External Quality Assurance

Who Controls the Control?

Zenobia Haffajee[1], Neeta Lal[1] and Julia Pagliuso[1]

[1] Royal College of Pathologists Australasia Quality Assurance Programs

Introduction

The RCPAQAP has trialled the assessment of laboratory in-house immunohistochemistry (IHC) control sections for two years in succession and the majority of participating laboratories were found to be satisfactory. However, the RCPAQAP experience for the assessment of special stain controls has been quite different. The approach towards the assessment of IHC in-house controls by the RCPAQAP is defined from observations from the last 2 years survey submissions.

Method

The assessment of participant IHC control sections was implemented in 2016. Controls were assessed as either Satisfactory, Unsatisfactory or No submission (if no control was submitted). Adequacy of selected tissue(s) should contain all target cells expected to stain. The advisory committee agreed that this component of the exercise was intended mainly for the participating laboratory to ensure quality control and satisfactory performance of the test kits/reagents used.

The assessment of control slides has always been part of the special staining exercise in the Technical Module. The assessment procedure is similar to the IHC controls.

Results Immunohistochemistry Modules

The assessment of 1732 participant IHC control sections across 27 exercises has proven that 94-100% of control sections stained satisfactorily when assessed against the relevant test external quality assurance (EQA) section (Fig. 1).

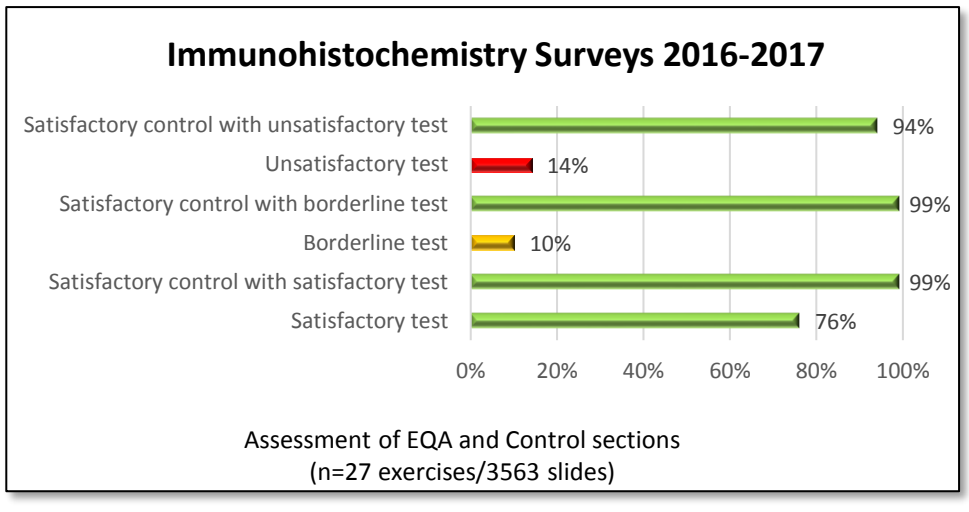

Fig 1: Immunohistochemistry survey results 2016-2017.

Those controls that were assessed as unsatisfactory were mainly due to methodology and antibody clone selection which affected the staining of the control. Only 1% of participants were noted to use an inappropriate control (ALK IHC survey for NSCLC) where participants used an anaplastic large cell lymphoma as the in-house control as the antibody clone used was specific to lymphomas and not lung adenocarcinoma.

References:

1. Quality Control in Modern Immunohistochemistry: Real-time Performance Characteristics and Quality. C.R. Taylor, MD, DPhil Appl Immunohistochem Mol Morphol ; Volume 25, Number 6, July 2017
2. Principles of Analytic Validation of Immunohistochemical Assays – Guideline from the College of American Pathologists Pathology and Laboratory quality Centre. P. L,Fitzgibbons; L.A. Bradley; L.A.Fatheree, et al. Arch Pathol Lab Me; Vol 123, Nov 2014
3. Proficiency testing in immunohistochemistry—experiences from Nordic Immunohistochemical Quality Control (NordiQC) M. Vyberg & S.Nielsen. Virchows Arch Vol 468:19–29, 2016
4. Quality and safety aspects in histopathology laboratory. Soniya Adyanthaya and Maji Jose. J Oral Maxillofac Pathol. 2013 Sep-Dec; 17(3): 402–407. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3927343/

Results Technical Modules

The assessment of 784 participant special stain control slides across 4 exercises showed that 42-77% of control sections stained satisfactorily against the relevant test EQA section (Fig. 2).

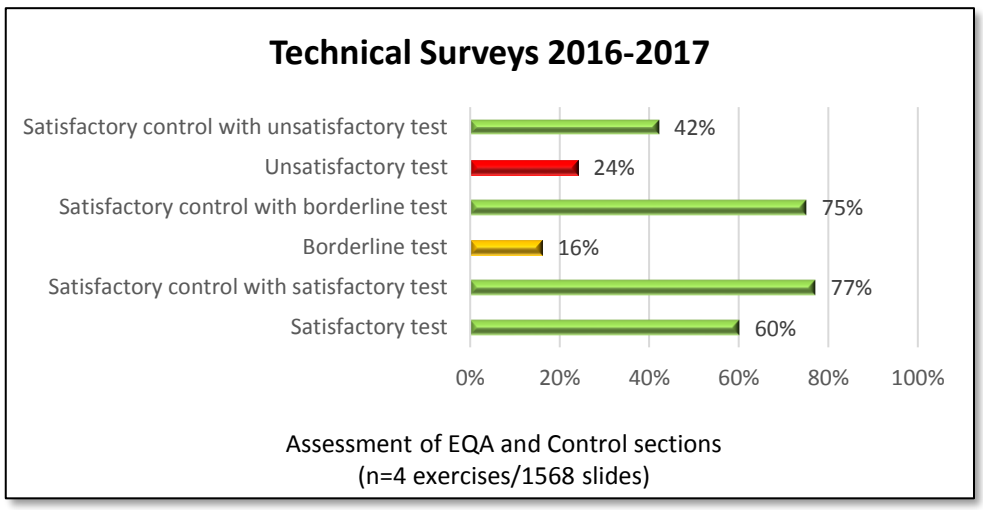

Fig 2: Technical survey results 2016-2017.

In 2016, the Gram staining exercise was provided to participants where in the first survey, only 56% of the control slides were categorised as satisfactory. The unsatisfactory controls failed to demonstrate the gram negative and positive organisms. In the repeat Gram stain exercise, an improvement of 21% was seen on the satisfactory results of control sections. Some participants followed the recommendations that were provided in Generic report and made changes to their methodologies for the repeat exercise.

Discussion

The RCPAQAP does not have a reference stain to assess each participant's control section, nor the equipment to consistently stain the participants' unstained control sections to enable a fair comparison. Therefore, the assessment of the control slide by the RCPAQAP is considered not reflective of the laboratory's overall mark.

The selection of using an appropriate control tissue when optimising staining for special stains and Immunohistochemistry (IHC) processes is crucial. Laboratories must validate their control tissue in-house. It is a valuable tool to monitor the specificity and sensitivity of the expected staining. Performance of the control tissue must be robust enough to reflect a low or high expression of the target area in special stains or the antigen in IHC stains at different levels[1-3].

1. It is advisable to include a composite section containing both a positive and negative control.
2. A tissue control with weak positive staining is more suitable than strong positive staining for optimal quality control and for detecting minor levels of reagent degradation. Ideally, a breast carcinoma known to have weak but positive staining is recommended to observe any reagent degradation.
3. If positive control tissues fail to demonstrate the expected staining results, the test section results should be considered invalid.
4. Cell-lines used as IHC controls are not considered as effective or appropriate when staining tissue test sections.

A robust methodology should be in practice to allow for variations in tissue fixation and processing as laboratories perform testing on external referral cases and not just EQA samples.

Conclusion

Laboratories should continue to submit a control as this is the required process for validating any staining procedure in-house. For the IHC survey exercises, control sections will not be assessed as part of the EQA exercise. If the test slide is deemed unsatisfactory, the control will be reviewed for appropriateness and comments provided if necessary. Controls submitted for the technical module will continue to be assessed.

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