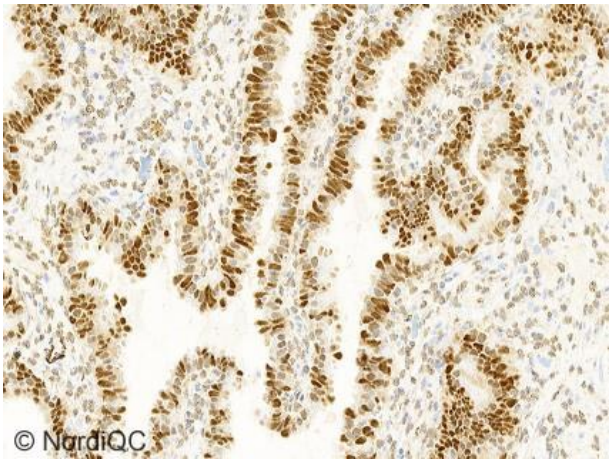

Fig. 6b
Insufficient PAX8 staining of the fallopian tube using the rmAb clone EP298 (Epitomics) at a too high concentration within a laboratory developed assay. False positive nuclear staining is seen in virtually all stromal cells. Compare with Fig. 2a - same field.

ON/LE/MV/RR 29.11.2017