AVALON HEALTH CARE INSTITUTIONS BOARD
(now part of Eastern HEALTH)
86 HIGHROAD SOUTH
CARBONEAR, NEWFOUNDLAND
CANADA A1Y 1A4
Telephone (709) 945-5111
Facsimile (709) 945-5158

# FACSIMILE MESSAGE

TO: Dr. R. Williams
VP - Quality, Diagnostic & Medical Services

FAX NO: 709-778-6307

FROM: Dr. Gary Baker, ACEO - Medical Services

DATE: 16 September 2005

NO. OF PAGES: 7 (including cover page)

MESSAGE: Urgent ☐ Confidential ☐ Original in Mail ☐

As per your request.

HealthCare
Corporation of St. John's

# MEMORANDUM

**FROM:** Mahmoud A. Khalifa, M.B.,B. Ch., PhD, FRCPC

**TO:** All Newfoundland Pathologists

**DATE:** February 16, 1998

**REF:** Reporting of estrogen and progesterone receptor immunohistochemical results

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As you all know, It has been suggested that assessment of estrogen and progesterone receptors (ER/PR) status in mammary invasive carcinomas be performed immunohistochemically (IHC) on formalin-fixed, paraffin-embedded tissues. This technique, although has its own limitations, has proven to be more practical and cost-effective than the traditional biochemical detection methods.

The division of Pathology at the Health Care Corporation of St. John's has been employing this technology for over a year. Recent audits correlating IHC with biochemical results in selected specimens where both techniques have been run in parallel have shown high accuracy of the introduced IHC detection. Results of these audits have been discussed in several meetings and are available for review.

As the technique was still in its introductory phase (**Phase 1**), I have been reporting results of the majority of cases to establish consistency and reproducible techniques. As we have come to a more advanced stage of this pursuit where this test could be done with a relatively high efficiency and reliability I came to believe that we are probably ready to move into the next two and final phases.

**Phase 2.** Each pathologist will be asked to report results of his/her own case as indicated by the brown staining of nuclei of the invasive neoplastic cells. This phase will start March 1, 1998, at which time your immunostained slides will be mailed back to you with positive controls whenever it is technically possible. With each run, I will still be responsible for reviewing the positive controls here in our laboratory and the slides will not be mailed to you unless adequate staining is noted in the positive controls. As we are all interested in making this transition as smooth as possible, I will be more than glad to continue being available to answer any questions and address concerns.

**Phase 3.** The division of Medical Biochemistry at the General Hospital will be addressed to officially discontinue performing steroid assessment by biochemical techniques. I have already spoken with Dr. V. Prabhakaran who is fully aware of this transition and is waiting for our signal to complete the switch. There is no proposed date for this phase yet.

Attached, please find a proposal for uniform reporting of ER/PR immunohistochemical staining. This proposal was discussed with many of my colleagues who mostly agreed with its content and accepted it as a policy. As I encourage you to adopt the attached proposal in your reporting to maintain uniformity, it should be clearly stated that this is only a proposal.

As you already know, there is a considerable host of publications addressing this issue. I will be glad to share any of the material I already have with you and I would extremely appreciate your feedback on this matter.

**Proposal for uniform reporting of ER/PR immunohistochemical assessment**

**FEBRUARY, 1998**

The report on a hormone receptor status will have three components.

1. The first component is a statement of whether the stain is "positive" or "negative". Positively is defined by nuclear staining detected in any number of malignant cells.
2. The second component is a rough estimate of the percentage of immunoreactive cells in the section examined. This estimate could be in the form of a range or a fixed number and is listed in parenthesis.
3. The third component is a comment regarding only ER (and not PR) immunoreactivity and is only to be included in the report if a small percentage of neoplastic cells (1-30%) is positive. The comment reads "Evidence from the available literature indicates that estrogen receptors immunoreactivity detected in less than 30% of neoplastic cells would most likely correspond to a negative result in a biochemical assay of the same specimen (Am J Surg Pathol 14:121-127,1990)".

**EXAMPLES**

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|---|---|
| **Example 1** | - ESTROGEN RECEPTORS, POSITIVE (70-80% OF CELLS).<br>- PROGESTERONE RECEPTORS, POSITIVE (80-90% OF CELLS). |

| | |
|---|---|
| **Example 2** | - ESTROGEN RECEPTORS, POSITIVE (1-5% OF CELLS). PLEASE, SEE COMMENT.<br>- PROGESTERONE RECEPTORS, NEGATIVE (0% OF CELLS).<br><br>COMMENT: EVIDENCE FROM THE AVAILABLE LITERATURE INDICATES THAT ESTROGEN RECEPTORS IMMUNO-REACTIVITY DETECTED IN LESS THAN 30% OF NEOPLASTIC CELLS WOULD MOST LIKELY CORRESPOND TO A NEGATIVE RESULT IN A BIOCHEMICAL ASSAY OF THE SAME SPECIMEN (AM J SURG PATHOL 14:121-127,1990). |

HealthCare
Corporation of St. John's

TO: PATHOLOGISTS, HSC, ST. CLARE'S AND OUT OF TOWN HOSPITALS

FROM: DR. G. EJECKAM, PATHOLOGIST, HSC

SUBJECT: ER/PR IMMUNOHISTOCHEMICAL STAINS

DATE: May 2, 2003

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I am glad to inform you that we have rectified the difficulties related to the immunostain of ER/PR, therefore, we can now resume regular request for these antibody stains. I will, however, like to bring the following information to your attention:

1. Results of the immunostains may be affected by:

   (a) Delayed fixation.

   (b) Over fixation.

   (c) Under fixation.

   (d) Uneven fixation.

   (e) Inadequate tissue dehydration.

   (f) Tissue reprocessing.

   The optimal fixation time for immunostains is 18 - 24 hours, in 10% neutral buffered formalin. If you use a different fixative, please specify that when you send your request.

   It is advisable to maintain a regular check on the PH of the buffered formalin even if it is procured commercially. Regular check and change of grades of alcohol in the Tissue Processor will eliminate inadequate tissue dehydration.

2. ER/PR false negative results increase in core biopsies, therefore, where possible restrict request to excision biopsies.

3. Check normal breast acini in your sections as internal controls. This is a second level control. Nuclear staining in normal breast tissue is heterogeneous and varies with menstrual cycle.

4. In carcinoma of the breast, most PR+ tumors are also ER+, however, 10% of PR+ tumors are ER-.
   Patients with PR+ tumors have significantly longer disease free survival than patients who are PR-.

5. Reporting of ER/PR:
   Several formulae are in the literature.
   FOR POSITIVE RESULTS:
   ER+ greater or equal to 5% nuclear staining.
   ER+ 10% of tumor staining.
   ER+ 1% - shown to benefit from endocrine treatment.

   Consensus Statement on Adjuvant Therapy of Breast Cancer, November 1-3, 2000, National Institute of Health. "Any positive nuclear ER immunostaining is considered to be a positive result and should be a definitive reason for instituting antiestrogen therapy for a patient." The medical oncologist may require percentage of tumor positivity.

6. Higher staining intensity does not reflect better results. This is a function of staining procedure and may alter. All cytoplasmic staining in ER and PR immunostain are to be considered as negative.

7. ER+ve tumors:

   - Tubular.
   - Mucinous.
   - Papillary.
   - Ductal (low nuclear grade).

8. Low nuclear grade tumors are usually positive for ER/PR and negative for Her2Neu while high grade tumors tend to be positive for Her2Neu and negative for ER/PR.

We are working on the remaining antibodies and hopefully all normal immunostains will resume soon.

Thank You,

Dr. G. Eapen

cc: Site Chief, HSC and St. Clare's
Barry Dyer
All Technical Staff on Immunohistochemistry