Quality Reassessment Review of the Immunohistochemistry Laboratory Health Care Corporation of St. John's

Prepared For:

Leadership Team of the Laboratory Medicine Program
Health Care Corporation of St. John's

Prepared By:

Trish Wegrynowski, BAS, MLT
Pathology Consultant
30 Woodbank Road
Etobicoke, Ontario
M9B 5C4

May 2, 2006

Quality Reassessment Review of the Immunohistochemistry Laboratory
Health Care Corporation of St. John's
Eastern Regional Integrated Health Authority

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1. Introduction

1.1 Executive Summary

The testing performed in the Immunohistochemistry Laboratory operated by the Health Science Centre Site, Health Care Corporation of St. John's was queried in May 2005 as a direct result of a change in a patient's ER/PR receptor status with the reassessment of the tumour.

In September 2005, the Pathology Laboratory's practices and procedures were evaluated. The inconsistencies identified in Immunohistochemistry and the total lack of Standard Operating Procedures throughout the entire Pathology Laboratory for both the Technical and Professional Staff, directly contributed to the lack of reproducibility associated with the ER/PR Receptor status.

1.2 Background

A peer review performed from September 20-23 2005 included both Technical and Professional staff at the Health Science Centre and St. Clare's site's Pathology Laboratory. The emphasis of the review was the Immunohistochemistry service.

Recommendations were prepared for the Leadership Team of the Laboratory Medicine Program in a report dated November 9, 2005.

Two of the Registered Technologists assigned to the Immunohistochemistry service have been sent to other institutions to view their processes since the Quality Review of the service. (Mount Sinai Hospital, Toronto, Ontario and Jewish General, Montreal, Quebec.)

A reassessment of the Immunohistochemistry Laboratory occurred from March 30-31 2006 at the request of Dr. R.J. Williams, Vice President, Quality, Diagnostic and Medical Services.

A Recommendation – Immunohistochemistry Service spreadsheet, compiled on December 16, 2005 and updated March 10, 2006 was reviewed prior to the reassessment.

1.3 Objective

The objectives of this review were as follows:

1. Evaluate the current practices and procedures within the Immunohistochemistry Laboratory.
2. Comment on the progress of the Immunohistochemistry Laboratory.
3. Provide recommendations detailing issues identified.

1.4 Scope

This review will be focused on the Immunohistochemistry Laboratory in particular and Pathology in general.

1.5 Methodology

The Immunohistochemistry Laboratory Technologists processes were assessed from March 30- 31, 2005. The process assessment was evaluated by interviews, the review of written material and observation. A brief discussion also took place with Mr. Barry Dyer and Ms. Catherine Parnell.

The intent of this review is strictly professional, and to share relevant knowledge and expertise. All recommendations are based on the College of American Pathologists and Ontario Laboratory Accreditation Standards.

2. Histology Laboratory

2.1 Fixation/Grossing

The fixation and grossing of the Surgical Pathology specimens has remained site dependant. The majority of the Breast cases still originate from the St. Clare's site. This review did not include a visit to the St. Clare's site and did not review any processes or documentation associated with the fixation of specimens at either site.

The Courier system has been enhanced. A "Stat" courier travels between the two sites four times per day. There is documentation available relating to the receipt of the Surgical specimens.

Frozen sections continue to be performed at both sites. I had an opportunity to inspect the Quick Section room at Health Science Centre on this occasion. Refrigeration storage is still not available for large or unfixed specimens.

Four Pathology Assistant positions have been recently created. This shall provide an opportunity to ensure that all fixation and grossing procedures at both sites are consistent and standardized.

Very informal protocols and documentation exist. Standard Operating Procedure Manuals do not exist.

Recommendations:

1. Standard Operating Procedures relating specifically to the Accessioning, Grossing and Fixation Procedures must exist for each tissue type to ensure the reproducibility and reliability of all test results.

2. Documentation must exist in regards to the Pathologist Assistants relating to the types of specimens and the extent of the examination they may perform and whether there is direct or indirect Pathologist supervision for each type of specimen the PA will gross.

   Documentation must also exist as to the performance of the Pathologist Assistants. They are to be evaluated by the Pathologists.

3. A Refrigerator in Operating Room Quick Section room at all sites.

   This has not been addressed since the assessment.

4. Suggest a time stamp for the receipt of specimens from the courier to avoid any unforeseen circumstances where the time of receipt could come into question by any of the parties.

2.2 Processing

The Tissue Processors are now all located at the Health Science Centre. The specimens which are fixed and grossed at the St. Clare's site are couriered to Health Science Centre. This should improve the reproducibility of the processing and eliminate duplication in the maintenance of the processors.

With the relocation of the tissue Processor from the St. Clare's site, the Technical Staff has been reassigned to the Health Science Centre. This has had a direct effect on the workflow as all processing, microtomy and staining takes place at the one site. This reduces the duplication of maintaining embedding centers at both sites and streamlines the Histology workflow. Also four additional Registered Technologist positions have been created. This should provide an opportunity to review staffing, competency, workflow and hours of operation of the Laboratory. This should benefit the Laboratory especially with the forecasted implementation of the Tissue X-Press Processor.

Procedure Manuals detailing the Standard Operating Procedures for the Tissue Processors do not exist. I did not have an opportunity to review the Processing area but was informed that Temperature monitoring and Maintenance documentation has begun.

The St. Clare site has 5 Pathologists who assess and evaluate the Surgical Breast samples. All paraffin embedded blocks are kept on site at Health Science Centre for 3 months and are subsequently stored at St. Clare's. This change in workflow expedites the service for all subsequent requested work.

Recommendations:

5. Standard Operating Procedures are to be written for the Tissue Processors.

6. Standard Operating Procedures are to be written for the Embedding Centers and embedding protocols for all tissue types.

7. Procedures for the handling of sub-optimal specimens must be developed and documented.

3. Immunohistochemistry Laboratory

3.1 IHC Staffing

The Immunohistochemistry Section is now staffed with three Registered Technologists dedicated to perform the staining, optimization and validation. The staff have also absorbed the microtomy function. One of the Technologists has been given the lead position.

The Registered Technologists have retooled the workflow and have established a rotation in the area allowing for maximum coverage.

A Medical Section Head has been established for the Immunohistochemistry Laboratory. It is my understanding the Section Head may be retiring this year and a Successor has recently been named.

Each Pathologist requests their Immunoperoxidase stains on a request form. The Pathologists from the St. Clare site fax their requests to Health Science Centre. As all blocks are on site, there is no longer a waiting period for the blocks to be retrieved and sent from the St. Clare's site. This has streamlined the process.

Lack of communication between technical and professional staff remains an issue. For example, recently the marker Low Molecular Weight Keratin was added to all Sentinel Lymph node biopsy protocols. The Immunohistochemistry Laboratory was not apprised of this prior to implementation. This had a direct impact on the Laboratory not only regarding the amount of Primary antibody and Detection System required for staining but on the workload in general.

Recommendations:

8. Lines of communication need to be enhanced to ensure uninterrupted workflow to accommodate changes in protocols.

9. Evaluate Succession planning at the Technical level as 2/3 Registered Technologists are and/or will be eligible for retirement in the short term.

3.2 IHC Documentation

The process of Documentation has recently begun in Immunohistochemistry. Key areas identified*:

- Assemblage of a Procedure Manual has been initiated. However, the Manual is not written in compliance with the Clinical and Laboratory Standard Institute (CLSI) guidelines.

- All antibody data sheets have been compiled however, formal documented validation is not present. Templates of examples of validation worksheets were provided during the initial assessment.

- Recorded Maintenance records of the Ventana Benchmark were present.

- NO Pipette and thermometer calibration of accuracy documented.

- Reagent and detection system validation initiated.

- Retirement of procedures and antibodies documentation commenced.

  Ensure documentation is evident in the Procedure Manual as to location of Retired documents and/or Procedures.

  Ensure that obsolete reagents are removed and only currently authorized reagents are available for use.

- Incomplete Corrective action and Error log present.

- Retired Procedures and antibodies information has been gathered. Maintain records for a minimum of two years.

Recommendations:

10. A Procedure Manual outlining all Standard Operating Procedures to be written in compliance with the Clinical and Laboratory Standard Institute (CLSI) using GP2-A4 guidelines for Clinical Laboratory Technical Procedure Manuals.

The Manual shall contain all procedures, methods, antibodies and documentation utilized in the service.*

11. Antibody Specification Sheets have been compiled in alphabetical order.

Formal Documented validation sheets needed for each working antibody detailing its specific requirements for use including the appropriate control tissue and staining pattern

Any change in lot number requires verification of the specificity of the antibody and documentation PRIOR to use. Stained slides used for validation to be kept for reference.

12. Microscope Maintenance and Documentation
The microscope must be set up for Kohler Illumination daily and recorded to ensure optimal resolution and contrast.

This has not been addressed since the assessment.

13. Documentation guaranteeing the Pipette accuracy and calibration.

The accuracy of the pipette delivery volume must be guarded to ensure the reproducibility of the antibody dilutions when using concentrated antibodies.

This has not been addressed since the assessment.

14. Digital Temperature readings do not suffice and thermometer readings are to be recorded.

A Standard thermometric device or reference thermometer (NIST certified or guaranteed by manufacturer to meet NIST standards) is to be available to check all thermometers used on temperature controlled instruments.

This has not been addressed since the assessment.

The refrigerator which contains all the antibodies and detection systems does not have a thermometer in it for daily readings.

This has not been addressed since the assessment.

The refrigerator containing the antibodies and detection systems is not on an alarm. An alarm system should be considered.

Documentation of temperature readings was found. However, there is no evidence of established acceptable limits and corrective actions required when the temperatures fall outside those limits.

15. Documented evaluation performed to ensure the sensitivity and specificity of all test results has commenced. The validation documentation must be stringent.

The Procedure Manual should contain the processes that are in place to assure that all reagents used are appropriately controlled.
Parallel testing of old versus new reagents is acceptable.

Include alternate Protocols in the Procedure Manual in case of a failure with the Automated Instruments, if this is applicable.

The pH is now verified for all pH-dependant reagents.

There must also be a process in place in the Procedure Manual for those instances where the pH is outside of acceptable limits.

16. New Equipment/Instrument selection criteria to be documented.

A generic Equipment selection criteria document could be established by the Pathology Manager regarding any new Pathology equipment purchase.

No evidence of a New Equipment Selection Criteria document was provided despite previous recommendation.

Evidence of training and competency of Technical Staff must be recorded. Evidence of competency/training on the Ventana Benchmark has been completed.

The new Ventana Stainer, Benchmark XT, is still in the evaluation process. Protocols and Records must be maintained as to the Calibration/Function Checks. Ensure both Function Verification and Performance Verification.

17. Corrective Action log to be maintained to record all issues and concerns. This tool will benefit both the Technical and Professional Staff.

18. A policy must be established relating to the non-specific false positive staining associated with staining from endogenous biotin. This is critical as the Laboratory utilizes an avidin-biotin complex detection system.

    Testing which requires pretreatments and heat induced epitope retrieval should be routinely blocked with avidin and biotin to avoid this issue.

*Not a mutually exclusive list.

3.3 Immunofluorescent Staining

Currently the Patient labelled specimen bottles sent to the Laboratory containing the Immunofluorescent sample are not retained after the specimen is sectioned.

No controls are used when performing this testing. This has not been addressed since the assessment.

Cover slipping of the slides is performed in a lit environment.

Recommendations:

19. All tissue samples and their respective labelled containers are to be retained for 2 weeks after the final report is issued. The container is kept in case of any issues concerning the specimen/patient information.

20. Interpretation of every staining procedure must be substantiated with the use of controls, both positive and negative. Controls must be handled exactly as the patient test samples. Positive controls assure that the specimen staining was correctly performed while negative controls assess non-specific staining.

    Using sections from previously confirmed positive cases offers the easiest and most practical way to obtain controls for Immunofluorescence studies.

21. To obtain the brightest staining with the lowest background, both the staining and the cover slipping should be performed protected from light.

3.4 Controls

External positive controls continue to be placed on every patient tested slide.
Negative controls are still not used as suggested in the initial recommendations.

Daily assessment of the external positive controls and documentation are not performed in the Immunohistochemistry Laboratory. Without assessing the controls, internal daily troubleshooting of the procedure is not occurring in the Immunohistochemistry Laboratory.

The Section Head of the Immunohistochemistry Laboratory has initiated training of the Registered Technologists in respect to assessing the control slide. No formal documentation was found.
A multi header microscope has been purchased for the Laboratory and was not yet assembled at the time of this visit. This will be an excellent teaching tool.

The Immunohistochemistry Laboratory is also beginning to establish a documented control tissue bank.

Recommendations:

22. Negative controls are to be stained and evaluated on each block of patient tissue being tested. The negative control assesses non-specific or aberrant staining in the patient tissue related to antigen retrieval and/or the detection system. Ideally, the section of patient tissue is treated in the same manner as the patient test. However, the patient section can be treated with the most aggressive pre-treatment and most sensitive detection system compared to the other antibodies requested on the case. The primary antibody is omitted from the test procedure and can be replaced with a negative reagent control either monoclonal or polyclonal. (Ventana has these products.)

Negative patient controls should be assessed by the Registered Technologist prior to the slides leaving the laboratory.

This has not been addressed since the assessment.

23. Negative tissue control blocks to be run for every antibody. A multi-tissue or a "sausage" block will serve this purpose. The control will assess the specificity of the antibody.

24. Immunohistochemistry Registered Technologists to be trained to assess the Quality of the external Positive and negative patient controls tested daily.

Signed documentation of this assessment must be retained. Retention of all QC records for at least 2 years.

25. The Pathology Laboratory is intending to change their processing equipment. The X-press Tissue processor uses very different technology and reagents than the historical Tissue processors.

Controls must be guarded to ensure that the patient testing is compared to control tissue that is handled in the exact same manner. They must both have had the same fixation and processing applied to them.

The effects of tissue processing and preparation on performance characteristics of each antibody should then be established and monitored through the use of the appropriate control tissue.

4 Surgical Reports

Each site continues to utilize their unique report headings on the Surgical Pathology reports. A standardized template or reporting format has not been established as of yet.

Recommendations:

26. Standard Report headings and templates for the Eastern Health Integrated Health Authority.

27. Standard reporting for all predictive/prognostic information. Investigate Synoptic reporting capabilities with Meditech, Medical Information Technology, Inc.

28. Results regarding Immunohistochemistry testing providing predictive/prognostic information must include information in the surgical report regarding the specimen processing, antibody clone and the scoring method used.

5. Quality Assurance

Great improvements have been made in this area. The laboratory has become involved in the External Quality Assurance Programs with the College of American Pathologists and the United Kingdom National Quality Assessment Scheme. Both of these programs can be used as benchmarks of peer-based performance.

The Immunohistochemistry Laboratory has participated in a Peer evaluation/education performance comparison program with the UK NEQAS and the tabulated results of the Immunohistochemistry Laboratories stained slides have been received by the Laboratory.

The Laboratory has also received the Journal of UK National Quality Assessment Scheme. This Journal is an excellent reference tool for the Technologists and Pathologists alike as it covers topics such as:

Guidelines used in validation.
Score staining pattern.
Technical parameters used by the participants.
Features of optimal immunostaining.
Features of suboptimal immunostaining.
Importance of good fixation.
Conclusions from the data and References.

Senior Administration has given approval and support for a Total Quality Management Program. The Quality Management system will encompass all processes relating to quality assurance with a major focus of continual improvement. There must be standards of performance A goal of the program is to provide a system which is as failure resistant as possible.

The Quality Management Program for the Laboratory will have representation from both the Technical and Professional staff. A Full time equivalent Registered Technologist has been designated to this position as has a .2 Full time equivalent of a Pathologist. The job description and Title of the Registered Technologist had yet to be determined. Also to be determined are the lines of authority, committee representation and delegated areas of responsibility.

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Recommendations:

29. The Quality Management initiative by the Eastern Regional Integrated Health Authority be shared with the other regions of Newfoundland to ensure the Best Medicine practices.

This initiative will assist in providing reproducible Immunohistochemistry results as the Health Science Center is the reference site for the province.

30. The Quality Management team should be involved in the quality improvement activities within the organization and with the user Physicians.

30. The Laboratory is to establish quality indicators to monitor the Laboratories contribution to patient care.

31. For a successful Quality Management team, the Laboratory management shall ensure that opportunities identified for improvement are dealt with.

32. Corrective action logs should be assessed from each area and include an investigation to determine the underlying root causes. The results of the corrective actions should be monitored to ensure they were effective in solving the original problem. Trends may also be identified which will aid in the development of policies and/or procedures.

6. Conclusion

Pathologist Assistants are in the process of being hired. Training has yet to be established. The training period will provide an opportunity for the Pathology Department to develop Orientation and Training records which can be used at a later date for Performance evaluations in respect to both General Performance and Competency.

A Procedure Manual for the Surgical Specimen Handling must be created. It should include documented instructions for the proper dissection, description and histological sampling of the various tissues. There must also be a clearly defined documented policy as to the type of specimens and the extent of the examination which can be performed by a non-pathologist. Bear in mind that all gross examination must be done by a Pathologist, Resident or under the supervision of a Qualified Pathologist.

The Pathologist Assistants will rotate between the Health Science Centre and the St. Clare's sites. This shall provide an opportunity to ensure that all fixation and grossing procedures at both sites are consistent and standardized.

The consolidation of the Tissue Processors to the Health Science Centre has streamlined the workflow, eliminated duplication and enabled the department to insure that the processing of all specimens is controlled. This should provide Management an opportunity to review staffing, competency, workflow and hours of operation of the Pathology Laboratory.

The Immunohistochemistry Laboratory has enhanced their practices since the initial Quality review. The area is now staffed by 3 non-rotating Registered Technologists. This has enabled them to begin working on the Standard Operating Procedures and Policies for the area. It has also provided them with the opportunity to begin formal validation of the antibodies, detection systems and reagents used.

The Director of the Immunohistochemistry Laboratory has begun teaching the Registered Technologists how to assess the external positive controls. This will be facilitated by the addition of a multi-header microscope in the Laboratory. After the training is completed and competency documentation is signed, evaluating the external positive and negative patient controls will become part of their scope of practice. This is essential, because the Laboratory director or their designee should be reviewing all controls slides each day of patient testing.

Also, keep in mind with the change of processing techniques, new control tissue must be collected to ensure that the patient samples and known positive controls are treated in the exact same manner. Testing of patient samples should not be done until after validation is completed.

The stringency required to ensure the reproducibility of all Immunohistochemistry testing is paramount. No antibodies should be used on patients until after documented validation is completed.

The Immunohistochemistry Laboratory has become involved in peer assessment programs. This has had a positive impact on the service.

All Procedure Manuals should be written in compliance with the Clinical Laboratory Standards Institute and in particular, the Clinical Laboratory Procedure Manual; Approved Guideline.

The Surgical reports should have Standard Report headings and templates for the Eastern Health Integrated Health Authority. This would ensure that all Clinicians received patient information in the same format.

Senior Administration has given approval and support to a Total Quality Management Program for the Pathology Laboratory. The impact of this decision will be far reaching. A major focus of this initiative will be Continuous Improvement as you strive to build a system which is as failure resistant as possible.

The Quality Management initiative by the Eastern Regional Integrated Health Authority could be shared with the other regions of Newfoundland to ensure the Best Medicine Practices for the province.