From: Heather Predham
To: Susan Bonnell;
Subject: documents
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Attachments: Interrogatory Questions1.doc
Affitdavit #1.doc

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as promised...I'll be in there in about 15 minutes

Heather

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2006 01 T 2966 CP

IN THE SUPREME COURT OF NEWFOUNDLAND AND LABRADOR
TRIAL DIVISION

BETWEEN:

VERNA DOUCETTE **PLAINTIFF**

AND:

EASTERN REGIONAL INTEGRATED HEALTH AUTHORITY **DEFENDANT**

Brought under the *Class Actions Act,* SNL 2001, c. C-18.1

AFFIDAVIT

I, Heather Predham, of the City of St. John's, in the Province of Newfoundland and Labrador, make oath and say as follows:

1. **THAT** I am a Risk Management Consultant/Assistant Director of Quality and Risk Management with the Defendant, Eastern Regional Integrated Health Authority ("Eastern Health") and was the Quality Initiatives representative in attendance at all meetings of the Tumor Board referred to in paragraph 19 of the within affidavit. As such I have been informed by pathologists and laboratory staff with Eastern Health of all activities of the Tumor Board including the retesting of breast cancer tumors and tissue samples more fully detailed in the within Affidavit. I am a registered nurse and completed a Bachelor of Nursing degree at Memorial University of Newfoundland. I make this affidavit as a representative of Eastern Health. The facts deposed in this Affidavit are true to the best of my knowledge, information and belief based on my review of medical literature and

my experiences and interactions with oncologists, pathologists and other medical professionals on the topic of breast cancer and breast cancer testing.

2. **THAT** breast cancers have many different characteristics and once a breast cancer tumor or sample is removed from the body, it is tested and analyzed to diagnose a patient to determine whether the type of breast cancer is invasive and whether lymph nodes are involved and, if so, how many.

3. **THAT** other features of the cancer including the size of the tumor, the hormone receptor status of the tumor, the tumor grade, the HER 2 expression, and tumor histology are also tested to assist oncologists in their determination of treatment options and the long-term health of the patient.

4. **THAT** the hormone receptor status of a breast tumor involves testing a tumor to determine whether the cancer cells have estrogen and/or progesterone receptors ("ER/PR"). Breast cancers that are either ER-positive or PR-positive or both may respond to hormone therapy, such as the drug Tamoxifen.

5. **THAT** literature which I have read suggests that approximately 75% of breast cancers are either ER-positive or PR-positive or both.

6. **THAT** hormonal therapy, chemotherapy and radiation are adjuvant therapies. The aim of adjuvant therapy is to decrease breast cancer recurrence rates and improve overall survival rates. Adjuvant therapies are generally additional treatments given after potentially curative surgery.

7. **THAT** immunohistochemistry is used to determine whether a tumor is ER-positive or PR-positive. To make the determination, laboratory technicians use antibodies to

visualize cellular proteins. Antibodies are molecules that are able to combine specifically with cellular antigens of interest. Using a good antigen at the right level is critical to the success of the test.

8. **THAT** testing to determine whether a tumor is ER-positive or PR-positive ("ER/PR testing") is a complicated procedure that involves more than 40 steps.

9. **THAT** there are no standardized laboratory procedures in Canada for immunohistochemistry testing. Likewise there is currently no national laboratory accreditation process for immunohistochemistry laboratories.

10. **THAT** hospitals throughout the province of Newfoundland and Labrador send tissue samples to the testing laboratory of Eastern Health for ER/PR testing once the fixation process is complete. Therefore, Eastern Health has no control over the pre-analytical or fixation phase of ER/PR testing for these tissue samples.

11. **THAT** there is a degree of subjectivity involved in ER/PR testing and, at Eastern Health, a number of different pathologists have been involved in interpreting the tests to determine the level of estrogen or progesterone positivity in a tumor.

12. **THAT** prior to April 2004, the Dako testing technique was used in Eastern Health's laboratories which required the manual boiling of tissue samples and also the measuring of minute mixtures of immunioperoxidase staining.

13. **THAT** in April 2004, Eastern Health installed the Ventana system for conducting ER/PR testing. This new system automated the process, thereby removing much of the human manipulation of samples.

14. **THAT** in May 2005 a patient, who had been diagnosed in 2002 with a lobular carcinoma of the breast and had been determined to be negative after ER/PR testing using the Dako semi-automated system, converted to positive after further ER/PR testing using the Ventana automated platform.

15. **THAT** in June 2005 Eastern Health conducted a case review of negative ER/PR tests that it obtained in 2002. Of the 25 cases retested, 12 converted from negative to positive. An additional 32 negative ER/PR tests were retested in July 2005 and 25 of the 32 cases converted.

16. **THAT** in early July 2005 Eastern Health decided to retest all negative ER/PR tests performed between May 1997 and August 8, 2005.

17. **THAT** in late July 2005 Eastern Health stopped reporting ER/PR in its laboratory and arranged for an independent, external laboratory to complete the retesting. In August 2005 Mount Sinai Hospital agreed to perform the retesting. All new cases were sent to Mount Sinai for ER/PR testing.

18. **THAT** in October 2005 Eastern Health received the first results from Mount Sinai Hospital. A Tumor Board was constituted and was composed of two oncologists, two surgeons, two pathologists, myself as the Quality Initiatives representative and one secretary. Its mandate was to review the results, assess the impact on patients and make treatment recommendations.

19. **THAT** in late January 2006 the final samples were forwarded to Mount Sinai Hospital for retesting and the final results were received from Mount Sinai in February, 2006.

Between February and May 2006 the Tumour Board continued to review results and make treatment recommendations.

20. **THAT** Eastern Health reviewed 2760 ER/PR tests conducted between 1997 and August 2005. Of those cases reviewed, 939 of the tests were originally reported as ER-negative. The negative test samples were sent to Mount Sinai Hospital to be retested. Results were obtained and reviewed for 763 patients.

21. **THAT** of the 763 patients whose samples were retested and results obtained, 433 patients saw no change in their ER/PR results and therefore no change in treatment was recommended. Specifically,

(a) 341 patients were confirmed negative by Mount Sinai;

(b) 28 patients were confirmed negative by the Tumor Board;

(c) 12 patients were confirmed positive; and

(d) 52 patients were determined to have ductal carcinoma in situ, and therefore no form of treatment would have been recommended.

22. **THAT** a further 13 patients saw no change in their ER/PR test results but a change in treatment was recommended as the standard for interpretation of what constituted an ER-positive test result had changed between the time of original testing and the Tumor Board's review.

23. **THAT** the ER/PR test results were different for 317 patients following retesting. Of the 317 patients, 104 patients required a change in treatment. Ninety-six of these patients were recommended for treatment with Tamoxifen or another aromatase inhibitor; 4 of these patients saw a change in their original diagnosis; and 4 of these patients originally had a degree of ER positivity but were negative on retesting.

24. **THAT** the remaining 213 patients whose ER/PR tests results were different on retesting did not require a change in the treatment that had been originally recommended for them because:

(a) 60 of these patients had a very low risk or recurrence;

(b) 148 of these patients had previously been treated with Tamoxifen or another aromatase inhibitor either at their request or their oncologist's recommendation following a review of the test results and their particular medical and family histories;

(c) 13 of these patients were not placed on Tamoxifen for their original disease but for subsequent metatstatic disease; and

(d) 5 of these patients received no treatment as they required assessment prior to any recommendation being made.

25. **THAT** 176 of the patients whose ER/PR tests were originally reported as negative are deceased. Of these 176 patients:

(a) 101 patient's samples were retested and results have been received;

(b) 2 patient's samples have been retested on request; and

(c) 73 patient's samples will not be retested unless requested by the families.

26. **THAT** based upon my involvement as a member of the Tumor Board, there was no one reason to explain why the respective test results converted on retesting and in many instances the cause of the conversions is unknown. Any number of the following factors may have contributed to the conversions:

(a) Where the samples were collected,

(b) How the samples were fixated;

(c) When the sample was tested initially;

(d) Who interpreted the initial results;

(e) What constituted a positive ER/PR test at the time of the original testing; and

(f) The technology used to perform the ER/PR testing for each patient, in particular, the antibodies used and antigen retrieval techniques utilized.

27. **THAT** in two cases, two different tissues samples were inadvertently sent to Mount Sinai hospital for each of the two patients. Mount Sinai Hospital advised that the slightly different results obtained for each patient, when the two different tissue sample test results were compared, may be explained by the fact that conducting testing of different portions of a single patient's tissue sample may render different results.

28. **THAT** in two further cases, Mount Sinai retested the same tissue samples for two patients. I am not certain whether the duplication of effort was inadvertent or intentional. In these two cases Mount Sinai tested the same tissue sample from the same patient twice and each time obtained different test results.

29. **THAT** for false negative ER test results and confirmed ER negative test results, I have been informed that controls were run in all instances and that documentation exists in some instances confirming that controls were run as part of quality assurance in place at the time.

30. **THAT** the focus of the Tumor Board and all persons involved with the retesting of breast tumor samples has been on patient care and the communication and implementation of treatment recommendations. The compilation of statistical information has only recently been addressed.

31. **THAT** I provide this Affidavit to the Court for the purpose of responding to the Application for Certification filed on behalf of the Plaintiff.

SWORN TO at St. John's, in the province of Newfoundland and Labrador, this day of January, 2007, before me:

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Heather Predham

2006 01 T 2966 CP
IN THE SUPREME COURT OF NEWFOUNDLAND AND LABRADOR
TRIAL DIVISION

BETWEEN:

VERNA DOUCETTE **PLAINTIFF**

AND:

EASTERN REGIONAL INTEGRATED HEALTH AUTHORITY **DEFENDANT**

BROUGHT UNDER THE *CLASS ACTIONS ACT*
BEFORE THE HONOURABLE MR. JUSTICE THOMPSON,
CASE MANAGEMENT JUDGE

ANSWERS TO INTERROGATORIES

In answer to the Interrogatories of the Plaintiff dated March 30, 2007, I make oath, as a representative of Eastern Regional Integrated Health Authority, and say that to the best of my knowledge, information and belief, based on my review of medical literature and my experiences and interactions with oncologists, pathologists and other medical professionals on the topic of breast cancer and breast cancer testing, as follows:

1. *As to paragraph 20 of your Affidavit dated February 9, 2007, how many ER/PR tests were done on the Dako system from May 1997 to April 2004?*

Answer: There were 2214 ER/PR breast tissue tests conducted on the Dako system from 1997, when the Dako testing commenced, to April 1, 2004. Some, but very few, lymph node tissue samples as well as metastatic tissue samples may be included in this figure.

2. *How many ER/PR tests on the Ventana system from May 2004 to August 2005?*

Answer: There were 495 ER/PR breast tissue tests conducted on the Ventana system from April 1, 2004 to August 1, 2005.

3. *How many ER/PR tests were done on a year to year basis, stating total number of tests and total number of negatives for each year:*

Dako system	Total Tests	Negatives
May 1997 to December 31		
January 1, 1998 to December 31		
January 1, 1999 to December 31		
January 1, 2000 to December 31		
January 1, 2001 to December 31		
January 1, 2002 to December 31		
January 1, 2003 to December 31		
January 1, 2004 to December 31		
Ventana system		
April 2004 to December 31		
January 1, 2005 to July 31		

Answer: The following is a summary of the total number of breast tissue ER/PR tests conducted on a year to year basis and the total number of clinically negative tests each year. In 1997, when testing commenced on the Dako system, a test was clinically positive if tumour tissue cells stained at 30% or more. This standard changed at the beginning of 2001 such that if tumour tissue cells stained at 10% or more, then the test was deemed positive.

Dako system	Total Tests	Total Negatives
May 1997 to December 31	137	57
January 1, 1998 to December 31	147	76
January 1, 1999 to December 31	360	126
January 1, 2000 to December 31	370	170
January 1, 2001 to December 31	374	143
January 1, 2002 to December 31	344	147
January 1, 2003 to December 31	373	89
January 1, 2004 to April 1, 2004	109	16
Ventana system		
April 2004 to December 31	381	41
January 1, 2005 to July 31	114	19

4. *As to paragraph 21, of the 330 (763 less 433) false negatives found on retesting by Mount Sinai, how many occurred while the Dako system was in use?*

Answer: My Affidavit dated the 9th day of February 2007 reviewed test results from the perspective of treatment change rather than a change in test results. Of the 330 remaining patients calculated by question #4, a further 13 patients of the 330 patients calculated did not see a change in their test results but a change in treatment was recommended as the standard interpretation of what constituted an ER-positive result had changed between the time of the original testing and the Tumour Board's review. Of the remaining 317 patients, whose test results were different on retesting at Mount Sinai, a further 4 had a change in their diagnosis and another 4 saw their test results change from positive to negative. Therefore, there were 309 patients whose test results were different on retesting at Mount Sinai and 306 of those patients' original test results were obtained using the Dako system.

5. *As to paragraph 25, what criteria were used in the selection of the 101 patient samples for retesting?*

Answer: The 101 patients referred to in paragraph 25 of my Affidavit were not "selected" for retesting. A decision was made by an Ethics Committee during the retesting process that no further tissue samples for deceased patients would be sent for retesting unless a request was made by the deceased patient's family. At that time, 101 of the 176 deceased patients' tissue samples had been retested. A further 2 were retested upon request.

6. *As to paragraph 25(c), were the families or attending physicians of the 73 deceased patients notified that there would be no retesting?*

Answer: The families and attending physicians of the 73 deceased patients were advised through press releases and general advertising that the tissue samples of deceased breast cancer patients could be retested at the family's request.

7. As to paragraph 25 (a) and (b), of the 103 deceased patients originally reported as negative and not retested by Mount Sinai, where was the retesting done and what were the results (ie. false negatives)?

Answer: As of today's date there are 105 deceased patients whose results have been retested at Mount Sinai. Of those 105 patients, 68 saw no change in their results, 1 originally clinically positive result, on retesting, was determined to be clinically negative, and 36 patients' test results changed from clinically negative to clinically positive.

8. Were the false negatives reported to the families or attending physicians?

Answer: Through press releases and general advertising the families and attending physicians of deceased patients were advised that they could request the breast tissue test results.

9. How many of the deceased patients were originally tested on the Dako system, and on retesting, were false negative?

Answer: Of the 36 patients that saw a change in their test results, all were originally tested on the Dako system.

10. As to paragraph 29, what controls were run in all instances?

Answer: Technical controls were run in all instances. Technical controls are the inclusion of confirmed positive control patient tissue samples.

11. What is the hospital policy on documentation of controls and on retention of the documentation?

Answer: There is no written hospital or lab policy on the documentation of controls and the retention of such documentation. The lab policy, based on the manufacturer's protocol, was that a lab technologist would run a technical control with each batch of tests. In 1997 and 1998 all test results were interpreted in St. John's by one pathologist; therefore, only one control was required. However, in 1999 test results were sent to pathologists outside St. John's for interpretation. Therefore,

several controls might be run for a single batch of tests such that each pathologist interpreting results would receive a control slide in addition to the patient's or several patients' test results. For tests interpreted in St. John's, the technical control slide would be filed with the test slides and maintained for 20 years.

As part of the lab's policy, the technologist would enter the date, time and number of tests run and number of controls run into the meditech computer system. By 2001, with computer upgrades, technologists included more particulars regarding the type of tests run. The pathologist would then sign out the slide(s) from the lab and produce a lab report. The report(s) should refer to both the technical and internal controls run.

12. *What were the controls used during the analytic phase (from paraffin section to the staining machine – antigen retrieval)?*

Answer: See responses to questions 10 and 11.

13. *Does the documentation show the controls were working in all documented cases?*

Answer: Not all pathologists referred to the technical and internal controls in their reports. I estimate that in 50% of all cases the pathologist referred to the technical controls in his or her report.

14. *What antibodies were used by Eastern Health while the Dako system was in use? (Estrogen and Progesterone).*

Answer: From 1997 to December 2000 the 1D5 ER clone was used and the 1A6 PR clone was used. From December 2000 to April 1, 2004 the 1D5 ER clone was used and the PgR 636 PR clone was used.

15. *What staining procedures were used at Mount Sinai in performing the retesting, Dako or Ventana?*

Answer: Mount Sinai used the Dako system.

16. *What antibodies, both progesterone and estrogen, were used by Mount Sinai?*

Answer: On retesting at Mount Sinai the 6F11 ER clone was used and the PgR 1294 PR clone was used.

17. Please provide a copy of the bench procedure for antigen retrieval during the use of the Dako system?

Answer: Please see the bench procedures for 1D5 ER clone, 1A6 PR clone, and PgR 636 PR clone attached.

SWORN TO at St. John's, in the province of Newfoundland and Labrador, this day of May, 2007, before me:

Heather Predham