COMMISSION OF INQUIRY
ON HORMONE RECEPTOR TESTING

BEFORE THE HONOURABLE JUSTICE CAMERON - COMMISSIONER

July 30, 2008

Appearances:

Bernard Coffey, Q.C. . . . . Commission Co-counsel
Sandra Chaytor, Q.C. . . . . Commission Co-counsel

Rolf Pritchard/Jackie Brazil . . . . Her Majesty in Right of NL

Peter Browne/Jane Hennebury . . . . . Doctors Kara Laing et al

Daniel Simmons . . . . . Eastern Regional Integrated
. . . . . Health Authority
Darlene Russell. . . . . Members of the Breast Cancer
. . . . . Testing Class Action
Mark Pike . . . . . NL Medical Association
Jennifer Newbury . . . . . Canadian Cancer Society (NL Division)
David Eaton Q.C./
Blair Pritchett. . . . . Central, Western and Labrador-Grenfell
Regional Integrated Health Authorities
William Clark . . . . . Counsel for Dr. Banerjee

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Q. Mr. Coffey.
COFFEY, Q.C.:
Q. Commissioner, the next witness is Dr. Banerjee.
DR. DIPONKAR BANERJEE, AFFIRMED, EXAMINATION BY BERNARD COFFEY, Q.C.
REGISTRAR:
Q. Would you please state and spell your complete name for the Commission?
DR. BANERJEE:
A. My name is Diponkar Banerjee, D-I-P-O-N-K-A-R B-A-N-E-R-J-E-E.
REGISTRAR:
Q. Thank you.
THE COMMISSIONER:
Q. Mr. Coffey, we have a new solicitor with us this morning.
COFFEY, Q.C.:
Q. Yes, we do.
MR. CLARK:
Q. Yes, Commissioner, I'm William Clark. I'm here as counsel for Dr. Banerjee.
THE COMMISSIONER:
Q. Welcome, Mr. Clark.

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COFFEY, Q.C.:
Q. Commissioner, I have some new exhibits, please, I'd ask that be entered. They are P-2430 through P-2435 inclusive.
THE COMMISSIONER:
Q. Entered.
EXHIBITS ENTERED AND MARKED P-2430 THROUGH P-2435
COFFEY, Q.C.:
Q. Thank you, Commissioner. Registrar, could we bring up Exhibit P-2435, please? Doctor, is this the first page of your curriculum vitae, Doctor?
DR. BANERJEE:
A. It is.
COFFEY, Q.C.:
Q. Doctor, I'm not going to take you through it in detail. I'm looking at the last page here on the paper copy I have, it's page 30, so we'd be here for quite a while going through it. I'm going to ask you, please, Doctor, to outline for the Commissioner your educational and professional background?
DR. BANERJEE:
A. Certainly. So my undergraduate training and medicine, surgery was at Makarere Medical

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School in Uganda. Following that post graduate medical education in pathology and laboratory medicine starting at the University of Minnesota and then I moved to Ottawa and finished my training there, and as you can see, the -
COFFEY, Q.C.:
Q. It's actually at page 30.
DR. BANERJEE:
A. Sorry?
COFFEY, Q.C.:
Q. You're actually on page 30 of the -
DR. BANERJEE:
A. Yes, I am.
COFFEY, Q.C.:
Q. - CV, and you go right ahead, Doctor. You go right ahead.
DR. BANERJEE:
A. And so I finished my residency training in Ottawa. I did my Royal College Fellowship, and at the same time, I did a PhD program at the University of Ottawa. So that's the extent of my professional education.
COFFEY, Q.C.:
Q. So you would have finished up in Ottawa in

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1975/76?
DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. Where did you go from there, Doctor?
DR. BANERJEE:
A. My first faculty appointment was at the University of Western Ontario as an assistant professor, starting in, I believe, 1978, and I was there for several years and then moved to the University of Toronto, where I was full professor, and then at that time, I was also the head of cancer pathology at Princess Margaret Hospital and the Ontario Cancer Institute, and then I moved to British Columbia, where I was head of pathology department at the B.C. Cancer Agency and professor at the University of British Columbia, and the last 16 months, I've been the Executive Medical Director for the Provincial Health Services Authority Laboratories, that includes the Cancer Agency, Children's Hospital, Women's Hospital, Centre for Disease Control and Riverview Hospital in Vancouver.

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COFFEY, Q.C.:
Q. And just in terms of the years involved, if we could look to page two, please, that's the years of your actual professional life after your education. Page two, I take it, Doctor, we pick it up then, your career in 1979, there towards the top of the page, '79 to '87, you were the Director of the Immunopathology laboratory, University Hospital, London, Ontario. '87 to '91, the chief of pathology at St. Joseph's Health Centre in London. '87 to '91, the Chairman of Cell Biology Division of Lawson Research Institute, and then from '91 through '97, the chief of oncologic pathology and Medical Director of Laboratories, Princess Margaret. So I'm trying to give the Commissioner some sense of the years because you referred to Princess Margaret.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. You were, in effect, at Princess Margaret throughout the 1990s?
DR. BANERJEE:

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A. That's correct.
COFFEY, Q.C.:
Q. Toward the end. At the same time, we go back to the page before, if I could, I'm just going to--page one, at the bottom of the page, you had moved then by 1994 to 1998, were involved with the Department of Pathology at the University of Toronto and then from '95 to '99, the Canadian Reference Centre for Cancer Pathology, the Eastern Division, the Director and overlapping with that, '97 to 2000, the Medical Director Immunology and Immunopathology, the Department of Laboratory Medicine and Pathobiology at the University Health Network in Toronto, and from there, I gather, Doctor, you finished up in Toronto in 2000, just looking at this, and moved then, in 2000, out to Vancouver where you described where you are.
DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. Doctor, I take it then, Doctor, just looking at your CV, that you've been involved in immunopathology really since the end of the

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1970s, in one form or another?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Doctor, could you give the Commissioner, again, I appreciate it'll be just an overview, but an overview of your experience with immunopathology in your working lifetime, as to how it's evolved over time?
DR. BANERJEE:
A. Certainly. So immunopathology evolved over a long period of time. At the time I was undergoing training, immunopathology was confined to studying auto immune diseases and kidney diseases and the methodology was limited to using frozen tissue and fluorescence labelled antibodies to visualize particular proteins in a tissue. However, in the late '60s and early '70s, certainly in research labs, people published methods that would allow proteins to be identified in routinely fixed, i.e. formalin fixed tissue, which until that point was not possible, using very sensitive methods which were non-fluorescence based methods. So what we call

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Brightfield microscopy methods. That is, you can use a regular microscope to actually visualize where the antibodies bind to tissues by using a coloured product at the end of the reaction. So it would be a brown or red or blue product.
COFFEY, Q.C.:
Q. This would have come in -
DR. BANERJEE:
A. This would be, in terms of general usage, would have happened during the late '70s. So just after I finished my training as a pathologist, the early papers began to be published about the use of this method and looking at cancer markers, the earliest being CEA or carcino-embryonic antigen, and that became very interesting to me because until that point, cancer pathology was largely based on microscopic analysis of routinely stained sections, by which I mean hematoxylin eosin or H&E stained sections, and all of cancer classification is based on morphological appearance of cancers under the microscope and to this day, that's still a correct statement. However, because of the improvement in

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immunopathology methods, of the immunoperoxidase method, as it was called in those days, and now immunohistochemistry as a general term, it became possible to look at specific proteins that are known to be associated with specific cancer types or cell types.
So over the early '80s, the whole concept of using H&E as the sole method for classifying cancer changed into H&E plus immunohistochemistry which refined our ability to separate out cancers which were relatively poorly differentiated. The well differentiated cancers are not difficult to identify, but when they're poorly differentiated, they lose their appearance that would allow us to identify the cell type and they all start to look very similar, even though they're entirely different cancers, and immunohistochemistry allowed us to actually clearly identify different types of cancer and that's been a huge improvement in the tools available to pathologists.
So in immunohistochemistry, the predominant application is to help us identify

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the cell type in a different--in different kinds of cancers, so that you can classify the cancer more accurately. At the same time, it became possible to look at certain proteins which are important in terms of oncologists making a decision about what treatment to use in a given cancer and one of the earlier--the earliest examples of that is the hormone receptors in breast cancer. There are many other proteins which are not important as targeted therapies become a standard of care. So Herceptin therapy and, in the case of breast cancer, is targeted to one protein, which is HER2/neu as it's called, and the therapy only works if the protein is over expressed. So these kinds of tests are now called predictive tests. So they actually tell you whether or not a patient is eligible for a particular type of treatment.

The degree of accuracy and optimization of the methods becomes more critical as you use these tests to actually determine not whether a patient has cancer or not, but what kind of treatment is the patient eligible for, and it becomes very critical to get that

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right. I'll give you examples of why that is so.

I'll start with Herceptin therapy as the example. That's the prototype for targeted therapy and there are many more targeted therapies being introduced. So it's important to understand this point. The drug itself is expensive, so it costs--I forget the exact cost now, but it's something like $43,000 per patient. It will only work if the target is expressed in the patient's tumour cells and therefore if you have a method which has a high false negative or false positive rate, it creates a huge dilemma. Number one, let's take a patient who has been tested and was a false positive. The oncologist wouldn't know that. The oncologists depend on the labs to tell them whether something is positive or not. If the lab hasn't optimized the method and validated it, then the potential for false positive staining is very high in this particular situation. What that will do is that the patient will then be offered Herceptin therapy, even though it's not going to work, because the patient's tumour is

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actually negative. Now, you'll say well, it's just waste of money, but it's not just the cost, because the Herceptin drug is not a benign drug. It does have side effects, particularly cardiotoxic side effects. So it's not just the cost, but you can actually harm the patient with no actual clinical benefit. Take the other side of that coin and say if it's a false negative test, what happens? Then you're denying that patient therapy that she would have been eligible for and could have benefitted from. So that's an example of why testing has to be of high quality.

Take estrogen receptors, which has been around much longer in terms of our knowledge of estrogen receptors and the efficacy of estrogen receptor blocking agents such as Tamoxifen. So there again, if the receptor is expressed in the tumour cells, then there's a higher chance of that patient responding to Tamoxifen. I must point out that this is not a 100 percent relationship because there are patients who are estrogen receptor positive who may not benefit from Tamoxifen, for

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reasons that are not fully understood. One of the reasons is we have over simplified the whole issue of estrogen receptors and Tamoxifen therapy because there are many, actually several estrogen receptor types. It's not just one. And most of the antibodies we use currently in labs across the world tend to focus on one type, which is the estrogen receptor alpha molecule.

COFFEY, Q.C.:

Q. As opposed to the beta? In contra distinction to the beta?

DR. BANERJEE:

A. That's right, and there's the beta and the gamma. There's very little known about gamma, but certainly some knowledge on beta. And it turns out that Tamoxifen is not a straightforward drug because depending on where the estrogen receptor is expressed, it has different effects. If it's in the breast, it blocks it. If it's in the uterus, it actually stimulates the estrogen receptor. It turns out that the estrogen receptor alpha molecule actually when you add Tamoxifen to the tumour cells, there's a dual effect. One

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is blocking the receptor, so the estrogen will not have an effect. The other is actually stimulating the receptor, because Tamoxifen can do both. So in an individual patient, one could say that the estrogen receptor response to Tamoxifen could be a combination of inhibition and stimulation and it could vary with the individual.

Estrogen receptor beta, on the other hand, is a somewhat different receptor because Tamoxifen always blocks it. There is a small subset of patients who are estrogen receptor alpha negative, but estrogen receptor beta positive and in most labs, we are not testing for beta, so there is going to be a small subset of patients whose ER test may be called negative, but actually will benefit from Tamoxifen because they have the beta subtype being expressed. So that's something that has to evolve into standard of practice and hasn't happened yet.

COFFEY, Q.C.:

Q. And I take it that that is still in a state of development or flux?

DR. BANERJEE:

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A. That's right, yes. So now back to the issue of how well done the immunohistochemistry test has to be for oncologists to be confident in the result, and the story of estrogen receptors is quite a long one because initially, it started out as a biochemical test, which you've all heard about.

COFFEY, Q.C.:

Q. So Doctor, I take it when you started your training, in particular your residency, was it still estrogen receptor progesterone receptor testing still done by the biochemical assay?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. When you started out in your residency?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Perhaps then if you could take us then through that?

DR. BANERJEE:

A. So the biochemical test was a dextran and charcoal coated test which was a radioimmuno assay. Well, it's not radioimmuno assay.

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It's a radio ligand banding assay which looked at radio labels estrogen and how it bound to the receptors in breast tissue and that was done in biochemistry labs because it was a biochemical method and it required frozen tissue from the operating room. So the pathologist would do a quick section to see whether or not there was cancer in the tissue removed by the surgeon, and if there was a cancer, they would then take a part of it, freeze it, and send it to the biochemistry lab which would then do the test, and it was a quantitative test, so actual concentration of the receptor molecule would be actually reported, and by correlating with response to Tamoxifen thresholds of positivity that were clinically significant were established, and that was used for several years and the test tended to be centralized in one particular lab in a particular region. There was quality assurance program where labs would compare their results with one another.

COFFEY, Q.C.:

Q. Doctor, just so the Commissioner can get some background on this, why was it -- at the time

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what was your understanding about why the biochemical assay process tended to be centralized?

DR. BANERJEE:

A. I'm not sure exactly what led to the centralization policy, but virtually every province went that route, and this is based on recommendations from the biochemist community that would have made that recommendation, largely to ensure that the expertise required for that test was available, and if you have the test done by multiple labs, I think it would have been very expensive. The reagent is very expensive. These are radioactive molecules, not easy to handle, etc. So there were several reasons for centralization.

COFFEY, Q.C.:

Q. And they were centralized and there was quality assurance, quality control measures?

DR. BANERJEE:

A. Yes, and labs had voluntarily compared their results with one another to keep the quality assurance going. So that test evolved. So to try and move away from radioactive materials, when the first monoclonal antibodies were

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developed against the estrogen receptor and progesterone receptor proteins, many of the biochemical labs switched their methods to immuno enzyme assay, which essentially used the antibodies to detect the estrogen receptor protein in the cells. They're still using frozen tissue and solubilizing the estrogen receptor protein and using immuno assay to actually detect protein concentration. It's still a quantitative assay.

COFFEY, Q.C.:

Q. And these are still biochemist?

DR. BANERJEE:

A. It was still done by a biochemist because they would do other immuno enzyme assays for other disease categories. What people realized -- the oncologists realized that there was a subset of patients who would not respond to Tamoxifen in the expected manner, and we began to wonder whether part of the problem was when you have frozen tissue and you grind it up to do the biochemical test or the immuno enzyme test, and realizing that not all tumour tissue is pure tumour, there's always normal tissue around, including normal breast epithelium,

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that perhaps some of the biochemical results were based on the presence of normal epithelium which would be positive for estrogen receptors, and, therefore, some of these women where actually the tumour is negative for estrogen receptors, but the test was coming out positive because of the inclusion of normal tissue in the material that was being analyzed. So people began to wonder whether they could actually visualize where the tumour cells were and the normal cells were by using tissue sections and using immuno-fluorescence methodology. So the initial tissue based issues in receptor assays were immuno-fluorescence assays, they kept antibodies available from various vendors and these then became the standard in the early 80s because you could not visualize where the tumour cells were and where the normal cells were, and you could look specifically at the tumour cells and determine whether they were positive. Further evolution happened because as screening mammography became standard screening system, the women with breast cancer were being diagnosed earlier and earlier. So

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as a result, the tumour size and initial diagnosis was getting smaller and smaller to the point that some tumours are not actually palpable any more, so you can't actually feel a lump, you can only see an abnormal mammogram, and the surgeon would then have to use the mammogram appearance to decide what kind of procedure they're going to go through because there was no obvious lump that could be biopsied. So pathologists then had to deal with these kinds of cases where the location of the tumour was uncertain other than the mammographic abnormality, and that meant that you couldn't just freeze some breast tissue and set it for the biochemical test or do a frozen section estrogen receptor assay because frozen section morphology is not as good as formalin fixed tissue morphology. It's harder to interpret. So then people started to think about using those antibodies to actually detect the protein in formalin fixed paraffin embedded tissue, and the earliest papers that were successful in demonstrating the protein were published in the late 80s and the early 90s, but the -- and although the correlation

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with the biochemical test was pretty good, there was clearly a subset of cases that did not correlate. So there may be cases that would be biochemically positive, but by immunohistochemistry negative, and it was not always because of the presence or absence of normal tissue, and people began to suspect that the sensitivity of their method wasn't sufficient for immunohistochemistry to be completely reliable. So additional steps were introduced. By then people realized that formalin fixation tends to stabilize proteins in a particular way by cross linking different parts of the protein cell. The morphology was good, but the antibody binding sites of the antigens would be distorted, and since antibodies bind to proteins by recognizing shape, if you alter the shape of the protein, antibody may not bind any more. So they tried to figure out some ways of reversing that cross linking effect of formalin. Initially what they used were various enzymes that tend to break proteins into smaller pieces, with the hope that as you get the fragmentation of the proteins, that some of those hidden

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antigens where the antibody needs to bind to would be exposed and that was successful. However, the --

COFFEY, Q.C.:

Q. Is this the process we've heard of, this antigen retrieval?

DR. BANERJEE:

A. This is one of the early methods of antigen retrieval using enzymes.

COFFEY, Q.C.:

Q. Using enzymes, okay.

DR. BANERJEE:

A. But it was soon realized that because the enzyme preparations were not consistent from batch to batch, that there was variation, they could never have a perfectly reproducible method. Then somebody discovered the antigen retrieval method using heat, so initially using steam and now microwaving or even pressure cooking the sections that are already cut and placed on glass slides, and that seemed to work very well, and that's become the most commonly used antigen retrieval system now. Even in the automated systems like the Ventana System, that's the basic

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antigen retrieval method used. It's not perfect for all types of proteins. In many labs, there are certain antigens that they know would require enzymatic treatment and others would be okay with just the heat treatment. Estrogen receptor proteins are detectable after heat treatment quite well and it's quite reproducible.

COFFEY, Q.C.:

Q. And when would heat treatment have started to come into usage, Doctor, approximately?

DR. BANERJEE:

A. Probably about the mid 90s that this started to become widely known, and certainly in the late 90s and early 2000, it was just pretty standard. What helped is the immunohistochemistry reagent vendors and the manufacturers of automated staining systems introduced these as standard methodology to improve the consistency of the results in different labs. So the commercial industry side of this whole system drove that, and for good reasons, and improved their reproducibility from lab to lab. Having said that, one has to say that if you look at

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inter-lab variability in immunohistochemistry, particularly with the hormone receptors and HER2/neu, there is still variability even though the methods have been pretty much standardized now across the world. Then if you consider why there is that variability, it probably boils down to two major steps in the process. One is the quality of fixation. So if the tissue is not fully fixed because the formalin did not penetrate into the centre of the -- into the tumour mass, then the possibility of the estrogen receptor being lost through diffusion is actually quite significant. So tissue has to be adequately fixed. Over fixation doesn't seem to make much of a difference, but under fixation definitely has an effect on the quality of the morphology and the immunohistochemistry results. So that's one thing. The second thing is variability in the antigen retrieval method. Even though the method is the same, the conditions under which the method is used may vary from lab to lab. For instance, some people still use steam, some people use microwaving, some people use pressure cookers.

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All those introduce variability. The buffer medium that you're immersing the slides in also has an effect. So these are some of the remaining reasons for inter-lab variability. It's interesting that the biggest quality assurance program, which is the United Kingdom program, has published some data on their various proficiency testing programs, and looked at variability, and I don't know whether this particular paper has been discussed earlier in the Commission inquiry, but one of the conclusions was that the biggest reason for variability was the antigen retrieval methodology. When you read through that paper, there's a little section in the materials and methods that say that cases where fixation wasn't optimized and internal controls which are the benign breast epithelia cells were not present or did not stain were excluded from that study. I suspect that if you looked at the true variability, it would be greater than was what was reported in that paper.

COFFEY, Q.C.:

Q. Than even was reported, and that paper was --

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do you recall the approximate year, Doctor?
DR. BANERJEE:
A. Sorry?
COFFEY, Q.C.:
Q. The year of the paper?
DR. BANERJEE:
A. I'd say it was probably in '95 or '96, something like that.
COFFEY, Q.C.:
Q. Okay, so it was in the mid 90s. This is before Rhodes, is it?
DR. BANERJEE:
A. Sorry?
COFFEY, Q.C.:
Q. We've heard references to and seen references to a Dr. Rhodes in the UK. He published a paper around 2000 -- a series of papers beginning around 2000. Would this be before that?
DR. BANERJEE:
A. I think this was probably one of the first papers from that group, yeah.
COFFEY, Q.C.:
Q. And you've noted that cases that might have been, for the reasons you've indicated, cases

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that had apparent problems with fixation?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Or internal controls might be an issue?
DR. BANERJEE:
A. Right.
COFFEY, Q.C.:
Q. They were excluded from the study?
DR. BANERJEE:
A. They were excluded from the analysis of -- that was reported in the paper, but it didn't actually specify how many cases have that problem. So it would have been interesting to find out.
COFFEY, Q.C.:
Q. And even then there was inter-lab variability?
DR. BANERJEE:
A. Correct.
COFFEY, Q.C.:
Q. But they -- in that context, identifying the retrieval method, antigen retrieval method, as being the primary factor?
DR. BANERJEE:
A. That's right.

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COFFEY, Q.C.:
Q. Causing potentially the variability.
DR. BANERJEE:
A. Right. So --
COFFEY, Q.C.:
Q. I take it -- so, Doctor, in that regard then, are you suggesting that in so identifying antigen retrieval as the culprit, as it were -- -
DR. BANERJEE:
A. Uh-hm.
COFFEY, Q.C.:
Q. They, at least at that point, may have been excluding considering fixation problems?
DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. And the utilization of internal controls?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. As a potential problem.
DR. BANERJEE:
A. Right.
COFFEY, Q.C.:

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Q. Okay.
DR. BANERJEE:
A. I think the point they were trying to make and emphasize was that the false negative rates were seen mainly in the cases where the estrogen receptor concentration was very low, and that's where the main problems lie. So if it's a very high concentration, then I think most labs would call those positive even if the methods weren't optimized. So that was a good observation, but I think they lost an opportunity to address the fixation issues and the internal control issues.
COFFEY, Q.C.:
Q. Doctor, in your own experience and the institutions you worked in, when did you first encounter ER and PR analysis using the IHC method yourself?
DR. BANERJEE:
A. If I remember correctly, it would have been in the mid 80s that we were doing it by the frozen section method.
COFFEY, Q.C.:
Q. Frozen section.
DR. BANERJEE:

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A. And then by the early 90s, we had switched to -- it would have been around '95/'96 that we switched to the formalin fixed paraffin section method. In fact, in my own research, I had been trying to do that, at the time frozen sections was the standard because we realized that you can't always identify the tumour in fresh tissue for reasons I've explained before; tumour size is very small these days. It was a tough thing to do. Until the whole methodology evolved and antigen retrieval became possible and so on, it was very difficult to do that.

COFFEY, Q.C.:

Q. This was back in the days of frozen sections?

DR. BANERJEE:

A. That's right, so methods evolved and one thing I have to emphasize, this is a never-ending issues, methods will continue to improve, get better, new methods are introduced, there's new targeted therapies are introduced, all of that means that labs have to introduce new assays for a patient selection and it's critical for us to have, I'll use the word robust, quality assurance systems across the

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country to make sure that we don't have problems like this again.

COFFEY, Q.C.:

Q. Now, Doctor, just in relation to that because you had referred to the biochemists and regionalized centres for conducting the biochemical assay and they had, your understanding was they had quality assurance measures in place.

DR. BANERJEE:

A. Uh-hm.

COFFEY, Q.C.:

Q. Who recognized, I gather, across the country and perhaps throughout North America.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. What happened when the ER/PR testing moved from the biochemists to the pathologists in relation to quality assurance and kind of generalized standards, as it were, what happened? What was your -

DR. BANERJEE:

A. Well initially it remains centralized because immunohistochemistry was still relatively

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under-utilized technique and it was used mostly large teaching hospitals because we had to do it all manually, there were no automated machinery at the time. So there were dedicated technologists and usually dedicated pathologists with oversight of the lab and I was one of the directors of immunopathology very early on in my career. And everything had to be basically developed from scratch because there were no staining kits available, you had primary antibody and immunodetection systems all separately sold by the vendors and you had to put it all together in the right sequence and right concentrations and had to figure out what was optimal. Then as the industry grew so there were many vendors for antibodies and then the automated staining machines began to be introduced. The market for the vendors had to expand because the money was to be made on selling reagents and there was a much bigger menu of tests that could be done, et cetera. And with automation, it became possible for smaller hospitals to start to do these tests and so the centralization of immunohistochemistry

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soon changed to decentralized model across North America, and so hospitals that had very few cases to stain in a given week would be doing immunhistochemistry. And in my various positions, tended to be in mostly cancer centres, because of central review policies of cancer agencies I've worked with, we would see the results of these immunohistochemistry preparations from several different hospitals as part of our review process. And there was clearly quite a lot of variability in quality of fixation, quality of staining, et cetera. So in some ways by making it easy for labs to do this procedure, we lost the rigor of quality assurance and it's very easy to lump immunohistochemistry with other special stains that are normally done in pathology labs, but it's really oversimplification because immunohistochemistry is a very complex reaction between antibody and protein and each protein has its own characteristics in whether it responds to formalin in a particular way or responds to heat antigen retrieval in a particular way, all that has to be worked out very carefully and it's often difficult to

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have one protocol for everything. And smaller labs may not have the time or the expertise to figure that out, so they go by what the manufacturer says and in experienced labs, we use the manufacturer's data sheet as just a starting point, that's not the protocol we would use because, as I said, those proteins are very sensitive to fixation conditions and fixation is quite variable from lab to lab. Tissue processing itself is quite variable, even the morphology would look variable for the same reasons and therefore, it is not appropriate for any lab to just to take the manufacturer's protocols and say this is what they say you should use and expect it to work because it will not.

COFFEY, Q.C.:

Q. I take it there's an outside chance it might, but generally it would not.

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. You would have to tweak it in some way.

DR. BANERJEE:

A. Yeah, you'd have to set up the protocol for

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your own lab, which is not difficult, it's time consuming.

COFFEY, Q.C.:

Q. Doctor, could I have you repeat that?

DR. BANERJEE:

A. It's not difficult, it's time consuming, so the effort required is quite significant and I guess over the years most labs have not kept up with their workload, so in terms of staffing and all of that because of financial constraints in the system, so the amount of time available for people to work up a method is limited. So that's a big challenge for all of us, but to go back to that whole issue of not simplifying the complexity of immunohistochemistry, I think the vendors have unfortunately created a false sense of confidence amongst all clinical labs saying if you buy our machine, buy our reagents, it's going to work. And in general, it's true, however if you haven't optimized your, the initial steps that you go through in terms of fixation, processing and so on, no matter how good your immunohistochemistry technique is, there's going to be a subset of patients where

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there's been so much degradation of the protein that you cannot demonstrate it. So, that remains a problem and I think if you look at the recent literature on things like, you know, central lab results versus referring lab results and different cancer bio-markers. A good study came out, I can't remember the year, I think it was 2005 in the journal of the National Cancer Institute which showed that if labs only did a few cancer cases a month and this was the HER2/neu protein assay for Herceptin therapy, that their error rate was quite significant compared to the large central labs, which did several hundred cases a month, so that tells you that, you know, you have to see enough cases to be able to actually judge whether or not your technique is working properly. If you don't see a lot, then you don't see those patterns, you don't observe their trends or drifts. Sometimes from batch to batch, reagents don't work as well and you have to correct for that, so those are the nuances of immunohistochemistry that only very experienced technologists fully understand and the supervising pathologist

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fully understands. Beyond the technique, there's the interpretation bias, inter-observer variability in how we interpret results. So that interaction between the pathologist and the technologist is critical in this area. For every protein, you're looking for used controls, so you could use external controls and internal controls. External controls are tissues from a different patient which have been fixed differently and processed differently in a different time, et cetera.

COFFEY, Q.C.:

Q. Than the patient's tissue?

DR. BANERJEE:

A. That's right, so internal controls are good in terms of making sure your staining is working, but it doesn't necessarily tell you whether a negative result in a patient is a true negative result.

COFFEY, Q.C.:

Q. That is external controls don't necessarily do that.

DR. BANERJEE:

A. That's right because the two tissues have been

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processed from different days and perhaps the fixation was not identical, et cetera.

COFFEY, Q.C.:

Q. So they would have been fixed at, obviously, different times.

DR. BANERJEE:

A. That's right.

COFFEY, Q.C.:

Q. The external control, the patient whose tissue ended up as the external control was probably dealt with, fixed a year, six months, maybe years ago.

DR. BANERJEE:

A. Could be a much older case.

COFFEY, Q.C.:

Q. And it was fixed and then it went through tissue processing at a different time.

DR. BANERJEE:

A. Yes, and in general labs will pick external controls from a case that stained beautifully, right, so lots of protein in that tissue and then you're comparing it with another patient's biopsy which might have a lower protein concentration and if your method is not optimized, you could have a false negative

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and even know about it.

COFFEY, Q.C.:

Q. So you're saying then external controls then has its usage, but beyond external controls, is it important to -

DR. BANERJEE:

A. So the other control I would look for is an internal control, so certain proteins expressed in normal cells, they're not unique to cancer cells, so you'd look for those normal cells and make sure they're staining appropriately, so estrogen receptor is a good example, which is expressed by normal breast epithelium, so it should always be positive. The intensity may be different from the tumour cells because some tumour cells actually make more of the protein than normal cells; however, if the internal controls are there, so normal breast epithelium was there in the section and it is negative, then if the tumour is negative, there's no way of concluding that this is a true negative because there may be other reasons why the stain was negative. So the situation like that, we would have to look for a different block which had maybe better

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fixed tissue or if there was no normal epithelium in the tumour section we were staining, then we would seek another block which had some normal tissue from the same patient, so you could then compare the internal controls with the tumour. There are situations where there is no normal tissue to look at because it's a small biopsy, like core biopsies, whatever, and in that situation if the test is negative, one has to be cautious about calling it a true negative, so we would normally report it as not interpretable because of the lack of internal controls, or of the internal control is negative, we would simply look at other blocks to try and get a better fixed example from the same patient. If that fails, we would then have to question how the tissue was processed and in our organization since we are a reference lab for many other hospitals, we see that fairly frequently, fixation related problems in immunohistochemistry and so on. Our staining protocols are optimized for other people's blocks. If you optimize it just on our own processed tissue, we would probably have a lot

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of false negatives, so we have to tweak the system to make it more sensitive to deal with blocks that come from other hospitals.

COFFEY, Q.C.:

Q. That may--that are not as well fixed as the blocks that would come from internally.

DR. BANERJEE:

A. Or if the fixation is fine, there's something different about their tissue processing protocol, I would have situations where blocks from one particular hospital would never work for a particular test until I started to ask questions about, so why the morphology is great, fixation looks okay, why is it not working? And it turned out that in the tissue processor they were using a slightly different set of chemicals from the standard that was used elsewhere. So these are things that good technologists have to figure out as a troubleshooting exercise.

COFFEY, Q.C.:

Q. I take it that requires them to have a significant level of knowledge about the theory of what they're doing?

DR. BANERJEE:

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A. Yes.
COFFEY, Q.C.:
Q. And that would require the time that they could devote to that.
DR. BANERJEE:
A. Yes, and they would have to invest in the education of those people, have reference books, good workshops and so on, compare their slides with other labs and so on.
COFFEY, Q.C.:
Q. Doctor, the idea of utilizing internal controls for estrogen receptors and I take it that is equally true for progesterone receptors as well, you'd utilize internal controls.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Utilizing the IHC method, by what point in time would you have been aware that that was important, to utilize internal controls if you're doing an ER/PR by IHC?
DR. BANERJEE:
A. I think basically when we first set up the methodology even with the frozen sections,

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that would be the standard.
COFFEY, Q.C.:
Q. That would be back in the frozen section days.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. And certainly by the time paraffin blocks came along.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Now, Doctor, you have indicated that, just in passing you said that you've, of course, been associated with certain universities, medical programs which suggest to me that throughout your career you have taught residents?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. The utilization of internal controls for the purposes you've just described, is that the sort of thing that you would teach a resident who was on your rotation?
DR. BANERJEE:
A. Yes, so the way we teach residents is we sign

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out cases together, to use a double head microscope, we'd be looking at the same slides simultaneously. So, if you're looking at the immunohistochemistry preparation, then I would talk about, particular junior residents who are seeing it for the first time, how do you approach analysing this? What do you look for? How do you troubleshoot something that didn't work or if there's too much non-specific staining background, how do you recognize that? And how do you correct it by discussion with the technologists?

So, internal controls, it's a general rule because almost every tumour marker we look for in cancer is not unique to the tumour. It's a marker of the cell of origin. So, normal cells for which these cancers develop, become malignant, will also express this protein, not necessarily at the same concentration, but any particular marker you're looking for, there's bound to be some normal counterpart in that tissue that should be positive. So, you look for that because that's the best indicator that the test actually worked.

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COFFEY, Q.C.
Q. The process you're using.
DR. BANERJEE:
A. That's right. The other thing you look for is cells that should not be expressing their protein in normal cells. If they are positive, then you'd question the specificity of your test. So, those are some of the clues we look for in any slide that we're looking at. So, if there's excessive background staining, something could look positive, just because of non-specific staining and I've seen examples of that from many labs, where they're not paying attention to that particular issue and that leads to the false positive test. False negative tests are again not just estrogen receptors, but any particular tumour bio-marker we're looking for, if the normal counterpart of the tumour cell is not expressing the protein then your method is not sensitive enough.
COFFEY, Q.C.
Q. Not expressing it in the sense of the slide that you're looking at, it's not apparent in that normal tissue.

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DR. BANERJEE:
A. That's correct. And then you immediately question the sensitivity of the method. And it can be optimized. I would teach residents you can make anything look positive with immunohistochemistry and it can all be completely non-specific if your conditions are not right.
COFFEY, Q.C.
Q. But that would be not appropriate, I take it, you're saying you can do it, but, of course, it's not appropriate.
DR. BANERJEE:
A. Yes, so you have to recognize where the positivity should be -
COFFEY, Q.C.
Q. And where it should not be.
DR. BANERJEE:
A. - and where it should not be.
COFFEY, Q.C.
Q. And adjust your approach in the methods accordingly.
DR. BANERJEE:
A. That's right. So, that's why I was emphasizing the external controls are good in

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terms of making sure every run is appropriate, but it's not sufficient. You have to look at the internal controls.
COFFEY, Q.C.
Q. And Doctor, your understanding of that would go back to, well, what era, in terms of decade? Would it be '80s, '90s?
DR. BANERJEE:
A. Yes, well in a way because my research involved these technologies that, you know, I had to do all the work myself in my research lab anyways, it's a great way to learn about each of these proteins. So, in some ways I was perhaps more attuned to that with those kinds of problems than the average pathologist.
COFFEY, Q.C.
Q. Throughout the profession of pathology, the realization of the potential significance of internal controls, for example, in ER and PR testing, and from you perspective, and I appreciate you've worked in Ontario for quite a period of time in the '90s and then in British Columbia, what's your understanding or sense of when there was, kind of, generally,

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or would have generally been amongst your colleagues, an understanding of the importance of internal controls?
DR. BANERJEE:
A. It's hard to pinpoint that. I think -
COFFEY, Q.C.
Q. And I appreciate because in your world you're very--that is your world, in particular. I just ask you to reflect upon, for example, your dealing with regional hospitals because you've worked in reference hospitals, reference centres. The idea of encountering pathologists who were not familiar with were apparently alert to the utilization of internal controls. How far back would you have to go?
DR. BANERJEE:
A. I would say that the problem still exists. It all depends on the experience of the individual and whether or not the lab is set up so that there is oversight by a single individual and dedicated technologists. So, all of those variables play a role here. If you're in a situation where you've a practice where no pathologist has responsibility for

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the immunohistochemistry lab, then the risk of these things not being paid attention to, attention to detail is very high because in a busy practice you're trying to get your work done as fast as possible. So, you may tend to gloss over details like that, whereas if you were responsible for that service, the professional overseeing that particular section of the lab, then it would be your job to make sure that each slide that goes out was of high quality.
COFFEY, Q.C.
Q. And I take that if they were being interpreted by other pathologists, that those pathologists were aware of what they should be doing -
DR. BANERJEE:
A. Right, so I would have to say when we first got started in the whole business of immunohistochemistry and I was the--in 1979 I was the Director of Immunopathology for University Hospital. It was very clear that very few pathologists actually fully understood how to interpret those slides. And so the policy that I would look at every slide that went out of that lab to make sure things

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were okay. And over time, you know, because we had always discussed cases, rounds and have seminars for the residents, the other pathologists would be there and over time everybody sort of came up to speed on how to interpret these things and know what to look for and so on and so forth. It was also very clear that in those early days there was a lot of scepticism from pathologists about immunohistochemistry because they were so used to just looking at H&Es and making a diagnosis.

COFFEY, Q.C.

Q. So, this would be back through, as we go through the '80s?

DR. BANERJEE:

A. Yes. So, worldwide there was, actually, a lot of resistance to this technology being introduced. And people eventually realized that the H&E stain was not adequate for cancer diagnosis, particularly poorly differentiated tumours and some of the British publications in the early days, '70s, from I think David Mason and his group published a wonderful paper that went and looked at a hundred cases

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of poorly differentiated tumours which had been classified as poorly differentiated carcinomas, melanomas and lymphomas, et cetera and used immunohistochemistry to re-classify then and found a huge error rate in H&E based diagnosis, 40 - 60 percent being completely wrong.

COFFEY, Q.C.

Q. And this would be back approximately what time frame?

DR. BANERJEE:

A. Well, those were retrospective cases -

COFFEY, Q.C.

Q. Yes, but his paper would have been published approximately when?

DR. BANERJEE:

A. Probably the late '70s.

COFFEY, Q.C.

Q. Okay. So, and this is, Doctor, in terms of your accounting for the Commissioner, your own kind of experience as you went from the beginning of your career and progressed, being responsible for immunohistochemistry in your particular location.

DR. BANERJEE:

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A. Yes.

COFFEY, Q.C.

Q. Dealing with your contemporaries or more the point, people who are senior to you in terms of, as a pathologist.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.

Q. They'd been trained in earlier days.

DR. BANERJEE:

A. One of my senior colleagues called it immuno-mythology.

COFFEY, Q.C.

Q. Mythology, okay.

DR. BANERJEE:

A. Because he didn't believe it; things have changed.

COFFEY, Q.C.

Q. Doctor, I point out, even today, I take it, that you would understand that there would be pathologists that you might encounter or pathologists work that you might encounter where it was apparent that they did not fully appreciate, for example, the importance of internal controls for certain of these IHC

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processes.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.

Q. And Doctor, I take it then a pathologist who is being trained today, for example, in your institution, you would expect to be exposed to that.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.

Q. But were there any particular pathologists who graduated years ago was exposed to, it would be function of their actual training and/or their curiosity in terms of looking at the literature.

DR. BANERJEE:

A. Right, it's a combination of the two. So, you're training program would train you what the standard of the day was, but as you practice as a professional, you have to keep up with what goes on in the field and that keeps changing.

COFFEY, Q.C.

Q. And, in particular I take it, in relation to

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immunohistochemistry, it has changed significantly over the past two decades.

DR. BANERJEE:

A. In terms of the spectrum of molecules you can detect by the method, it's enormous, grown hugely.

COFFEY, Q.C.

Q. And Doctor, I'm going to return, I hope, to that whole subject a little bit later, but I understand that in the past you'd been involved with the Canadian Association of Pathologists.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.

Q. And you have been involved with the executive and, in fact, had served as the president.

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.

Q. As well I understand that you had met a gentleman named Dr. Donald Cook.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.

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Q. How did you know Dr. Cook?

DR. BANERJEE:

A. I think probably when I joined the executive I got to know him. I'd known about him before because he was a member of the association.

COFFEY, Q.C.

Q. And if we could bring up, please, Exhibit P-1992. Now, Doctor, these are handwritten notes of Dr. Cook and here he notes that, on Tuesday, August 2nd, 2005 at about 5:30, that would be local St. John's time, I take it, he's contacted you, I gather, by phone. He writes, "given range of our figure Diponkar feels we are in the range, may have a problem with the Ventana being too sensitive; may not have a problem with the old methodology, stressed the need for quality assurance and proficiency testing program. And a good idea to correlate with Mount Sinai and set up proficiency testing program with them. A bit concerned about us reporting negatives". Something "when negative internal controls and may suggest test invalid". He says, "don't admit to"--he notes you as saying, "don't admit to error with the old system as it was

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the technology of the day. Use a variety of controls and good idea to correlate with Mount Sinai". And he's noted here, "Ventana provides standardization and reproducibility". I appreciate, Doctor, these are just simply some handwritten notes and I just bring them to your attention because it is, as far as I can tell, I believe the first note of a contact with yourself, August 2.

DR. BANERJEE:

A. Right.

COFFEY, Q.C.

Q. Doctor, what do you recall about your initial contact with Dr. Cook which ended up in you coming to St. John's?

DR. BANERJEE:

A. So, what I recall was clearly he was concerned about the conversion rates between the old technique and the Ventana based method. And my initial thought was there was something wrong with the Ventana method optimization because Ventana instruments were being purchased by several hospitals during that time and had seen the results of their immunohistochemistry procedures. And

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initially if you just went with whatever the manufacturer tells you to use because this is almost a fully automated system where the re-agents are already pre-diluted. So, there's very little modification required by the technologists. But in general, I was noting a lot more background staining with that system because of the detection methodology was different from the DAKO methods. And so my initial thought was that possibly seeing a lot of cytoplasmic staining and calling that positives, something like -

COFFEY, Q.C.

Q. In the Ventana.

DR. BANERJEE:

A. That's right. So, that was my first immediate reaction, that maybe it hasn't been optimized. They've just started to use the Ventana system and maybe they're just getting non-specific staining and maybe the DAKO system was fine. So, that was my initial, sort of, reaction, but as I was talking to him and the issue of internal controls came up and the fact that tests that were being reported without consideration that the internal controls have

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to be positive concerned me. And then I started to wonder about other reasons why, that may be less than optimal staining protocol. We were definitely using a DAKO system ourselves. We've used it for many years and there's been no problem with it. So, I was quite sceptical about the DAKO being blamed as the culprit because it didn't make sense to me. And so I said, you know, don't jump to that conclusion yet and let me come and take a look at these slides because I hadn't seen their slides before. And then I might be able to figure out what was going on.

COFFEY, Q.C.

Q. So, don't jump to what conclusion?

DR. BANERJEE:

A. That there's something wrong with the DAKO system.

COFFEY, Q.C.

Q. Because your own institution was utilizing that technology, the DAKO, and others.

DR. BANERJEE:

A. It's being used by several institutions, Mount Sinai included.

COFFEY, Q.C.

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Q. So, you indicated that you would come to St. John's.

DR. BANERJEE:

A. Um-hm.

COFFEY, Q.C.

Q. If we could look, please, at Exhibit P-1979. Now, Doctor, these two e-mails of August 3rd, 2005, Dr. Cook's first one, the bottom of the page here.

DR. BANERJEE:

A. Right.

COFFEY, Q.C.

Q. He writes, "I certainly appreciate you coming to St. John's to review our immunohistochemistry lab during the dates of September 15th to the 16th, 2005. We will reimburse you for the costs. We'll keep in contact regarding the information you will need". And he does refer to your consultation fee and I do want to note that I'm not going to refer to it after, but in fact, you subsequently did waive your consultation fee, didn't you?

DR. BANERJEE:

A. I did.

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COFFEY, Q.C.

Q. And then you responded by saying, "Hi Don, I look forward to the site visit". So, I take it, Doctor, really within the day of contact with Dr. Cook, you'd arranged the timeframe and -

DR. BANERJEE:

A. That's right.

COFFEY, Q.C.

Q. - the other considerations. Doctor, I refer you then to Exhibit P-1969. And here, Doctor, actually let me go to page two first; this is a couple of e-mails. The first one from Dr. Cook, at the bottom there, indicates, "I'm assuming everything is still a go for your visit to St. John's in review of our immunohistochemistry service" and he asks you to give him a call. And then the same day, later the same day, you respond with your travel arrangements and where you're staying and you then indicated, right here, "for my site visit, I will need to review any lab procedure manuals and a random selection of IHC slides before and after switching to the Ventana platform, including positive and

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negative control slides, not just for ER and HER2/neu, but all antibodies on your menu. If you have cases stained with both old and new methods on the same block, those would be helpful as well".

Doctor, why was it then, just so the Commissioner understands, because you had been consulted really, initially, about the ER/PR.

DR. BANERJEE:

A. Um-hm.

COFFEY, Q.C.

Q. You'd been told by Dr. Cook, I take it, that had these number of retests and conversions.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.

Q. Had he told you at the time why there was retesting in the beginning and what had occasioned the retesting? Do you recall that?

DR. BANERJEE:

A. I recall the discussion around the initial patient that let to this whole investigation and the fact that they were going to retest other cases as well. I didn't know necessarily the extent of the retesting in

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terms of the numbers at that time.
COFFEY, Q.C.
Q. You just understood that there were a number of conversions. What they had retested, there'd been a number of conversions.
DR. BANERJEE:
A. That's right.
COFFEY, Q.C.
Q. And why then, Doctor, in kind of finalizing--because you'd be coming later, in fact, that week--the week of September 12. You weren't just going to limit yourself to ER/PR or HER2/neu slides. You wanted a wider selection. Why is that?
DR. BANERJEE:
A. So, what I was hoping to look for is some kind of pattern of non-specific staining or false negative staining as a result of some lack of optimization and methodology, particularly in the detection system side which would be similar, no matter which particular protein you were looking for. So, instead of looking just at ER/PR and HER2, I wanted to look at the full spectrum of what they did and just kept that view of what the problem might be

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due to.
COFFEY, Q.C.
Q. And this was in relation to Ventana stained slides, I take it.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. This wider view.
DR. BANERJEE:
A. I wanted to see both, both the stains through the DAKO system as well as the Ventana system, just to get an initial impression of whether there were some technical problems or not, and I wasn't necessarily assuming one thing or the other at that time.
COFFEY, Q.C.
Q. And you were asking for--review any lab procedure manuals.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. And why did you want to see those?
DR. BANERJEE:
A. I wanted to see whether the test optimization was done in the local lab or were they just

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following the manufacturers instructions for staining.
COFFEY, Q.C.
Q. And why would it be important to know the answer to that.
DR. BANERJEE:
A. Well, you know, I explained earlier, if you just take the manufacturers protocols, they may not necessarily work in your lab because there are other variables to correct for it.
COFFEY, Q.C.
Q. And what did you, in fact, find in that regard?
DR. BANERJEE:
A. I found, in general, again, I'm going to be fairly general, the DAKO system tended to have lower intensity staining no matter what you looked for.
COFFEY, Q.C.
Q. Probably if I could, I'll be visiting that, I'm just asking about the laboratory, were they using the spec sheets as it were or -
DR. BANERJEE:
A. Actually we didn't get into that.
COFFEY, Q.C.

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Q. Okay.
DR. BANERJEE:
A. I don't recall having seen any lab manuals at the time of the visit.
COFFEY, Q.C.
Q. That's what I was going to ask you because you had asked to see laboratory or lab procedure manuals.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. And you don't recall, in fact, being presented with any.
DR. BANERJEE:
A. Right.
COFFEY, Q.C.
Q. Did you ask at the time subsequently whether there were any?
DR. BANERJEE:
A. No, I didn't because by the time I'd seen all the slides, I'd figured out what the problem was.
COFFEY, Q.C.
Q. Yes. Exhibit P-1942. Doctor, this is two e-mails of September 13th, 2005, the first at

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the bottom of the exhibit here is from Dr. Cook to yourself. He thanks you for your e-mail of September 12. He indicates he will pick you up. He says "I will drive you first to St. Clare's site where I will provide you with background information including a review of the IHC slides before and after the Ventana platform. The focus will be on ER and PRs, however I will try to get as many representative IHCs from other antibodies as possible. Following this I will take you over to the General site where the cutting and staining procedures are done and also have you meet with key individuals at that site. I had asked the chief tech to provide you with the lab procedure manual. I will fax you a copy of the terms of reference of the IHC review this afternoon. I assume"--he refers to your fax number and he says, "I will also try to arrange an exit interview with key leadership people from the organization on Friday afternoon. Let me know if this is okay". And you respond by saying, "thanks, the arrangements and exit interview are fine".

If we could, please, Exhibit P-1283,

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Doctor, that is the background--these are terms of reference, External Quality Review of the Immunohistochemistry Service. And the Commissioner has seen these before, we all have here. I take it this was faxed to you?

DR. BANERJEE:

A. That's correct, yes.

COFFEY, Q.C.

Q. Doctor, back in early August you'd agreed to come to St. John's, what was your understanding of the terms, if any, under which you were coming and the purpose of your visit, at that time, early August?

DR. BANERJEE:

A. My understanding was that I was being asked to figure out what the problem was with their immunohistochemistry service, and I was approaching it from the point of view of an experienced immunopathologist who could troubleshoot for them and advise them about how they could improve the process.

COFFEY, Q.C.:

Q. These terms of reference when you look at them, the purpose is noted to be "To review the operation and make recommendations as to

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the processes involved and the service of the laboratory medicine program", and you're described as the external quality review consultant who will take direction from and make recommendations to the leadership team of the laboratory medicine program, and they talk about the time frame and the responsibilities are listed there, and then there's a case summary, which includes as well a reference to the -- as it turns out it's a lady named Peggy Deane, which has been referred to here at times as the index case, and four other patients, and then reference to what had happened up to that point in time in terms of the retesting and he notes -- this terms of reference notes, "Of the 57 retested on the Ventana System, 38 now show positive results", and a reference to the sensitivity of the Ventana System now being in question, and finally, "The report of the external quality review shall be in writing and include the team's recommendations. The recommendations will be shared with involved staff members", and it notes, "The peer review, its conclusions and a final report are protected

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under the Evidence Act, and as such the final report will not be available to any third party, and as well the final report is protected from any subsequent legal proceedings". Now, Doctor, I will ask you this because I'll be asking you your views later on in relation to this idea of peer review, quality assurance, and protection in legal proceedings, but at the time you agreed to come, was peer review or external quality assurance, was that on your mind or discussed between you and Dr. Cook, the idea that this would be a peer review?

DR. BANERJEE:

A. I think it was understood that the whole procedure would be protected under the Evidence Act.

COFFEY, Q.C.:

Q. Right from the beginning?

DR. BANERJEE:

A. Right from the beginning, but, you know, possibly each province does it differently, so unsure what to expect and what the actual procedure was going to be. Certainly in other jurisdictions, in Ontario, and in British

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Columbia, somebody from risk management would actually be driving that process, and it wasn't the case here.

COFFEY, Q.C.:

Q. It wasn't the case here.

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. It was Dr. Cook. Doctor, just again so the Commissioner can perhaps put this into context, have you ever, yourself, conducted peer reviews of other peers or been involved in that?

DR. BANERJEE:

A. Yes, those would be based on individual pathologists being reviewed as opposed to a program review of this type, or external reviews of an academic department when they're looking for new leadership or whatever.

COFFEY, Q.C.:

Q. So you have done external reviews of an academic department when you've been asked to --

DR. BANERJEE:

A. Yes.

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COFFEY, Q.C.:

Q. When they're looking for a particular -- like, a head of a department?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. You've done that in the past, and you've been asked to be involved in peer reviews of individuals?

DR. BANERJEE:

A. Correct.

COFFEY, Q.C.:

Q. Have you ever been involved in this sort of a review, the one that occurred here in St. John's, a review of a whole department or system?

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. This is your first.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Do you know of any other such review that has occurred?

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DR. BANERJEE:

A. Anywhere else in the country, you mean?

COFFEY, Q.C.:

Q. Yes, that you're aware of.

DR. BANERJEE:

A. Yes, I was asked about another one, which they turned me down as a reviewer for some reason. Probably I was too expensive or something.

COFFEY, Q.C.:

Q. But I take it that as you've been involved in your field for decades, that this is a relatively rare -- as far as you know, a relatively rare approach?

DR. BANERJEE:

A. Yes, doing a system review of a particular aspect of a lab based on concern about the quality of the results, yes, that would be unusual.

COFFEY, Q.C.:

Q. Exhibit -- Doctor, I'm going to ask you -- I'll be referring you to a couple of documents, but I'm going to ask you to tell the Commissioner -- it's about five to eleven, Commissioner, so rather than embark upon that, perhaps we could take the morning break, and

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I'm going to come back and ask you to recount then what you recall about what happened, Doctor, when you arrived in St. John's in September.

DR. BANERJEE:

A. Right.

COMMISSIONER:

Q. Okay, we'll take the morning break.

(BREAK)

COMMISSIONER:

Q. Mr. Coffey.

COFFEY, Q.C.:

Q. Thank you, Commissioner. Dr. Banerjee, could you tell us then please about your visit to St. John's in September, 2005?

DR. BANERJEE:

A. Certainly. If I recall correctly, I met with Dr. Cook who took me to St. Clare's site first, then the General site, and at the St. Clare's site, we looked at selection of cases that he had put together for my review, which included the ER stains from the DAKO System and the Ventana System, and other immunohistochemistry preparations that I could sort of look at a pattern of the staining

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problems that they're having. So we sat down and looked at the slides together using a double-headed microscope. For each case we looked at, I had some comments that I made. I didn't record my observations on a piece of paper because I was really looking for patterns across multiple cases, and at the end of that review, I could see where the problems were, and it was a combination of fixation problems as well as optimization of the stain protocols. Clearly the DAKO System had a lower intensity staining than the Ventana System, which to me would suggest that there was either a problem with antigen retrieval or the antibody concentrations being used, or the detection system concentrations being used, were not optimal. We did discuss the issue of the internal controls, which I could see was a major problem in that all of the cases that he showed me that had converted between the DAKO and the Ventana Systems have the same kinds of characteristics, i.e. fixation not being adequate. The second thing was that many of the cases which included the benign breast epithelium showed no staining of the benign

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epithelium for estrogen receptors, and to me that would invalidate the particular report on that case since the internal controls did not work. Now since the Ventana System was picking up more positive cases, then one would have to conclude that fixation was not the only culprit since if the protein was completely destroyed because of inadequate fixation, neither system would have produced a positive result without creating huge background staining. So there was a combination of fixation problems and method optimization that led to the false negative staining, which because the Ventana System has really pre-diluted the reagents and has the antigen retrieval process built into the machine, it has, to a large extent, overcome problems related to fixation. However, I don't believe it can be completely overcome as there's surely some protein loss because of fixation problems. So those were my conclusions, and I verbally gave it to him, and commented about the need for dedicated technologists who understood how to troubleshoot, and the fact that they did not

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have a designated pathologist responsible for that service, and that was a major concern of mine. So it boils down to accountability for the quality assurance system in the lab, and that seemed to be -- if you want to look at the root cause of quality problems, it relates to accountability and who is responsible for quality.

COFFEY, Q.C.:

Q. Doctor, I'm going to ask you a little bit more about that. Before we go on, you were shown a variety of slides that Dr. Cook chose?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. The slides for estrogen receptors for the DAKO slides and the corresponding Ventana slides for that particular patient, approximately how many patients ER slides would you have dealt with?

DR. BANERJEE:

A. It was not a large number. I think it was roughly about 20 cases.

COFFEY, Q.C.:

Q. About 20.

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DR. BANERJEE:

A. Yes, plus other cases for different --

COFFEY, Q.C.:

Q. Yes, and the others -- there would be 30 odd, I take it, of the other cases.

DR. BANERJEE:

A. Approximately.

COFFEY, Q.C.:

Q. In total, but they were other stains, not ER stains?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Not ER stains, they were other stains.

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. And I'll ask you what you found with respect to those in a moment, but the sampling of 20 cases that -- and all of which had converted.

DR. BANERJEE:

A. Uh-hm.

COFFEY, Q.C.:

Q. You understood from the ER DAKO slide to the ER Ventana slide --

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DR. BANERJEE:
A. Correct.
COFFEY, Q.C.:
Q. Had all converted. Doctor, a sample size of 20, of course, is not necessarily all that large. How comfortable did you feel at the time that you had identified the source of the problem, as it were?
DR. BANERJEE:
A. I was pretty comfortable because I could see the recurrent problems around the fixation and the lack of positivity in the internal controls. So I didn't feel that I needed to see more cases. If I only found one or two cases of that nature, then I would have said this isn't enough for me to make a conclusion.
COFFEY, Q.C.:
Q. If out of the 20, there was only one with a fixation problem --
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Or an internal control that was present, but hadn't stained, you would have had to go looking for something else?

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DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. Doctor, just while we're on this because you've referred to it just now, and just so I don't omit to go back to it, you referred to the idea of organization and root cause?
DR. BANERJEE:
A. Uh-hm.
COFFEY, Q.C.:
Q. Perhaps we'll come back to that because that's in your report itself and you addressed that, and we'll address it then.
DR. BANERJEE:
A. Right, okay.
COFFEY, Q.C.:
Q. Did you discuss the management issue or the organization issue with Dr. Cook at the time?
DR. BANERJEE:
A. I did, and one of his concerns, and obviously it was frustrating him, was the fact that he was the clinical chief of the lab, but he did not have any authority over the technologist, budget, space, etc, and that was under the jurisdiction of the program director who was not a lab physician.
COFFEY, Q.C.:
Q. And Dr. Cook expressed that to you at the time?
DR. BANERJEE:
A. Yes, and so did the other pathologists that I've interviewed.
COFFEY, Q.C.:
Q. I was going to ask you then, Doctor, at the St. Clare's site, did you speak with anyone else at the time, do you recall?
DR. BANERJEE:
A. I didn't keep notes, and my recollection is not very good, but I met with pathologists individually. I think I spent the greatest time with Dr. Edgecombe, whom I had known from my previous training in Ottawa, he was a trainee at the same time.
COFFEY, Q.C.:
Q. So you would have seen him on your visit in September at the General Hospital site, I take it?
DR. BANERJEE:
A. That's right.
COFFEY, Q.C.:

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Q. While you were at St. Clare's that day, do you recall if you spoke with Beverley Carter, Dr. Carter?
DR. BANERJEE:
A. I did speak with her, but I can't remember where it was.
COFFEY, Q.C.:
Q. So it was brief, I take it --
DR. BANERJEE:
A. Relatively brief, yes.
COFFEY, Q.C.:
Q. So you're with Dr. Cook, you examined the slides, the conversation you referred to. What if anything did you notice about the non ER slides, this other sampling of slides? What do you recall about those?
DR. BANERJEE:
A. What I recall about those were in the DAKO System the intensity was rather pale, the staining intensity, not what I would accept as a very good result, and again looking at internal controls for the various proteins that we were looking at, there were clearly cells that should have been positive that were not. So I said this isn't optimized for these

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particular tests as well. In looking at the Ventana, the intensity was certainly higher, but there was also more background staining, which is what I had expected to see, because all other labs were having the same problem with the Ventana System.

COFFEY, Q.C.:

Q. These were labs --

DR. BANERJEE:

A. Which were all not, you know, optimizable.

COFFEY, Q.C.:

Q. So I take it the Ventana slides, there was more background staining than from your perspective you would want?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. And you attributed that to a failure to have optimized the Ventana System?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. Did you discuss those two aspects of the matter with Dr. Cook?

DR. BANERJEE:

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A. Yes, I did.

COMMISSIONER:

Q. Excuse me, Mr. Coffey, I'm not sure this is the right place to go down this road, but can you tell me a little more about what you're looking for when you're optimizing?

DR. BANERJEE:

A. Yes, certainly. So what we look for is -- I think the starting point is what manufacturer of the reagent would say this the dilution you use, etc, and this is the antigen retrieval method you should use. That's the starting point, but we then go through a process whereby we do multiple dilutions of the primary antibody, and try different heat -- antigen retrieval protocols, enzyme versus heat ,and then optimize the detection system which is a set of reagents that bind to the primary antibody, and all of that is what we call a checkerboard type of titration process. So what we're looking for is a crisp intense staining in the cells that you expect to be positive with a clean background, no staining at all in cells that are expected to be completely negative, and once you've done

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that, you then look at a range of examples of clinical samples to make sure that that is the correct setting for that test. So it corrects individual variations that might result from changes in fixation protocol, etc. Remember we are reference labs, so we do that because we know that when we get tissue blocks from other hospitals, they're not all going to be identically processed, so we have to modify our technique accordingly, but in a lab that only works with their own processed tissue, it's a little easier to actually establish the optimal protocols.

COMMISSIONER:

Q. Okay. So then as I understand what you're saying -- I think from other witnesses, I've understood a little bit about the process in the sense of you have these parameters of what you might want to use, and then you use incremental amounts, etc.

DR. BANERJEE:

A. That's correct.

COMMISSIONER:

Q. And examine the result, but the -- what you -- the test of it, as it were, is what you see on

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the slide, and that is in terms of these things about minimizing background, optimizing what should be positive being positive, and what should be negative not showing, as it were?

DR. BANERJEE:

A. That's correct.

COMMISSIONER:

Q. Okay, and then in your case, because you're using or dealing with material which comes from different locations, you would want to make sure that the best choice for ideal circumstances will work with the varieties of fixation, etc, that you would expect to deal with?

DR. BANERJEE:

A. That's correct.

COMMISSIONER:

Q. Okay, and you said something this morning about being able to make anything positive, so how do you -- is it the fact that you have a known quantity on that slide that you're really doing the test, the initial test on, what makes you confident that, in fact, this is the appropriate thing?

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DR. BANERJEE:
A. No. In fact, you know very little about how much of that protein is actually there in the tissue.
THE COMMISSIONER:
Q. Okay.
DR. BANERJEE:
A. There is no gold standard. So what you really look for is the cell type that should be expressing that particular protein, whether it's positive or not, because you can recognize different cell types just from the morphology of the cells.
THE COMMISSIONER:
Q. Okay.
DR. BANERJEE:
A. And based on the literature and examples from the studies that established the method, you then understand the intensity or expectancy. Intensity is not going to be identical for every type of protein, so it would depend on the protein. I think more important than intensity is the location of the positive reaction. So for something like estrogen receptors, which is a nuclear protein, one

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would not expect to see it in the cytoplasm of the cell. So it has to be a nuclear stain, and if you see anything outside of the nucleus, then one would again question whether the method has been optimized or not. So each protein you're looking for has particular characteristics about where it is expressed, what is known about how much of the protein is expressed in the cancer cell, etcetera, and that knowledge is really based on cancer cell lines which have been analyzed quantitatively for the protein, but translating that into clinical samples is quite difficult because there is no quantitative method in immunohistochemistry yet. It is a semi-quantitative method because there's so many steps of amplification required to create the sensitivity of the method that it loses its linear relationship to protein concentration. So no matter how automated the process is, it is a semi-quantitative--the end result, the interpretation of the result is very semi-quantitative and I think trying to standardize the grading of intensity is probably asking too much. Standardizing based on the

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percentage of cells being positive is perhaps more logical than trying to grade intensity, because it's not a linear relationship with the protein concentration.
THE COMMISSIONER:
Q. So that the person involved in this process has to be a person who is current with the literature?
DR. BANERJEE:
A. Yes.
THE COMMISSIONER:
Q. And the studies have made some, presumably, determination about the validity of some of these studies?
DR. BANERJEE:
A. Yes.
THE COMMISSIONER:
Q. And the key thing is what you know, on the basis of those studies, about what you should see?
DR. BANERJEE:
A. That's correct.
THE COMMISSIONER:
Q. And what the results should be. Okay, thank you.

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COFFEY, Q.C.:
Q. Doctor, just on that point the Commissioner has raised with you, for example, in British Columbia, Vancouver, I take it that's where you're based at work, you're providing or you see and deal with blocks that come from different hospitals?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Variety of hospitals, and in this optimization process, you account for the fact that we're not just dealing with blocks from the second floor of our own building. These are blocks from a particular region or even a larger -
DR. BANERJEE:
A. The whole province.
COFFEY, Q.C.:
Q. The whole province, in effect, in your case. So that sort of an optimization process, which I take it has to occur in respect of each stain that's utilized?
DR. BANERJEE:
A. Um-hm.
COFFEY, Q.C.:

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Q. If, at Eastern Health, the General Hospital, you visited in September 2005, is providing the same service, in effect, in terms of IHC, to the entire province here and in the course of doing so, is receiving blocks from hospitals, a number of hospitals throughout Newfoundland and Labrador, the same, not only optimization for their own fixation quality locally would have to occur, but as well, they would have to take into account the fact that they are going to be processing blocks from all over the province?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. The same sort of process would have to occur. Perhaps with fewer IHC tests here in St. John's, but the same process that occurs in Vancouver would have to occur here.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. The approach that is utilized in Vancouver in that regard, does the protocol used vary depending upon the hospital you get the block

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from or is it just the one--for example, for ER, is it -

DR. BANERJEE:

A. No, that would be too difficult to do. So we end up with a bit of a compromise. There are protocols designed to work with virtually all the material we receive. If there's a particular problem with a particular hospital, then we would discuss that with that hospital. But in British Columbia, I don't see that as a major problem, for whatever reason. I think it's a smaller province than Ontario and there are fewer hospitals involved and there's a lot more of a cohesive network of people who have been working together for many years. It's not really a problem there.

COFFEY, Q.C.:

Q. And Doctor, just while we've on it, because you've indicated that when you were looking at these slides with Dr. Cook, the approximately 20 ER--pairs of ER slides and the other slides as well, the non-ER ones, you referred to and noted the fact that you'd recognized fixation problems?

DR. BANERJEE:

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A. Yes.

COFFEY, Q.C.:

Q. Fixation issues. What is it that caused you to reach that conclusion, based upon what you saw? What is it that you were seeing that led you to that result?

DR. BANERJEE:

A. See, basically, you start out with the routinely stained section, that's the hematoxylin eosin stained preparation or H&E stain preparation, and you look at general sort of morphology of the tissue and how crisp the cells are. Are they easily identified or they look smudgy, etcetera, and the staining intensity is appropriate or not and that gives you, immediately, a reasonably good clue as to whether the tissue is well fixed and well processed, and as a general rule, if the tissue hasn't been well fixed or well processed, no matter what you do subsequent to the tissue being processed, in terms of special stains or immunohistochemistry, the results will not be optimal and even the morphology of the cells are distorted so that it may be difficult to actually identify the

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cancer type or whether there's cancer or benign tissue in there, particularly with smaller biopsies. So these are all kind of fundamental things you look for, and I could see that right from the get-go, looking at the H&E, that there was a problem with fixation.

COFFEY, Q.C.:

Q. And that's just the H&E slides that you saw at St. Clare's?

DR. BANERJEE:

A. That's right. And then, so if I describe the distortion a little more. So what you might see would be excessive shrinkage of cells. So there'll be gaps around the cells, between the stroma and the epithelium, for instance, or the nucleus would be swollen up or not as well defined as you would like to see, and the nucleus stains would be pale or very dark, depending on whether there's shrinkage or swelling and so on. So if you then choose a block which tells you that the tissue hasn't been fixed and processed adequately and you do the heat antigen retrieval on a section that's been cut and placed on a slide, the likelihood of that tissue actually staying on the slide

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is very low. It tends to fall off because it's a very harsh treatment, that high temperature. Or it starts to wrinkle or parts of it falls off or parts of the tumour might fall off, so you can't interpret your stain and so on. So it's critical to have that initial processing step optimized. Otherwise you have these kinds of problems. The morphology gets worse after the heat antigen retrieval and if you have bad morphology to start with, it just looks worse and worse. So it just compounds the problem.

COFFEY, Q.C.:

Q. Doctor, that sort of recognition of fixation not having been optimal or, in fact, having been relatively poor, looking at the H&E stained slides, would any pathologist who had gone through the residency program in Canada, for example, would they recognize that, do you think?

DR. BANERJEE:

A. Not necessarily, because it depends on--like if you were in training program in a teaching hospital that hadn't optimized its fixation process, you wouldn't recognize that there was

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a problem because every case would look similar and you sort of work around the problem.

COFFEY, Q.C.:

Q. Okay.

DR. BANERJEE:

A. I'll give you some anecdotal experience about that. When I first moved to London, Ontario, the University of Western Ontario, I specialized in lymphoma pathology, so these are lymph nodes with lymph gland cancer, and I could see that they had a fixation problem because they would place the entire lymph node in formalin, leave it in for hours and then cut it and process it. And of course, formalin takes a long time to penetrate tissue and fix it. It takes hours. So the thicker the tissue, the longer it'll take, and the centre of the tissue, in the meantime, would start to degrade because it hasn't been fixed yet. So I changed the protocol, saying you know, you have to take the fresh lymph node and slice it into thin slices, two to three millimetres maximum thickness, then fix it, and you'll see much better morphology, and what happened was

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because the morphology suddenly became better, people actually had difficulty in recognizing the cancer because now they're looking at cells which are bigger and looked horrible, in terms of malignant characteristics, and so there's a new learning curve for that because if you're used to badly processed tissue and you still can make a diagnosis, you're sort of reading through the artifact and if you remove the artifact, then somehow you have to reset your mind about, you know, how to interpret morphology all over again, and we have to go through that.

So if a hospital hasn't done that, then all of the residents in training will learn to read through the artifacts and they'll accept that as normal, and I think another factor that leads to this is that virtually all pathology training programs, the first year of training tends to focus on autopsy pathology, and certainly my training was like that as well. So the first year is just doing hundreds of autopsies, until you learn the pathology, and then you were allowed to go into surgical pathology as the next phase.

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Autopsy pathology, you're already starting with degraded tissue because cells start to degrade as soon as the patient dies, and of course, it takes hours before you actually begin the autopsy. So when you look at the morphology from autopsy tissue, it looks terrible, but you learn how to read that. So then when you go to surgical pathology and if your fixation is terrible, then you'd say "well, this is sort of what I'm use to anyway." So you'd sort of perpetuate that problem.

COFFEY, Q.C.:

Q. And so it's depending upon the local fixation practices from place to place, you wouldn't find it surprising to come in--for example, in your case, when you arrived here in St. John's, September 2005, and noted what you interpreted, saw interpreted as fixation issues on these slides, is it possible that Dr. Cook, for example, just would not have recognized it as a problem in the same way that you did?

DR. BANERJEE:

A. It is possible. It would depend on where he

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had trained and where he had practised, whether he had seen other examples. IF your practice is limited to the local professional practice, then you may see only a spectrum of quality. If you were in our situation, because we are looking at tissue from not only other hospitals in the province, but across the country, from other parts of the world, we saw a full spectrum of what's good and what isn't good, and we learned from that as well ourselves.

COFFEY, Q.C.:

Q. So Doctor, is there anything else you recall about the visit to St. Clare's that day?

DR. BANERJEE:

A. No, it's quite vague in my mind.

COFFEY, Q.C.:

Q. And you then, I take it, were taken over to the General Hospital?

DR. BANERJEE:

A. That's right.

COFFEY, Q.C.:

Q. And what happened there?

DR. BANERJEE:

A. So there, I actually went to the lab that does

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the immunohistochemistry and talked to the technologists, looked at how the lab was set up. I wasn't particularly looking at how they do their work, but I was just asking them questions about what else they did and it was clear that they were not dedicated to that section in the lab, that they had other responsibilities elsewhere and they had felt it was hard for them to keep up with the knowledge base required to do a good job, but that's not unusual. This is a common problem across the country.

COFFEY, Q.C.:

Q. And your purpose in going to that site was what, the General Hospital site? Did you look at slides at the General Hospital site, do you recall?

DR. BANERJEE:

A. I don't recall whether I saw another set of slides. I don't think so.

COFFEY, Q.C.:

Q. So then your purpose then -

DR. BANERJEE:

A. It was more sort of interviewing other pathologists at that site.

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COFFEY, Q.C.:

Q. You've indicated that you did, while you were in St. John's, at that time, speak to Dr. Ejeckam?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. And you had known Dr. Ejeckam before?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Could you tell the Commissioner how it was you happen to know Dr. Ejeckam?

DR. BANERJEE:

A. Well, when I was in training in Ottawa, he was also a trainee, at not the same hospital I was in, but we met at the Canadian Tumour Reference Centre. We were both doing a month elective time there, and we got to know each other, and I've seen him off and on over the years and I know that he was very interested in immunohistochemistry, and certainly very knowledgeable, and so I asked him his opinion of what was going on. He sort of confirmed some of my conclusions. He was clearly not in

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charge of the lab, but he sort of had a -

COFFEY, Q.C.:

Q. Okay, I was going to ask you about that.

DR. BANERJEE:

A. - he really wanted to do something about it.

COFFEY, Q.C.:

Q. Doctor, so before September 2005, you understood that Dr. Ejeckam had more than a passing acquaintance with IHC techniques?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. He knew more than the average pathologist about it?

DR. BANERJEE:

A. I think so, yes.

COFFEY, Q.C.:

Q. And then finding him here on the ground, as it were, in St. John's, in the course of doing this, you would have, as you've indicated, asked him "what do you think is going on, Gershon?"

DR. BANERJEE:

A. Um-hm.

COFFEY, Q.C.:

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Q. What was it--do you recall what it was he told you? And not only what was going on, but his position here in St. John's?
DR. BANERJEE:
A. Right. So he was obviously quite concerned about the quality of the immunohistochemistry lab and he sort of volunteered to try and help the lab to do a better job and he spent a lot of time actually teaching the technologists and providing them with reference books and textbooks, but clearly he didn't actually have the authority to make the additional changes that were required, and this was a recurrent theme amongst the pathologists, that they didn't feel they had any authority to change the way the lab was functioning.
COFFEY, Q.C.:
Q. Do you recall at that time, well do you remember what Dr. Ejeckam did--you speak about or did you learn while you were in St. John's at the time, either from him or anyone else that back in 2003 that Dr. Ejeckam had, for a period of time, stopped or caused to be stopped the utilization of eight stains, two of which were ER/PR, were you made aware of

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that while you were -
DR. BANERJEE:
A. Yes, he did discuss it with me and I think shared a memorandum here, circulated at the time as to why he wanted to stop the service and he introduced some changes in the lab that improved the staining process.
COFFEY, Q.C.:
Q. Do you recall if he told you what those changes were?
DR. BANERJEE:
A. I think working with the technologists to optimize each of the stains. At the time they were using, I believe they were using the DAKO system.
COFFEY, Q.C.:
Q. DAKO. Anything you recall about your meeting with Dr. Ejeckam at the time?
DR. BANERJEE:
A. Well we spent a fair bit of time talking about his role and he was perhaps a little concerned that I would sort of finger him as the culprit and I assured him that that wasn't what I was there for. I was trying to figure out whether from his observations that my conclusions were

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actually on the right track and he did come up with the same observations that I had.
COFFEY, Q.C.:
Q. And was it your understanding in speaking to him at that time that he had his own views or his own vision for perhaps what he wanted to achieve here -
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. - but was not able to.
DR. BANERJEE:
A. That is correct.
COFFEY, Q.C.:
Q. That would summarize it, I take it.
DR. BANERJEE:
A. Uh-hm.
COFFEY, Q.C.:
Q. What then happened, Doctor? You had your round of interviews, did you meet with Mr. Terry Gulliver or Barry Dyer?
DR. BANERJEE:
A. Yes, I did.
COFFEY, Q.C.:
Q. At the General site?

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DR. BANERJEE:
A. Correct.
COFFEY, Q.C.:
Q. What do you recall about that?
DR. BANERJEE:
A. I recall both gentleman as very eager to do a good job and they're very much in touch with the industry side of lab operations. The issue of accountability and governance, I did not discuss with them. They felt that they were perhaps not as appreciated by the pathologists as they would like, in terms of bringing innovation to the lab and that acquired some new equipment which was sitting idle because the pathologists weren't interested, so to me, that suggested that there wasn't a team approach to building the department and there was some separation of medical and technical staff in terms of planning quality assurance and so on.
COFFEY, Q.C.:
Q. And we understand as well, we're heard or understand that you met with a Dr. Dan Fontaine?
DR. BANERJEE:

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A. Yes.
COFFEY, Q.C.:
Q. And had you known Dr. Fontaine before?
DR. BANERJEE:
A. I had known about it but I hadn't personally met him until that visit.
COFFEY, Q.C.:
Q. And in what context then here in St. John's did you meet him at the time?
DR. BANERJEE:
A. Just one of the few people that I interviewed and I think he was my host for dinner that first night.
COFFEY, Q.C.:
Q. We understand as well, I gather that you met with Dr. Denic, did you meet Dr. Denic at the time?
DR. BANERJEE:
A. Yes, I did.
COFFEY, Q.C.:
Q. And again, what was the purpose of your meeting with Dr. Denic?
DR. BANERJEE:
A. Just to get his impression about what the solution should be. We spent probably a

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significant amount of time talking about a problem with retaining pathologists on staff and a high turn over which Dr. Cook had also discussed with me and it was pretty well known across the country that pathologists in this province were not paid at the same level as some of the other provinces and they kept losing staff to other provinces for that reason. So I felt that that was perhaps one of the factors that led to perhaps a lack of continuity on the medical side of running the labs. When you don't have that stability, it's hard to develop a team.
COFFEY, Q.C.:
Q. Doctor, I understand that this visit to St. Clare's and the General would have occurred your first day, your first full day in St. John's.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Anything else other than going to dinner that evening, anything else that you were involved in that day?
DR. BANERJEE:

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A. I can't think of anything right now.
COFFEY, Q.C.:
Q. How about the next day?
DR. BANERJEE:
A. Yeah, I think the next day was more, sort of more discussions about my observations with Dr. Cook and then I remember the exit interview, there were a number of people in the room, not just pathologists and I basically summarized my findings and then headed to the airport after that, sent in my written report within a few weeks.
COFFEY, Q.C.:
Q. Doctor, we do have some notes that refer to this exit interview, if I could ask, please, Exhibit P-2148? Now I appreciate these are not your notes, Doctor, but they are of an exit interview of September 16th, 2005, it's described as an external review there and your name is there, description of who you are or the position you had at the time. And there's a note here in paragraph one, "providing a comparable service with the rest of Canada. In some areas we are above average. There is lots of potential in the division of

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anatomical pathology with both pathologists and managers wanting to"--and it's very difficult for me to read, but I gather the point was -
MR. BROWNE:
Q. "Achieve the same end point".
COFFEY, Q.C.:
Q. "Achieve the same end point which is a good quality reliable service." Thank you. Doctor, do you recall telling the people in the exit interview that from your perspective they were providing a comparable service to elsewhere in the country?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. And in what context was that said?
DR. BANERJEE:
A. In the context of a full spectrum of hospital--slides from various hospitals I've seen over the years, in terms of their peer groups, if you like.
COFFEY, Q.C.:
Q. And the peer group in this context would be which group?

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DR. BANERJEE:
A. Combination of teaching and non-teaching hospitals.
COFFEY, Q.C.:
Q. Now that comment, was that made in relation to the ER/PR or -
DR. BANERJEE:
A. Immunohistochemistry in general.
COFFEY, Q.C.:
Q. Immunohistochemistry, generally, okay.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. The absence of internal control tissue or the presence of it and it's non-staining in the cases that you had look at the day before, had you ever encountered that before?
DR. BANERJEE:
A. Oh yes.
COFFEY, Q.C.:
Q. In other places.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. And I wanted to ask you about that, when you

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arrived in St. John's and looked at the slides, particularly those first 20 or so pairs of slides, were you surprised by what you saw?
DR. BANERJEE:
A. No, not really.
COFFEY, Q.C.:
Q. And why is that?
DR. BANERJEE:
A. We've seen it before, many times.
COFFEY, Q.C.:
Q. That people would have reported slides that either didn't have internal--ER slides that didn't have internal controls or had them and didn't stain appropriately.
DR. BANERJEE:
A. Right, yes.
COFFEY, Q.C.:
Q. You'd seen that in the past.
DR. BANERJEE:
A. Uh-hm.
COFFEY, Q.C.:
Q. Before you arrived in St. John's, had you anticipated seeing that or -
DR. BANERJEE:

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A. No, actually I was thinking more about non-specific background staining as the culprit, perhaps difficulty in interpretation -
COFFEY, Q.C.:
Q. In relation to the Ventana.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Perhaps overcalling, as it were.
DR. BANERJEE:
A. Yes, that's right.
COFFEY, Q.C.:
Q. But when you first saw the 20 pairs of slides and the attendant H&E stained slides -
DR. BANERJEE:
A. I changed my mind about that.
COFFEY, Q.C.:
Q. But what you were seeing didn't surprise you?
DR. BANERJEE:
A. No.
COFFEY, Q.C.:
Q. Doctor, here there's a note here, No. 2, there are issues, deals with the problem of--refers to a problem of adequate fixation of tissue, effect the reliability of immunoperoxidase

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testing, and need for pathology assistants and I'll be taking you through the report itself, but paragraph 3 then, you refer to the need for highly specialized immunoperoxidase concerned technologists, dedicated to that, you talked about the technologist issue being dedicated. One thing you refer to here is the issue of proper documentation and the antigen retrieval method, which is paragraph four. So what, if anything, had you learned about that?
DR. BANERJEE:
A. Well I think they were clearly using Ventana's protocol for antigen retrieval, but the machine can be set to several combinations of temperature and the duration of the heat treatment and I wasn't clear whether they had gone through that process to optimize it because there was no documentation of how they actually decided which of the various protocols available in the Ventana system was actually chosen. So I wanted to make sure they went through a process of optimization and then documenting that, so that the technologist would use that in the future runs.

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COFFEY, Q.C.:
Q. And then in paragraph 5, there's a reference to the need for subspecialization and that would be amongst the pathologists?
DR. BANERJEE:
A. Amongst the pathologists.
COFFEY, Q.C.:
Q. And reference to with an adequate compensation package and I'll be talking to you a bit more about that, so the issues discussed in the main during the exit interview, at least according to the notes here, were the fixation aspect of the matter, the need for dedicated technologists, attention being paid to proper documentation and optimization of the antigen retrieval methodology and the need for subspecialization amongst pathologists. Do you recall during that exit interview if the idea of or the concern about internal controls came up?
DR. BANERJEE:
A. I don't think there was much discussion about that.
COFFEY, Q.C.:
Q. How about Dr. Cook? You had told Dr. Cook

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about this the day before.
DR. BANERJEE:
A. Right, so I thought that was covered under the discussion about fixation.
COFFEY, Q.C.:
Q. Doctor, what I want to ask you is when you raised the matter of internal controls with Dr. Cook, do you recall whether or not he, at the time appeared already aware of that?
DR. BANERJEE:
A. He seemed to be aware of that, but the initial phone call in the conversation, the initial phone call, I was surprised that they were allowing those reports to go out without the internal controls being positive.
COFFEY, Q.C.:
Q. Had he raised it during the phone call initially or had you -
DR. BANERJEE:
A. No, I had questioned him on that point because I wanted to make sure that the interpretation was not the issue, didn't seem to be.
COFFEY, Q.C.:
Q. And when he said that no, he knew or by then knew that some cases were being reported

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without the internal controls that's being stained positive and he told you that, you thought well maybe interpretation may be an issue here too?
DR. BANERJEE:
A. Right, he raised the point about cases where the internal control was negative, but the tumour was positive, which as I said, that's okay, so when both are negative, it's hard to make a conclusion.
COFFEY, Q.C.:
Q. That came up during that August 2nd phone call?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. And it would have arisen then again, I take it, on September 15th, the first day you were in St. John's looking through the microscope together.
DR. BANERJEE:
A. Right, discussed that, every example we looked at.
COFFEY, Q.C.:
Q. Exhibit P-0046 please? Now, Doctor, this is a

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copy, well the first page is your covering letter of October 17th, 2005 to Dr. Cook and it's Re: "External Quality Review of Immunoperoxidase Service". Signed by yourself and then the second page of the exhibit is, of course, the cover page of the report. Before I delve into this, we understand at the time you were in St. John's, Dr. Bob Williams, Robert Williams was the VP Medical?
DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. Do you recall meeting with Dr. Williams?
DR. BANERJEE:
A. Yes, I did actually, I think probably twice, I can't remember the exact number of meetings I had with him, but definitely the exit interview was in his administrative office area.
COFFEY, Q.C.:
Q. So he was present for that?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. You note here, Doctor, "Please find enclosed

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my report" and you offer to clarify any issues that may arise, and then you stated, "In addition, please convey to Dr. Williams that beyond the specifics of my report, there should be recognition of the following issues that have bearing on the sustainability of the quality laboratory program. No. 1, pathologist compensation should be competitive with those of other provinces; otherwise your department will face ongoing staff turn over as pathologists move to more rewarding positions elsewhere. Unless this revolving door syndrome is dealt with, it will only lead to the deterioration of the quality of staff as you will continue to lose your best people. No. 2, "For high quality cancer program in the province, your department must invest in subspecialization, continuing education and central pathology review for the entire province in order to provide the highest quality of service in cancer diagnosis, so that your oncologists can manage their patients optimally. All cancer patients deserve the same standard of care, regardless of where they live. Accurate pathology

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diagnosis, grading and staging are essential for clinical decision making and these activities cannot be compromised. With the two recommendations implemented, you will be able to attract and retain the best pathologists." Now, Doctor, I take it the two recommendations in this context are those two above?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. Because there are a number in your report itself. Doctor, the reference to "central pathology review for the entire province" what are you referring to there?

DR. BANERJEE:

A. What I'm referring to is, well if you look at how patients with cancer are diagnosed, the initial diagnostic procedure could be a biopsy or a resection by a surgeon and that could happen anywhere, in any hospital with surgical facilities. And usually the report is then generated by the local pathologists at that hospital. It's my personal belief that to be a good cancer pathologist, you'd need to see a

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significant number of cases every year to keep your skills up and in some of the smaller community hospitals, they don't see enough cases to achieve that level of skill. I also believe that cancer pathology should be practised by people who have received additional education and training beyond the Royal College certification, particularly in high volume cancer centres either in Canada or the United States. So I personally recruit people with at least one or two years of post Royal College certification experience in a specific area of pathology, preferentially in a cancer centre. The reason for that is cancer is a complex disease, there are many different kinds. The common cancers are easy to diagnose because people are familiar with them, but the uncommon cancers presenting as if they are a common cancer is where the problem lies, so there may be under-diagnosis, under-grading, over-grading, all of that sort of thing. I know from my own experience in Toronto and now in Vancouver that in general there is--when you do a central review, that's done before the patient actually begins

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treatment at one of the cancer centres, that you tend to uncover some details that the oncologist actually needs to make a decision about the best management of that patient. We have quantified that and when I was at the Princess Margaret Hospital, I did a survey of how many changes were made as a result of that central review that would affect patient management. It was not an insignificant number, on average of 26 percent, so that's a pretty big number. British Columbia, it's in the order of 15 percent. We also see cases from other provinces and patients have been referred to, BC Cancer Agency and the discrepancy rates could be even higher than the 15 percent we see in BC. If you then convert that into something other than statistics, and you say all right, how many breast cancer patients are diagnosed every year in the province? In BC we have about 2700 cases a year, multiply that with 15 percent discrepancy rates, so you have several hundred patients who are maybe undercalled or overcalled that would receive the wrong treatment.

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COFFEY, Q.C.:
Q. In the absence of this central -
DR. BANERJEE:
A. In the absence of the central review. And this is not surprising, this is reported widely in the literature and every jurisdiction these kinds of problems exist. The American Cancer Centre, by rule, will always review the outside pathology before a patient is treated, unless it's an emergency situation. In Canada there is no such rule, except--and some cancer centres lack, BC Cancer Agency and the Princess Margaret Hospital et cetera, and the reason why this is not widely practised, a pathologist don't like to be second guessed or have their work reviewed by someone else, a natural sort of reaction.
COFFEY, Q.C.:
Q. I take it that's not peculiar you expect of pathologists.
DR. BANERJEE:
A. Sorry?
COFFEY, Q.C.:
Q. That's not peculiar or unique to pathologists.

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DR. BANERJEE:
A. No, many, any professional would be uncomfortable with that situation; however, if you translate the statistics into the individual patient, then it becomes very clear that ethically this is what we need to do because I've been accused of wasting taxpayer's dollars by doing central reviews, I say, it's okay, I'm looking at what the patient needs and that's what I'm basing my policy on.
COFFEY, Q.C.:
Q. And so at the time you wrote this in October of 2005, from your perspective and again, you're coming in from the outside to Eastern Health and in particular, St. Clare's and the General Hospital sites, bearing in mind what you were then given to understand about how cancer patients were treated in the province, all the IHC staining being done at the General Hospital, the original diagnosis often being made elsewhere, that even in the context of this province, to set up a central pathology review for the entire province, was appropriate you -

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DR. BANERJEE:
A. Yes, I believe every province should have some kind of central review policy.
COFFEY, Q.C.:
Q. And that would not be limited to ER/PR or breast cancer.
DR. BANERJEE:
A. No.
COFFEY, Q.C.:
Q. It would be across the board.
DR. BANERJEE:
A. Across the board. We tend not to review cases where the management wouldn't change, if somebody presents with metastatic disease and there are very few options for the patient, then we wouldn't do the review.
COFFEY, Q.C.:
Q. But for, certainly primary cancers, initial diagnosis of cancer -
DR. BANERJEE:
A. Yes, and the policy is developed with discussion with oncologists about we ensure that we're not being frivolous about the central review and it's done for the right reasons.

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COFFEY, Q.C.:
Q. Now this central pathology review, I take it that, the idea of that, that's an across the board thing, that's not a particular patient or is it every 10th patient or every patient -
DR. BANERJEE:
A. No, it's every patient. Historically, I mean, even at the Princess Margaret Hospital when I first arrived there, it was--the second opinion was triggered by an oncologist looking at the original report and saying, you know, something doesn't sound right or doesn't fit, I had better get this reviewed. And then explain to them that if you only go by whether the report looks right or wrong, I could create a report that looks beautifully correct, but could be completely wrong because the data in the report may be totally wrong. And how do you know that? So that led to, you know, I went to the Medical Advisory Committee and persuaded them to change that policy, so that every patient in certain categories would be reviewed centrally.
COFFEY, Q.C.:
Q. Just, I want to clarify, Ms. Chaytor asked me

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to clarify this, is this all patients, all cancer patients across the board or is it cancer patients just in particular categories?

DR. BANERJEE:

A. It would be certain cancer types where treatment options are multiple and hinge on particular characteristics of the individual patient pathology, yeah.

COFFEY, Q.C.:

Q. Does breast cancer fall into that category?

DR. BANERJEE:

A. It does.

COFFEY, Q.C.:

Q. If we could then look at the body of the report itself, I will tell you this, the Commissioner has seen this report a number of times and various parts of it, in the incident problem case, you note here in the second paragraph, "It should be noted that invasive lobular carcinomas are frequently ER positive 92 percent." And you have a footnote there for that cited, "Thus the initial negative result should have been questioned."

DR. BANERJEE:

A. Right.

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COFFEY, Q.C.:

Q. And we look, the particular article in question you've sited in the footnote is the Journal of Clinical Oncology 2005 and that, I take it, is what you cited for the 92 percent. Doctor, had the patient originally, of course, been tested in 2002, was it generally known in 2002 and before 2002 that invasive lobular carcinomas should be ER positive?

DR. BANERJEE:

A. Yes, it was known. I used that reference because that actually quantitated the positivity rate.

COFFEY, Q.C.:

Q. I'm sorry?

DR. BANERJEE:

A. It had actually provided a quantitation of the positivity rate.

COFFEY, Q.C.:

Q. A quantitation, the figure of 92 percent.

DR. BANERJEE:

A. Yeah, in general practice it's almost virtually 100 percent.

COFFEY, Q.C.:

Q. And you say, "Thus the initial negative

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results should have been questioned." Now, from your perspective, questioned by whom?

DR. BANERJEE:

A. By the pathologist and the oncologist, both. Both groups should have been aware.

COFFEY, Q.C.:

Q. You go on to note then, Doctor, you talk about and I take it the four other patients previously tested were also retested and that, in fact is referred to in the terms of reference, I believe, and in any case you would have become aware of that while you were here in St. John's dealing with Dr. Cook and company. The conversation rate would be based upon figures given to you by Dr. Cook.

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. Then you, under review of cases, you reviewed a number of cases from the retrospective testings with Dr. Donald Cook and that would be the ER cases?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

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Q. That retrospective group and that would be, as you quantified it here, approximately 20 such cases?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. And you conclude your comment here by saying, "It is apparent that too much reliance is being placed on external positive controls with no attention paid to internal controls". I take it that your conclusion, "No attention being paid to internal controls", is based upon what, what kind of reasoning were you using there?

DR. BANERJEE:

A. Oh, that cases were being called positive -- negative, rather, even though the internal controls were either not there, there's no normal epithelium to look at, or if it was present, it was negative as well. So in our practice, we would not report those, we would call them inconclusive.

COFFEY, Q.C.:

Q. And then, Doctor, you refer to a literature review of the DAKO versus Ventana

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immunostainer performance.
DR. BANERJEE:
A. Right.
COFFEY, Q.C.:
Q. And you note that that particular study published in '98 may not be relevant, and in any case, I take it, Doctor, as we'll see later in your report, the problem in St. John's, from your perspective, wasn't per se the DAKO or the Ventana systems?
DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. Perhaps through utilization?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Doctor, here there's a note, you begin at the bottom of the page here by saying, "Fixation time in formalin does not affect the ER results as long as two millimetre thick slices of tissue are placed in fixative within fifteen minutes of surgical excision, and adequate heat induced antigen retrieval is performed". Would that mean that any minimum

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amount of time, fixation time?
DR. BANERJEE:
A. No, I should have provided more detail there. There is a minimum time of six to eight hours that's recommended in the literature. In general, I think, the smaller the biopsy, the less time required. That's just a general guideline. The larger samples like the lumpectomies and mastectomies require more time than that just because of the volume of tissue involved.
COFFEY, Q.C.:
Q. Doctor, you do go on then at some length and discuss this matter fixation. On the top of the second page, you note, "Since the Ventana System did detect ER protein in previously negative cases, one must conclude that even if there was partial loss of ER protein due to poor fixation, the failure of the DAKO System was largely due to inadequate antigen retrieval or inadequate antibody and/or detection system optimization, or a combination of these factors", which I take it is a written form of what you told us earlier --

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DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. You told Dr. Cook. The second last sentence here in this paragraph, Doctor, you write, "It remains possible that even with complete optimization of antigen retrieval and immunostaining protocols, if fixation is not optimized, there will be an irreducible number of false negative cases".
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. So I take it -- do I understand that to mean then in my layman's terms that no matter how careful you are with your antigen retrieval and immunostaining procedures, if the fixation is done poorly enough, then no matter what we do in the lab, it will not be able to correct the problem?
DR. BANERJEE:
A. That's correct, yes.
COFFEY, Q.C.:
Q. Doctor, the choice of antibodies, could you explain -- tell us, please, just expand upon

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this a bit in terms of what antibody was being used here in St. John's, and from your perspective, the advantages and disadvantages of switching?
DR. BANERJEE:
A. If I recall correctly, they were using the 1D antibody, which is widely used. The other widely used one is 6F11, and in some labs 6F performs better than ID5; in other labs they're about equivalent. They're both capable of demonstrating the protein in formalin fixed tissue provided to the antigen retrieval. Now in the last few years, additional anti -- monoclonal antibodies have been developed which are derived from rabbits as opposed to mice. Now rabbit immune systems are a little different from the mouse in that they seem to have more stronger reaction to whatever the immunizing antigen is. So rabbits historically have been used for the preparation of antibodies, polyclonal antibodies, not monoclonals, and rabbit antibodies tend to have higher affinity to bind more tightly to the antigen that they're directed against. So now that the technology

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to develop monoclonal antibodies from rabbits has been introduced, some of the newer antibodies are coming out with much higher affinity than the mouse antibodies, and in various labs that have compared the mouse antibodies with the rabbit antibodies, they find that the rabbit antibodies are of such affinity that even if you don't do antigen retrieval, they will yield a positive result, which is interpretable quite easily. So one could debate whether or not they need to switch, but in general in our hands the SP1 antibody seems be more reproducible, less variation from case to case, but others have found that if you compare the 1D5 and SP1, clearly SP1 is better, but if you compare with 6F11 and SP1, in one report there is no difference; in another report the SP1 is better. So the differences are fairly minor, but the intensity is a little better with SP1, it's easier to interpret, and cases that have been negative by 1D5 have turned out to be positive with the SP1, even in our lab. So there is some benefit to switching, but again if you haven't dealt with the fixation issue,

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it's probably not the area to invest in.

COFFEY, Q.C.:

Q. Yes. In fact, we do come across if we jump ahead to recommendation 3, in this context you're only comment was consideration should be given to switching to SP1, you weren't telling them to switch to it, you were just pointing out here, I take it, the pros and cons as known at the time to you, and ultimately in your recommendation leaving it to them?

DR. BANERJEE:

A. Uh-hm, yes.

COFFEY, Q.C.:

Q. Doctor, you've noted here, inter-laboratory variability, "A number of publications indicate poor concordance between laboratories for ER assays, especially for the weakly positive cases", and this is attributed to variation in antigen retrieval protocols", citing footnote seven and eight, and when we look, we'll see that footnote seven is an American Journal of Clinical Pathology article of 2002, and then an article in 2001, or publication. Doctor, in particular, could

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you, if you can, please, elaborate a little on the reference to "especially for the weakly positive cases".

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. You alluded to this earlier too.

DR. BANERJEE:

A. Right. So if you look at the publication that compared the biochemical test with the immunohistochemistry assays, the discordance between the two methods were particularly prominent in the cases with low estrogen receptor content from the biochemical assay. So it's clear that even immunohistochemistry might miss positive cases in that range of concentration, and those particular publications, I actually don't have copies with me right now, but there's a similar publication which I mentioned earlier, which is from the UK quality assurance program, the Rhodes and Jasani paper. That sort of came to similar conclusions and they thought the antigen retrieval was the main culprit for the inter-lab variability, but as I mentioned

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earlier, they also excluded cases that had fixation problems, so -- they didn't quantify that.

COFFEY, Q.C.:

Q. And weakly positive cases are problematic, in particular, why? I take it there's so little --

DR. BANERJEE:

A. Yes, there's not enough protein. So if your method is not sensitive enough, you'll have a negative result. However, from a clinical perspective, those patients are eligible for Tamoxifen therapy and may respond. So it could lead to denial of therapy to women with low positive (unintelligible).

COFFEY, Q.C.:

Q. Doctor, you go on here then with your conclusions about the reasons for test failure. You posed the question, "Is the DAKO System faulty", and I take it that, in effect, in the course of coming to St. John's, that was one of the questions posed to you?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

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Q. And you say this us unlikely, and then you give the reason for test failure was most likely due to, and you - lack of test optimization, including antigen retrieval method and antibody detection system titration as positive controls showed a weak staining in general, and internal controls failed in all the false negative cases, and we've already discussed most of this. One thing I do want to ask you about is "positive controls showed weak staining, in general".

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. What are you referring to there?

DR. BANERJEE:

A. So those are the external positive controls that they were using for each run, and when I looked at them, they were of lower intensity than I would be used to seeing in our lab.

COFFEY, Q.C.:

Q. And what, if anything -- bearing in mind that these positive controls were generally staining weakly, from your perspective as a pathologist, what if anything should be the

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thought process when faced with that kind of a positive control that's staining weakly? What should that alert you to, if anything?

DR. BANERJEE:

A. So my concern would be that you've chosen a positive control with detectable staining, but it was of low intensity and that was probably your best case because that's how labs choose their positive control, and if that's the case, then there's something wrong with your methods, not sensitive enough, because I've seen a lot more intense staining in our lab.

COFFEY, Q.C.:

Q. So I understand this correctly, if that positive control slide is staining --

DR. BANERJEE:

A. Uh-hm.

COFFEY, Q.C.:

Q. But if that's the most intense -- you're saying to the Commissioner, what your understanding as an outside would be, if that's your most intensely stained positive ER slide that you have, then that can't be correct?

DR. BANERJEE:

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A. That's right.

COFFEY, Q.C.:

Q. Because there would be patients who would be better than that, more positive staining, more intense positive staining?

DR. BANERJEE:

A. Correct.

COFFEY, Q.C.:

Q. And, therefore, that should have alerted the reader of the slide to there's something wrong with the process here generally for ER?

DR. BANERJEE:

A. That's right, but --

COFFEY, Q.C.:

Q. And it wouldn't be particular to that run then, I take it, it would be in general?

DR. BANERJEE:

A. In General, yes. The positive control -- the external positive controls is usually one block from one case that they keep using over and over again. So it's the same tissue, newer sections being cut from the block and then used in the stain, but just to go back to that discussion, it would also -- I mean, looking back at why that would be the case, it

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would also suggest that when they were setting up the staining protocols, that they hadn't actually received or asked for examples from other labs. So ask for positive control from a different lab, for instance, with the original lab slides, immunohistochemistry preparations to compare with, because if you have no comparator, how do you set your threshold. If you're using your own external positive controls and you say, well, this is as intense as it's getting, then you think that's probably okay because you haven't seen other examples where the intensity is much greater than that.

COFFEY, Q.C.:

Q. Doctor, if--I'll ask you this. If an external positive control that you are seeing on a routine basis and it's staining the way you would expect, it's strongly--you're looking for a strong positive. You're expecting that and you're seeing that, one day to the next, and then on a particular day, on a Thursday, you happen to see external positive control had stained, but it's not nearly as strong as it was in the weeks before that, what, if

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anything, would that cause you to inquire into?

DR. BANERJEE:

A. Yes, so that would trigger us asking the technologist, you know, "what has changed? Have you got a new batch of antibody that needs to be reoptimized, you know, retitrated?" That kind of discussion needs to occur. Sometimes a block--see, as you cut into the block and you put the block back in storage, the technologist usually puts more wax on it to cover the cut surface, because once you expose the cut surface to oxygen, all proteins will deteriorate over time. So that's why we don't precut sections for immunohistochemistry. We try to cut fresh sections from the block. So sometimes a block itself will deteriorate or you're cutting deeper into the tumour and there's tumour heterogeneity which will also account for loss of intensity. Different parts of the tumour may express different levels of protein.

COFFEY, Q.C.:

Q. So I take it the point being that, you know, faced with that situation, it's time to make

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inquiries of the technologist?

DR. BANERJEE:

A. Yes, and that might lead to choosing a different block. So just to finish up the discussion about the external controls. It is not appropriate to choose the most intense case as your positive control, because your clinical cases may have lower protein concentration. So it's better to have two or three different samples. One is a low expresser and medium and high expressing tumour. And really concentrate on the lowest protein concentration case and make sure that's always positive, because that's where your threshold is.

COFFEY, Q.C.:

Q. And Doctor, in terms of then external controls, you know, such external controls, I take it in evaluating whether or not external control is staining appropriately, one would--the individual in question would have to have some expectation and experience with what to expect?

DR. BANERJEE:

A. That's correct.

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COFFEY, Q.C.:

Q. In order to make any kind of valid judgment about it perhaps?

DR. BANERJEE:

A. Yes. You almost have to have a mental image of what it looked like the last time or go back and get those slides and say, you know, has this really changed, because the control slides are kept on file, so you can always go back to them.

COFFEY, Q.C.:

Q. And you did see external control slides when you were in St. John's?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Paragraph two, Doctor, "is the Ventana system too sensitive?" and you've indicated "there's no evidence it creates false positive results." You did note the system here in St. John's, I take it, still requires optimization to avoid non-specific cytoplasmic staining?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

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Q. Are you talking about Ventana in general or just St. John's or both here, the system still requires--bearing in mind that you had seen non-specific cytoplasmic staining?

DR. BANERJEE:

A. Right. It was definitely the Ventana system being more sensitive than the protocol being used on the DAKO system, but as I said, you know, it's a matter of switching protocols on the Ventana system to reduce that non-specific staining.

COFFEY, Q.C.:

Q. Doctor, paragraph three, you pose the question, "is there a problem with tissue fixation?" You note "there appears to be inadequate attention paid by the grossing pathologist to the thickness of tissue slides, quality and adequacy of fixation and there's no standardized fixation protocol that everyone adheres to." Now what led you to believe or to reach those conclusions?

DR. BANERJEE:

A. I think the fixation problems were evident in the morphology of the slides I was looking at and it was clear that there wasn't actually

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written down policy about standard fixation protocols and that since all of the pathologists were taking turns grossing, that would lead to variability in the quality of fixation. I think part of the issue is that when the pathologist is grossing tissue, they have other things waiting for them to do like a stack of slides on the desk back at the office, etcetera. So there's a tendency to move quickly and do your work quickly and that could lead to variability as well.

COFFEY, Q.C.:

Q. So did you actually, yourself, witness at the time pathologists, you know, cutting tissue too thickly or -

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. - this was something, an observation based upon just the sheer number of pathologists and residents who are rotating through that?

DR. BANERJEE:

A. That's correct. I didn't actually observe them grossing.

COFFEY, Q.C.:

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Q. But in knowing the numbers that went through there and based upon your experience, you inferred that there would be differences in the thickness and the approach?

DR. BANERJEE:

A. Yeah, it's nothing unusual. You see that everywhere.

COFFEY, Q.C.:

Q. Doctor, then paragraph four deals with the issue of internal controls. Is there anything further, just looking at that, that you'd want to elaborate upon in paragraph four?

DR. BANERJEE:

A. Not really, I think we've gone over that.

COFFEY, Q.C.:

Q. Yes. You've already noted that from your perspective, because of the condition of the internal controls, in terms of at least the slides you looked at, that in your view, where the internal controls hadn't stained and they were being reported as negatives -

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. - the tumour, then they should not have been

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released in that context?

DR. BANERJEE:

A. That is correct

COFFEY, Q.C.:

Q. Or at least looking further into the matter?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. The idea, Doctor, here, the notion here that you pose here, "it should have been noted in the reports as uninterpretable due to the failure or absence of internal controls." I take it then you're not against the idea of a pathologist saying, in writing, "look, for this and this reason, I'm not prepared to make a call"?

DR. BANERJEE:

A. Right. For instance, if there were no other blocks to go to, for instance, let's say it's a small core biopsy and there was a single block and that wasn't properly fixed, you're basically stuck with that, and you can't interpret that case.

COFFEY, Q.C.:

Q. And then you just can't, then that's what

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you'd tell the oncologist?

DR. BANERJEE:

A. So in that situation, the oncologist, you know, would say that the core biopsy was not sufficient for us to assess the estrogen receptor content and they would wait for the lumpectomy or mastectomy specimen and repeat the test on that.

COFFEY, Q.C.:

Q. Doctor, other system flaws--well, first of all, I should ask you, is there anything further, Doctor? You're satisfied that that covers the issue of internal controls?

DR. BANERJEE:

A. I think I'm satisfied, yes.

COFFEY, Q.C.:

Q. Then "other system flaws observed" and you refer to the lack of dedicated immunohistochemistry technologists and the rotations--you know, the rotation system is being used and the potential consequences of that for their inability to gain in-depth knowledge or expertise. Now "lack of an officially designated pathologist as director of immunohistochemistry service.

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Technologists thus get conflicting feedback from a large number of pathologists" and you go on to note "there is no accountability for the quality of the service." I want to ask you about two aspects of this, Doctor. What led you to believe that the technologists were getting conflicting feedback?

DR. BANERJEE:

A. I think during my conversation with them, they would say Doctor so-and-so would say "I want it done this way," and somebody else would say, "no, I don't agree with that. I want it this way," and so on, and they would be confused because nobody was actually coming up with a consensus direction for them.

COFFEY, Q.C.:

Q. And you go on and you conclude by saying, "there is no accountability for the quality of the service" and I take it you were linking that with the lack of an officially designated pathologist as director of immunochemistry service?

DR. BANERJEE:

A. Right, so it seemed that the pathologists felt it was not their responsibility to make that

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lab better because it was run by non-medical personnel, management, and the technologists didn't really have a sufficient knowledge base to troubleshoot by themselves, so it naturally led to suboptimal results.

COFFEY, Q.C.:

Q. Paragraph four here, you refer to "lack of subspecialization amongst pathologists." I take it that you saw subspecialization, as you indicated, perhaps "led at the time to a lack of in-depth knowledge about IHC technical interpretation details and pitfalls." Your conclusion about that lack of in-depth knowledge, was that based upon, for example, the internal controls issue in the ER slides?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. It was apparent to you that, in your world, if you knew the difference, you wouldn't report the case?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. And that is if you, a pathologist, knew the

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difference, you wouldn't report it, and as these were being reported, you were drawing the inference that they perhaps didn't know-- or you're assuming they didn't know about the internal controls?

DR. BANERJEE:

A. That's correct. I also remember I saw some other preparations which were not ER/PR related and could see that if people were accepting that quality and reporting on them, then there was something missing in their own knowledge base.

COFFEY, Q.C.:

Q. Paragraph five, you talk about the "disconnect between laboratory program director, division manager, clinical site chief and laboratory director in decision making" and you go on then to talk about "the organizational charts indicate a complex separation of reporting structures" and this is all written out there, Doctor. I'm going to ask you to generally describe then, for the Commissioner, your understanding of how it was functioning here and your concerns about the way it was functioning.

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DR. BANERJEE:

A. Well, the way it was set up was that the clinical chief, i.e. the lab director, Dr. Cook, had no jurisdiction or authority over the technical side of the lab. That meant budgets, staff, you know, how they were hired, who was hired, who was--whether they were being trained, etcetera. He had no authority over that. So in looking at the org chart that existed at the time, it would seem that there was a dual management structure. There's the medical side and the technical side, each reporting separately to the Vice President of Medical Services, Dr. Williams. So in essence, Dr. Williams was the lab director.

COFFEY, Q.C.:

Q. Yes, that's--in essence, that's -

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. - the one person who's responsible for the entire lab was Dr. Williams?

DR. BANERJEE:

A. For everything, that's correct.

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COFFEY, Q.C.:
Q. Under that organizational arrangement?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. And I take it it was your understanding that Dr. Williams, in fact, had really perhaps no day-to-day contact with the lab itself?
DR. BANERJEE:
A. Not on a day-to-day basis, nor would he have, in his own training, and I can't remember what his specialty is, but certainly not a lab physician.
COFFEY, Q.C.:
Q. Doctor, you had noted above, in paragraph two, you had concluded there by saying "there is no accountability for the quality of the service" and did that have anything as well--it's stated in the context of the lack of a Director of Immunohistochemistry there.
DR. BANERJEE:
A. Right.
COFFEY, Q.C.:
Q. But did that also, from your perspective, have anything to do with the lab structure itself,

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in terms of who ultimately was accountable for this?
DR. BANERJEE:
A. I mean, looking at the structure, I'd say there was no accountability for quality because there are two aspects to quality. One is the technical quality assurance piece, quality controls, etcetera. But there's the professional interpretation side, which is also part of the quality, and if the two sides are so separate they don't talk to each other, then there is no real accountability. They're only looking at parts of the process, not the entire process.
COFFEY, Q.C.:
Q. And based upon the org chart, at least that you had seen, and your understanding at the time, that connect only finally occurred in the person of Dr. Williams, the VP Medical?
DR. BANERJEE:
A. Yes, that's correct.
COFFEY, Q.C.:
Q. You do conclude paragraph five by saying "superior outcomes could be achieved by ensuring better linkages between technical,

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managerial and medical leadership"?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Doctor, from your perspective, you certainly suggested a director of immunohistochemistry?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Paragraph two. How about having one particular individual in charge of the lab who is actually day-to-day involved with the lab?
DR. BANERJEE:
A. I certainly believe that is necessary. That's my opinion. There are lots of differences of opinion on that point across the country, including my own province. But I do believe that in the eyes of the courts, the law, the medical director is responsible for the quality of the lab.
COFFEY, Q.C.:
Q. I take it at least in the province where you are?
DR. BANERJEE:
A. Definitely in British Columbia, and that means

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total authority over all aspects of lab operations.
COFFEY, Q.C.:
Q. Doctor, you, in paragraph six, suggest that there should be "attendance by medical and technical staff at various conferences with a focus on new technology should be encouraged" and you "encourage consensus driven innovation should be the goal" or you say that that should be the goal. You then refer to pathology assistants, "dedicated pathology assistants to ensure gross room consistency in tissue handling, trimming and fixation." I take it that that has the advantage of cutting down on the sheer number of people involved?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. In St. John's, it could be 15 to 20, for example, pathologists, I gather, involved in breast grossing.
DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. And you would limit it to whatever the number

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required?
DR. BANERJEE:
A. Right.
MR. COFFEY:
Q. What are the advantages then, in a practical way, of having pathology assistants, from your perspective?
DR. BANERJEE:
A. Well, there are two advantages. One is that you can train them to follow protocols and they tend to follow that religiously because they don't believe that they have enough medical knowledge to decide when the protocol needs to be modified, so they tend to be consistent because of that reason alone. Secondly, by having pathologist assistants doing the grossing, it frees up the pathologists to do their other work, which is the microscopy, attending patient care rounds, etcetera, and that feeling of being rushed all the time goes away and cutting corners because of lack of time then is dealt with.
MR. COFFEY:
Q. In particular, to use the phrase, you just used "cutting corner" as a word, like feeling

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time pressure -
DR. BANERJEE:
A. That's right.
MR. COFFEY:
Q. - to get your tissue handing done, your trimming done -
DR. BANERJEE:
A. Um-hm.
MR. COFFEY:
Q. - would no longer then apply to the pathologists because they wouldn't be involved in it, unless they happened to be asked to be consulted on a particular matter, the pathology assistants would be doing it?
DR. BANERJEE:
A. And that's exactly the way it should be set up, so that the pathologist is still responsible for the grossing but the way that larger hospitals have done that is the pathologists will actually spend the first part of the morning of the afternoon with the pathologist assistants taking a quick look at what the specimens are, what the nature of the specimens are and providing specific instructions if there's some unusual specimen

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to deal with. But in general, the experienced pathologist assistants become very good at handling complex cases as well.
MR. COFFEY:
Q. And, Doctor, then you make a series of recommendations, they're numbered one through ten here. Subspecialization for pathologists is the first; section medical direction for immunohistochemistry service is the second. You already canvassed those. Consideration being given to switching to SP-1.
DR. BANERJEE:
A. Um-hm.
MR. COFFEY:
Q. Dedicated technologists, and the appropriate number of the IHC. Doctor, under the paragraph 4 you note, "technologists should be capable of quality assurance of each staining run and not release slides if internal and external controls have failed. QA, QC failures noted by the reporting pathologist should be documented and reviewed periodically by the section medical director with corrective measures implemented as soon as possible." The reference to the technologists not

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releasing the slides if internal and external controls have failed, I take it that that suggests that perhaps they should be involved in the reading of internal and external controls?
DR. BANERJEE:
A. Oh, yes. And they have to--they can't do it without looking down a microscope, so they need to be trained as to what to look for. They're not necessarily experts in histopathology, but over time they gain enough experience by looking at slides with the pathologist, section medical director, for instance, and then can get to that level of comfort, particularly with specific tests where that, that needs to be reported. Not all labs do that. I think it has two benefits: one is the QC, QA activity becomes much more stringent; the other thing is that technologist actually learn a lot more about what they're doing as a result of that interaction with the pathologist.
MR. COFFEY:
Q. And but you, as you just acknowledged, there are different approaches by various

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laboratories across the country to whether the technologists examine the external controls alone or look at the internal and external controls?

DR. BANERJEE:

A. That's correct.

MR. COFFEY:

Q. And in any case, whichever of the two or of both it's your view and you were suggesting, I take it that, they should be, of course, appropriately trained?

DR. BANERJEE:

A. Yes.

MR. COFFEY:

Q. If they're going to be involved, they need to be trained?

DR. BANERJEE:

A. Right.

MR. COFFEY:

Q. Doctor, then, you then conclude by saying that in five you refer to a necessity for tumour pathology, "pathologist leaders must regularly attend appropriate educational and scientific conferences to stay current." And I take it tumour site pathologists leaders would be the

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kind of subspecialists, as it were?

DR. BANERJEE:

A. That's correct.

MR. COFFEY:

Q. The leaders in breast, the leaders in lung, whatever?

DR. BANERJEE:

A. Um-hm.

MR. COFFEY:

Q. Whatever system you're dealing with?

DR. BANERJEE:

A. Yes.

MR. COFFEY:

Q. Pathologists assistants are referred to here, should be hired and trained. The Sakura continuous flow tissue processing system to allow the implementation of it, they should jointly redesign work flow practices. The Sakura system, Doctor, because it's referred to earlier in your report, as well, were you advising them to adopt the Sakura or not?

DR. BANERJEE:

A. Well, they had already acquired the system but it wasn't actually in action because it was a decision made without input from the

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pathologists so there was an immediate push back from the pathologists. I actually believe that eventually that will be the standard down the road. Not many hospitals have adopted that system. It's a different kind of tissue process, it uses microwave technology that reduces processing time from overnight processing to one hour or two hours at the most but doesn't deal with the fixation issues, that is a separate issue. And it's a continuous flow system, so it's not a batch processor. And so if you're familiar with lean manufacturing practice that's now being adopted by health care systems, we are moving away from batch processing to single flow processing and that for the individual patient biopsy means very short turn around times, but it means pathologists and technologists have to completely redesign how they work during the day, so it's a complex thing to do.

MR. COFFEY:

Q. And you do note here, they should joint--they would have to jointly redesign their work flow practices -

DR. BANERJEE:

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A. Right.

MR. COFFEY:

Q. - if it's going to work at all.

DR. BANERJEE:

A. Yeah.

MR. COFFEY:

Q. You at paragraph 8 say "The Ventana system is performing adequately and with improvement and standardization of fixation protocols there's no reason that the service could not be resumed without further delay." That would be the ER/PR service in this context?

DR. BANERJEE:

A. That's correct.

MR. COFFEY:

Q. But you were saying there was improvement in and standardization, improvement in and standardization of fixation protocols were certainly going to be necessary?

DR. BANERJEE:

A. Yes.

MR. COFFEY:

Q. And perhaps even optimization?

DR. BANERJEE:

A. Absolutely, yeah.

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MR. COFFEY:
Q. There's a reference then to external quality assurance programs such as CAP or NEQAS, the laboratory should prescribe to them. At the time do you recall whether or not it was your understanding that they were--were they, at that point, involved in either of these?
DR. BANERJEE:
A. No, they were not.
MR. COFFEY:
Q. And then the organizational chart should be redesigned to provide better joint technical and medical accountability, planning and communication. So, Doctor, I take it that in paragraph 10 you weren't really saying you should have a medical director in charge, per se?
DR. BANERJEE:
A. I wasn't saying that, but I wish I had said that.
MR. COFFEY:
Q. Yes. But in any case, the organizational chart would be required to be, from your perspective, redesigned to ensure that at least everybody knew everybody else's role and

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they interacted appropriately?
DR. BANERJEE:
A. That's correct.
MR. COFFEY:
Q. To achieve the best result. If we could, Commissioner, I'm going to go on then to -
COMMISSIONER:
Q. Time to break?
MR. COFFEY:
Q. If you would, please?
COMMISSIONER:
Q. All right. We'll reconvene at 2:15.
(LUNCH BREAK)
COMMISSIONER:
Q. Please be seated. Mr. Coffey.
COFFEY, Q.C.:
Q. Thank you, Commissioner. Registrar, Exhibit P-1312, please? And, Doctor, this is an exchange of e-mails from October 21st through the, well, actually, and the 22nd between yourself and Dr. Cook. And the first of them on the 21st he acknowledges receipt of your report. And you responded by saying "Hi Don, best of luck." Doctor, you know, having had the opportunity to come to St. John's

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September, make your observations, go away and think about it and make your report and reduce it to writing, Doctor, from your perspective at the time, could the problems have been detected earlier, do you think?
DR. BANERJEE:
A. I believe so. I think the problems should have been detected earlier and I think Dr. Edgecombe was probably one of the first people to judgely--raise some concerns about the immunohistochemistry service. I think the whole transition from the biochemistry test and the immunohistochemistry test should have been handled in a different way to get the correlations done, comparisons done between the two methods before you switch over to the new method. And that's our task because, I mean, it's a permanent task because in our business new methods are constantly being developed and for us to switch from an existing method to a new one there is a process we have to follow to make sure it's validated.
COFFEY, Q.C.:
Q. Now we have heard evidence from Dr. Khalifa,

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who was the physician who, in effect, introduced ER/PR IHC methodology to the province and there was certainly some correlation effort in the first year or so involving the biochemical assay that was then being done in St. John's and the ER/PR IHC slides that the lab at the General Hospital was producing. Even after that, between '97 and then you showed up in 2005 and you understood Dr. Ejeckam had some concerns dating back to certainly 2003?
DR. BANERJEE:
A. Right.
COFFEY, Q.C.:
Q. What is it then that you think in terms of who, and not so much the individuals as is what groups might have been able to identify that there was a problem earlier and what do you think they might have seen to do so?
DR. BANERJEE:
A. I think probably rather than trying to solve the problem through internal review and process redesign that would have been probably the best time to get some external experts to come in and take a look.

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COFFEY, Q.C.:
Q. And when was that, Doctor?
DR. BANERJEE:
A. So as soon as the concerns were raised in 2003 I think that would have been the right time to bring in some external consultants just to make sure that the methods were set up correctly. Because even though Dr. Edgecombe had raised his concerns, I mean, I wasn't clear what external benchmarks were available to him to make the judgment whether they were doing the task or not.
COFFEY, Q.C.:
Q. And, Doctor, you did, when you were here in September of 2005, see these slides for approximately 20 patients. And we understand that most of those slides probably were from the year 2002, is our understanding because most of the retesting that had occurred involved 2002.
DR. BANERJEE:
A. Possibly. I don't quite remember it, so -
COFFEY, Q.C.:
Q. And you wouldn't have reported that. I'm saying we understand it because we've seen, of

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course, and heard evidence concerning what year, the year from which particular patients had been retested up to the point you arrived.
DR. BANERJEE:
A. Um-hm.
COFFEY, Q.C.:
Q. And in the main it was 2002 cases. Doctor, with that in mind, for example, in looking at those particular slides, if the pathologist at the time who examined them had been aware of the internal control requirement and had noticed that particular internal controls weren't staining and they were reporting the tumours as negative, if inquiries had been made at that point, for instance, well, I can't report this and in fact this is the second one I've seen in a month or whatever.
DR. BANERJEE:
A. Um-hm.
COFFEY, Q.C.:
Q. Do you think any inquiries at that point, if there had been inquiries made then, you know, people who were faced with that might have recognized the problem at the time?
DR. BANERJEE:

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A. I think so, yes.
COFFEY, Q.C.:
Q. If we could look at, please, at Exhibit P-2095? Doctor, page 92, please? Doctor, this is two e-mails, October 23rd, one from Dr. Cook to yourself, and the subject is a possible agenda item for CAP meeting in November. And he writes, "Hi Diponkar, Mr. George Tilley, CEO of Eastern Health and Bob Williams, VP, have asked me if we could discuss the issue of national standards for immunohistochemistry at the Canadian Association of Pathologists. Maybe we could put on the agenda for the November meeting as an item we could bring to the federal minister of health. This could be part of a much larger issue such as national standards of practice for laboratory medicine in Canada. I would appreciate your thoughts. Regards, Don." And you responded the next day saying "I agree, this is an important topic that needs discussion. We should add it to the agenda along with the national standards of practice topic." And I will be asking you more about this, Doctor, but. So as we get

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into the last week of October of '04 Dr. Cook raised this with you and you were certainly, at that point you were president, I take it, of the association?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. And this November meeting, where was that to occur, do you recall where?
DR. BANERJEE:
A. I can't remember. It was either Ottawa or Toronto.
COFFEY, Q.C.:
Q. Okay. And I'll be asking you a bit more about, to elaborate upon what happened then and what has happened since concerning national standards for immunohistochemistry and generally for the practice of laboratory medicine. If we could look at Exhibit P-0662? And here, Doctor, I take it, this is a letter of October 24th, 2005. It's addressed to yourself, it's from Dr. Cook, copied to Dr. Williams. It's Dr. Williams' copy we have. And I take it this is just the formal request reflecting the e-mail we just looked at?

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DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. Exhibit P-2095, please, 2095? Page 45. Doctor, this is a letter on Canadian Association of Pathologists letterhead, it's from yourself, it's to Dr. Cook. And this is responding to his letter of October 24th and advising him that "I've asked that this topic be placed on the agenda for the November meeting." And the topic in question is national standards for immunohistochemistry testing.
DR. BANERJEE:
A. Right.
COFFEY, Q.C.:
Q. Exhibit P-0679. Doctor, this is, in particular, the e-mail of November 2nd at the bottom of the exhibit here. It's from yourself. Daniele -
DR. BANERJEE:
A. Saintonge.
COFFEY, Q.C.:
Q. Saintonge. Who is Daniele Saintonge?
DR. BANERJEE:

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A. She works at the Royal College and provides administrative support to Canadian Association of Pathologists.
COFFEY, Q.C.:
Q. And you had asked her, "Could you please add the following item to the November agenda." And national standards for laboratory immunohistochemistry--laboratories immunohistochemistry testing. "Dr. Cook and I," that's yourself, "will speak on this topic." Doctor, what then happened in November, do you recall?
DR. BANERJEE:
A. As I recall, we discussed the need for national standards, and wondered how to bring this to the attention of both the federal and provincial jurisdictions of health care. Since we didn't feel that the Canadian Association of Pathologists in its current configuration and membership would really be able to do much without the resources required to set up such a system, that we needed help from both provincial and federal governments to do this properly.
COFFEY, Q.C.:

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Q. And so that was yourself and Dr. Cook, I take it, raised that at the time?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.:
Q. And was there any decision as to how to go forward at that point?
DR. BANERJEE:
A. So the decision was made that I would write to various stakeholders in the business of cancer care across the country and solicit their support in approaching provincial and federal governments on this particular issue, which I did.
COFFEY, Q.C.:
Q. And I'll be asking you in a more general way to take the Commissioner through what had happened before that in this regard and what has happened since. Exhibit P-1973. Here, Doctor, there's two e-mails of December 2nd, 2005. The first of them is from Dr. Cook to yourself and the subject is institution of ER/PR services and it says, "As I mentioned to you in Ottawa", perhaps where the meeting then was --

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DR. BANERJEE:
A. Yes, that's right.
COFFEY, Q.C.:
Q. "We will be receiving funding for the upgrading of your immunohistochemistry services. We will be planning a number of meetings with our keys pathologists and technical people concerning implementation of recommendations. I would appreciate your advice and guidance, and I wonder if you can participate in some of these meetings in a conference call. I predict there will be a number of differing options on how to implement and when to decide on a start up date. I would certainly welcome an outside perspective in helping me achieve a consensus approach to full implementation", and you responded saying, "Hi Don, yes, I would also request that Dr. Malcolm Hayes and our head technologist, Bev Thomas, also be invited to join at least for some of the meetings so we can benefit from their experience. Regards, Diponkar".
DR. BANERJEE:
A. Uh-hm.

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COFFEY, Q.C.:
Q. Doctor, why did you suggest that if you were to be involved in this, that you would want Bev Thomas and Dr. Malcolm Hayes involved?
DR. BANERJEE:
A. Dr. Malcolm Hayes is one of our best pathology experts, and at the time he was also overseeing the immunohistochemistry lab at the BC Cancer Agency, and Bev Thomas at the time was the head histotechnologist responsible for that service, and she had considerable experience and skills in immunohistochemistry, so I felt that she could provide some detailed technical guidance to people at Eastern Health.
COFFEY, Q.C.:
Q. Exhibit P-2008. Doctor, this is an e-mail of December 5th, 2005, from Dr. Cook responding, I take it, to the last e-mail I just looked at, "Thanks for your help. I will contact you when I have the meetings arranged. Regards, Don". Doctor, were there ever such meetings, at least that you were involved in?
DR. BANERJEE:
A. I was not involved in any. I wasn't aware of

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when the meetings were actually held.
COFFEY, Q.C.:
Q. Exhibit P-2036. Doctor, this is two e-mails; one from Dr. Cook of January 13th, 2006, to yourself. It involves the subject -- he styles it as ER/PR issue, and he says, "Dr. Kara Laing, out clinical chief, oncology, received a phone call from an oncologist in Fredericton, New Brunswick, stating that problems with ERs and PRs have been identified for a particular year from a Fredericton lab and was looking for information on what happened and how we handled the issue. Dr. Laing advised the oncologist that a more thorough review, other than the year in question, is needed. As for an explanation as to what is happening in Fredericton lab reports, they have a pH issue according to Dr. Laing. I anticipate that this may spread to other regions in Canada as the problem becomes more widely known. From a Canadian Association of Pathologists perspective, I think we need to stay on top of this issue and liaise very closely with the Canadian Association of Oncologists and be ready for possible media

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interviews. I will keep you posted. Regards, Don", and you responded the Monday following that saying, "Thanks". Doctor, the issue -- the ER/PR issue, as Dr. Cook styled it here, other than St. John's, has that arisen anywhere else in the sense of since that time in this kind of a -- become public, anyway?
DR. BANERJEE:
A. I haven't been made aware of similar issues. Other than this e-mail, I didn't get any further information about the Fredericton lab problem.
COFFEY, Q.C.:
A. And at the end of his e-mail, he refers to the Canadian Association of Oncologists, and liaising closely with them. How much liaising from your perspective has gone on between the Association of Pathologists and that of oncologists?
DR. BANERJEE:
A. Very little.
COFFEY, Q.C.:
Q. It's not --
DR. BANERJEE:
A. And historically, there hasn't been much, and

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I don't believe there's any current interaction.
COFFEY, Q.C.:
QQ. And do you think that there should be?
DR. BANERJEE:
A. Oh, absolutely, because we are all dealing with the same patient population.
COFFEY, Q.C.:
Q. Exhibit P-2006. Doctor, again this is an exchange of e-mails between yourself and Dr. Cook, February 20th. He says, "In regard to the ERs and PRs, we are in the implementation phase of many of the recommendations brought forth by the review process. We are hoping to restart this system by the end of March. I would appreciate if you could fly to St. John's sometime near the end of March and review the progress we have made. We would value any observations and recommendations that you make regarding implementation of the system. We will, of course, reimburse you for your expenses and time involved. I look forward to hearing from you and hope you can visit", and then you got back to him the next day saying, "I have left you a voice mail

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message. Please call me", and your cell number, "and send me an e-mail if the dates I've suggested will work for you", and you advised him of your then current location. Doctor, up until toward the end of February of '06, other than that e-mail exchange where Dr. Malcolm Hayes is referenced, and Bev Thomas, had you been at all involved otherwise with this?

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. So this is the - your reintroduction to the idea of re-implementing ER/PR in St. John's, your involvement, potential involvement in it?

DR. BANERJEE:

A. This is the first time I was aware of that.

COFFEY, Q.C.:

Q. Yes, and to your knowledge, I take it, no one else from your institution had been involved up to this point?

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. Doctor, at that point in time -- up to that

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point in time, had you been aware of Trish Wegrynowski's involvement?

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. And, in fact, we will now come to your coming back to St. John's in the spring of 2006. You weren't aware of her involvement then either, I take it?

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. When did you first become aware that the chief technologist from Mount Sinai was involved in this?

DR. BANERJEE:

A. I think after this Commission of Inquiry was announced.

COFFEY, Q.C.:

Q. Okay. Doctor, in the meantime in terms of what else was going on, Exhibit P-0165, please.

DR. BANERJEE:

A. That's not the right --

COFFEY, Q.C.:

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Q. No, no, P-0165, not 2165, 165, please. Thank you. I'm going to go to page two first, Doctor. Now, Doctor, this is a letter on Canadian Association of Pathologists letterhead, February 1st, 2006. It's addressed to the Honourable John Ottenheimer, Minister of Health, here in St. John's. The subject is "re; laboratory medicine specialist pathologists in Newfoundland". It's signed by yourself as President of the Canadian Association of Pathologists, and generally a description of the various positions you then held underneath your signature at the University of British Columbia and the British Columbia Cancer Agency, etc. Now, Doctor, how was it you came to write this letter?

DR. BANERJEE:

A. Well, I think during my first visit to Eastern Health, and during my discussions with the pathologists, the whole issue of retention and turnover of pathologists was raised, and I think the current head of pathology was in the middle of negotiations with the Government on compensation levels for pathologists and he asked whether I would be willing to support

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their case by writing a letter as President of the Canadian Association of Pathologists, and I agreed to do that because I could see that compensation was certainly a big factor in the whole retention issue. So I prepared this letter and had it transferred to letterhead and submitted to the Minister at the time.

COFFEY, Q.C.:

Q. And, Doctor, you do write here, "80 percent of all medical decisions are based on laboratory reports issued by pathologists, yet pathology services usually cost less than 5 percent of the health care budget in most jurisdictions". That figure of -- and I appreciate this is being written in early 2006, "80 percent of all medical decisions are based on laboratory reports issued by pathologists", that sort of a figure, where would you have gotten that from at the time?

DR. BANERJEE:

A. That's sort of a generally accepted figure in the literature and that's across the board in terms of lab services. I would say in an oncology setting, you're probably looking at a higher percentage that drives clinical

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decision making.
COFFEY, Q.C.:
Q. Higher than 80?
DR. BANERJEE:
A. Higher than 80.
COFFEY, Q.C.:
Q. And you note -- you go on to say, "We are facing a severe and growing pathologist manpower shortage across the country, and Newfoundland is likely to face a crisis very soon". You then go on to say, "Unless you are prepared", and that is "you", I take it, in the royal sense, the Government of the day" -
DR. BANERJEE:
A. Um.
COFFEY, Q.C.:
Q. "prepared to address, in the immediate future, the fact that pathologists in your province are among the lowest paid professionals in the nation, please do not be surprised if your province experience even greater difficulty in attracting and retaining pathologists than you face now. Not addressing is false economy, as patient care will be adversely affected by the lack of high quality pathologists in the

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province. You have already experienced a recent example of the effects of not investing in high quality pathology when the errors in breast cancer estrogen receptor status were discovered, affecting hundreds of patients in your province."

Doctor, in referring there to "the lack of high quality pathologists in the province," what were you--and then "not investing in high quality pathology" in the next sentence, what are you referring to there?
DR. BANERJEE:
A. I'm referring to the fact that if you have a compensation issue and you haven't addressed it, then the potential of keeping your best pathologists in the province would be damaged since they would seek employment elsewhere in the country or perhaps even outside of the country, and no matter what else happened, you know, compensation is definitely a factor that influences professionals in terms of where they practice. So it's kind of a fundamental sort of economic fact. The problem of-- there's a difference in the two sentences. One, I'm talking about high quality

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pathologists and retaining them, and the second sentence is talking about high quality pathology, which is more of the infrastructure in which these professionals would work. So you can't just improve compensation without dealing with all of the other issues about how to run a high quality lab service, which means you have the right number of technologists, appropriately qualified technologists, you have the right equipment, the appropriate budget for supplies, etcetera. All of that is part of the equation. So if you're cutting corners, cutting costs, ultimately this is quite predictable as to what's going to happen, and this is a long standing issue in Newfoundland, not something that happened overnight.
COFFEY, Q.C.:
Q. And so in this last sentence in the second paragraph, you here seemingly attribute the recent example of errors in breast cancer estrogen receptor status, which is from your perspective, you understood it affected hundreds of patients in this province, were ultimately caused by not having invested in

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high quality pathology, and pathology in a wider sense than just the pathologists?
DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.:
Q. The whole system?
DR. BANERJEE:
A. Um-hm.
COFFEY, Q.C.:
Q. I take it then, Doctor, that the lack of money has the--or lack of money, particularly a lack of investment financially over an extended period of time has what effect or could have what effects, in the clinical laboratory setting?
DR. BANERJEE:
A. I think it affects the kind of expertise you can keep in your laboratory. It affects the infrastructure, the quality of the equipment, the age of the equipment, whether using current technology or not, all of that is affected by lack of investment.
COFFEY, Q.C.:
Q. I take it, you then go on to say here, Doctor, "historically your province has relied heavily

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on foreign trained pathologists who are unlikely to stay on in the province as more attractive jobs come up elsewhere in the nation" and you ask that "this cycle be broken by promoting and protecting your best assets." I take it, in effect, by increasing their compensation or at least addressing the issue is what you were urging here?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. Now Doctor, and we're going to look at the response in a moment, but here, were you in any way suggesting that foreign trained pathologists had caused the problem here?

DR. BANERJEE:

A. No. Actually, what I'm saying is that if you have a retention problem and you're dependent on foreign trained pathologists to fill your vacant positions, and you haven't dealt with the compensation issue and the infrastructural problems, there's nothing going to hold them in this province, because they don't have family connections, etcetera. So they're more likely to leave than say people who grew up in

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this province, were educated in this province. They're frustrated in their jobs, but couldn't leave because of their family connections. So that's the point I was trying to make.

COFFEY, Q.C.:

Q. Page one of this exhibit, Doctor, is the response that came more than two months later. It's dated April 18th, 2006. It's addressed to yourself. It's from Tom Osborne, the Minister, and I should tell you here, Doctor, that Tom Osborne has testified here and he has told the Commissioner that other than you being the president of the Canadian Association of Pathologists, he had no idea at all that you had been involved in reviewing the lab here in St. John's. So I'll just let you know that. He does conclude by--he acknowledges, at the end of the second paragraph, "all parties have recognized that physician compensation is about one of the many challenges facing this specialized group" and the group in question, I take it, are the laboratory medicine specialists referred to in the first paragraph. He then says "I do take exception to your suggestion that the recent

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errors in breast cancer screening experienced in this province were as a result of not having invested in high quality pathologists." He attributes -

DR. BANERJEE:

A. Um-hm.

COFFEY, Q.C.:

Q. - doesn't make the distinction between the two sentences that you did. Were you suggesting, had you ever suggested that the pathologists here were not high quality pathologists? Were you ever asked that question?

DR. BANERJEE:

A. No, not really, but I could see how they would interpret my letter along those lines, but I think I've explained to you what I meant by that and how do you assess quality of pathologists without checking their work? And I was only looking at one aspect of the work, so I don't believe I've done a thorough review of that to come to a conclusion about their quality.

COFFEY, Q.C.:

Q. And your review had been in respect of just the ER/PR staining?

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DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. And perhaps a little bit more IHC generally?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. And you had found certain things that were, from your perspective, wanting or lacking in that regard?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. In that particular field, and that was it?

DR. BANERJEE:

A. Um-hm.

COFFEY, Q.C.:

Q. You go on to say, there has been--well, not you, I'm sorry, Mr. Osborne went on to say "it has been recognized that the tests associated with this procedure are fraught with errors in reproduction, as well as changes in national standards." Now would you have disagreed with that assertion?

DR. BANERJEE:

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A. I would say it's not fraught with errors of reproduction. It's certainly not an easy assay to do. And there were no national standards to compare against, so I'm not sure what he means by that.

COFFEY, Q.C.:

Q. And so in address--or speaking of the procedure being fraught with errors in reproduction, you would have disagreed with that. I take it your position would be that it can be done correctly. You just have to go about it properly?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. Doctor, he concludes by saying "your letter suggests that the pathologists employed by Eastern Health are less than qualified, which is a great disservice to your peers represented by your organization," and that's the letter of February 1st. At the time, did you feel that you had suggested that the pathologists employed in Newfoundland were less than qualified?

DR. BANERJEE:

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A. No, I didn't feel that.

COFFEY, Q.C.:

Q. Did you ever respond to this letter, Doctor?

DR. BANERJEE:

A. I did not.

COFFEY, Q.C.:

Q. Did you ever talk to anybody else or communicate with anybody about it?

DR. BANERJEE:

A. I might have joked about it with colleagues.

COFFEY, Q.C.:

Q. Do you recall--with colleagues, would that be within British Columbia? Did you ever talk to anybody in Newfoundland about it, that you recall?

DR. BANERJEE:

A. I don't recall specifically discussing it, other than that I didn't receive a very constructive response from the Minister.

COFFEY, Q.C.:

Q. Now Doctor, we understand that you did return to St. John's. If we could look, please, at Exhibit P-2148? In particular, Doctor, I want to take you to page three of this. These are notes of what is styled an exit meeting, April

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25th, 2006. You'll see your name is there as number one, Dr. Bob Williams, Dr. Donald Cook, Dan Fontaine, Gershon Ejeckam. It says Bev Fontaine; presumably that should be Bev Carter.

DR. BANERJEE:

A. Carter.

COFFEY, Q.C.:

Q. And Dr. Joy McCarthy. Doctor, can you tell us, please, then what you recall about your second visit?

DR. BANERJEE:

A. So my second visit, I reexamined some of the slides that were more currently or recently prepared, and I could see that there was a significant improvement in their quality, intensity of staining. Background problems had been dealt with, so there were clean backgrounds. The internal controls seemed to be working in the cases I looked at. We also again looked at other immunohistochemistry preparations other than estrogen receptors.

COFFEY, Q.C.:

Q. So the slides you're talking about just now, they're estrogen receptor slides?

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DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. So you also looked at others, I'm sorry?

DR. BANERJEE:

A. That's right, and when I looked at the other stains, other than the receptor stains, they also showed significant improvement in the quality of the staining, the specificity of the stain or the right cells were staining and the cells that were supposed to be negative were negative, etcetera. So I was quite happy with the improvement I saw.

COFFEY, Q.C.:

Q. What was the situation in respect of fixation?

DR. BANERJEE:

A. Fixation, there was still remaining problem. Again, I didn't look at a very large number of slides from different hospitals. It's hard to--hard for me to give you a general sort of impression of how well the fixation issues had been dealt with, but I was under the impression that they were certainly moving in the direction of getting pathologists assistants and I felt confident that the

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variability in fixation and tissue processing would have been dealt with and clearly some of the improvement in immunohistochemistry was related to better fixation, but it was not entirely resolved, from my recollection.

COFFEY, Q.C.:

Q. And Doctor, during your second visit, do you recall where it was you actually--like where you went?

DR. BANERJEE:

A. Not really.

COFFEY, Q.C.:

Q. Okay, you just--your second visit compared to your first, was your second visit a shorter or more focused?

DR. BANERJEE:

A. I think it was, yeah, a little shorter, but I think we were essentially in the same locations as before when we were looking at the slides.

COFFEY, Q.C.:

Q. Doctor, there's a note here, or at least these notes, I understand that these are Dr. Cook's, he attributes the following comments to Dr. Ejeckam, and the notes do indicate Dr. Ejeckam

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was present. Actually, well perhaps I'll begin with what he attributes to you. "Pleased to see recommendations have been implemented. Reviewed ER and PR stains. Stains are working," that may be okay, I'm not sure. "Lab is performing as well as expected. Good to see dedicated technologists. Good to see"--I apologize, I'll just go up here. "Good to see dedicated medical supervisor of lab. Good to see external QA. Some variability is a function of tissue from other hospitals, still present. 8. Need to set out guidelines--or send out guidelines to other hospitals regarding fixation. 9. Fixation and processing of tissue needs to be standardized. 10. No hesitation in restarting the lab" and in that context, you mean ER/PR?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. So I take it that suggests, at least to me, Doctor, that you, during your visit, became aware that some of the tissue at least was coming from other places?

DR. BANERJEE:

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A. Right.

COFFEY, Q.C.:

Q. And fixation and processing of tissues needs to be standardized and the guidelines for other hospitals, regarding fixation, had to come from somewhere, and perhaps be sent out from St. John's?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Then there are notes or references to Dr. Ejeckam's comments. "Need to have a stipend for director of immunohistochemistry. Need to recognize workload. Need time for monitoring" that should perhaps be, "the lab and documentation need clerical support. Need clerical support for document control," which is indicated to be supported by yourself. "Need CME," continuing medical education, "for the techs. Need succession plans for younger people into immunohistochemistry" and he goes on from there, "preferably people" and he describes the type of individual he'd be looking in a succession plan, and attribute to Dr. Ejeckam, "can start ER/PR immediately, and

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work on optimization of HER2/neu."

Doctor, your overall sense then, you know, bearing in mind what you saw when you came in April of 2006, and during the meeting you had, the exit meeting, was what, compared to what you'd seen in September?

DR. BANERJEE:

A. Well, it was much improved, and I think the results were interpretable and the whole issue of internal controls had been addressed. So I felt that they were doing as well as most hospitals that I've seen.

COFFEY, Q.C.

Q. Now here on the second page of the notes, fourth page of the exhibit, toward the end, attribute to you, Banerjee saying "breast pathologists must get together with oncologists to discuss ongoing issues". And I should point out that they attributed, above that, certain comments during the meeting to Dr. McCarthy. "And have to do literature review to decide what cut-off to use or is to be" -

DR. BANERJEE:

A. Yes.

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COFFEY, Q.C.
Q. - "to get on track, have to"--it says something to NCIC guidelines, 10 percent cut-off, need to get standards across the country, set up a breast site group, pathologists, radiologists, surgeons and oncology". So, was it your view that they should set up a breast site group here?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. And in terms of the interaction of pathologists with oncologists, the advantage of a breast site group would be what, in that regard?
DR. BANERJEE:
A. The advantage would be that there would be appropriate forum for discussion about that policies, guidelines about clinical decision making based on pathology observations and how that should be reported and to make it standardized in terms of reporting. And also when there's debates about what is the appropriate cut-off point for calling something positive or negative, that should be

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based on a thorough literature review which oncologists and pathologists have to do together to then decide whether they're going to use one percent or ten percent. Most people are now using one percent as their cut-off. And again, the formation of the site group allows a new development to be planned for and new lab tests to be introduced in a systematic manner.
COFFEY, Q.C.
Q. Exhibit P-0049, please. Doctor, was there anything else of note during your time in St. John's that we haven't covered, that the Commissioner should know, do you think?
DR. BANERJEE:
A. I think the only thing that perhaps didn't come out during this discussion today was the HER2/neu testing for herceptin therapy, that I felt was not ready to be restarted until they had finished their validation against the gold standard method in situ hybridization and I'm not sure exactly what happened with that, whether that's still not being offered locally or whether that's already being offered. So, I don't have much information on that.

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COFFEY, Q.C.
Q. And looking at this, Doctor, it's a letter of May 23rd, 2006 on page one of the exhibit and it's to Dr. Williams and you send a copy of your report based on your last site visit, your report on immunohistochemistry service. We look at page two of this, cover page, May 21st, 2006 and you've indicated, at the request of Dr. Williams, you reviewed the performance of the IHC lab on April 24th, 2006 in order to determine whether the quality of IHC has improved since your last visit and "whether my previous recommendations have been implemented". You've already addressed, just now, your view as to whether it had improved. I take it here under the charts we have here, Doctor, that follow, you simply listed your prior recommendations verbatim and made a comment upon them.
DR. BANERJEE:
A. Right, yes.
COFFEY, Q.C.
Q. And I'll jus simply go through them. The first of them was the idea of pathologists subspecializing and you noted here, "in

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progress" you are advised at that point.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. One pathologist should be appointed as section medical director for the IHC service, is recommendation number two. You noted, implemented, Drs. Fontaine and Elms were appointed.
DR. BANERJEE:
A. Right.
COFFEY, Q.C.
Q. Doctor, in that regard, in terms of a person being the section medical director for IHC, from your perspective and you do have, I gather, a significant amount of experience as an IHC director yourself, what sort of training or experience should such a director have? Because I take it, from time to time, of course, the director will change, people will move on or their term will expire. What sort of training should the person have?
DR. BANERJEE:
A. I think that they definitely need to have spent some time in one of the reference

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laboratories within the US or in Canada to make sure that they have understood what it will take them to be effective as a section medical director and to be able to help the technologist to troubleshoot and make sure that when they select the technologists for the lab that it's done with technical knowledge in mind. So, yes, I think that requires some additional training and it would depend on where they went and how quickly they saw the full spectrum of even the histochemistry procedures and sign out with whoever is in charge of the lab at the training site. So, it could be something that would take a month, maybe a couple of weeks depending on the volume going through that particular lab.

COFFEY, Q.C.

Q. Doctor, is there a formal training program that you're aware of for a person who might be a section medical director for an IHC service?

DR. BANERJEE:

A. No, there is no such formal training, but it can be arranged through correspondence with a particular lab that you want to go and train

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at, some kind of visiting scientist kind of arrangement could be made. We also run workshops at the annual meeting of the association which often covers details of immunohistochemistry, but in the context of specific tumour types and so on.

COFFEY, Q.C.

Q. So, right now, such training, such as it exists is on an informal basis.

DR. BANERJEE:

A. It is.

COFFEY, Q.C.

Q. And should involve a reference laboratory.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.

Q. And the extent of the period of time required would depend upon the individual pathologists background and experience to date.

DR. BANERJEE:

A. Yes, right.

COFFEY, Q.C.

Q. Then in paragraph three here, the consideration should be given to switching to the SP-1 and I take it, you've noted here, it

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was under discussion. Do you recall what the situation was, under discussion, why was it still under discussion or -

DR. BANERJEE:

A. No, it's just that I don't think they had decided to make the switch yet because their existing antibodies seemed to be working better, So -

COFFEY, Q.C.:

Q. And you had seen slides stained with the -

DR. BANERJEE:

A. Yeah.

COFFEY, Q.C.:

Q. - recently then and from your perspective they were fine?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Paragraph 4 on the next page, I apologize, is the No. 4 recommendation. And then you've noted here, and this deals with the appropriate number of technologists being dedicated to the IHC service and accountable to the section medical director. You've noted, "Implemented, three dedicated

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technologists have been assigned to the service. However, a succession plan is required now in order to minimize future problems related to attrition due to retirements. The phenotype of future staff for this section should be based on their knowledge based and minimum educational standards as this area will experience much expansion and highly skilled staff are required for implementing new antibodies, probes of FISH, troubleshooting and maintaining high standards. University graduates at BSc or MSc level should be recruited and trained to perform IHC/FISH at reputable laboratories." Doctor, to your knowledge are there any standards for IHC technologists?

DR. BANERJEE:

A. No, there are not that I am aware of. I made this recommendation because this is a recommendation I make to any hospital lab in any part of the world because this is an area that's expanding very rapidly, and as I said, as new targeted therapies become available it's going to be critical to do these tests as

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accurately as possible. And I think investing in well trained technologists is extremely important, otherwise we will continue to have problems with immunohistochemistry tests, particularly the newer ones that we will be obliged to provide.

COFFEY, Q.C.:

Q. Which, I gather, you anticipate that they have recently and will continue into the future to require more and more scientific knowledge just to even understand what it is you're doing?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. As a technologist?

DR. BANERJEE:

A. Yes. The danger is that if you don't do that, you're at the mercy of the vendors of machines and reagents who will tell you that they have worked out all the bugs and we just run with it.

COFFEY, Q.C.:

Q. And her, Doctor, paragraph, or recommendation No. 5, this is the tumour site pathologists

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leaders must attend appropriate educational and scientific conferences. You understood that was in progress?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Ongoing medical education. "Pathologist assistants should be hired and trained." You've noted it's implemented, three PAs were hired. And you go on to say, "Issues around qualifications and training to be discussed with senior human resource consultants, as these are individuals who will perform delegated medical tasks requiring a minimum level of education (currently the Canadian Association of Pathologists) guidelines indicate that these should be at a master's level, with formal training as PAs."

DR. BANERJEE:

A. Okay.

COFFEY, Q.C.

Q. So, the Canadian Association of Pathologists did have, at that time, had guidelines as to what the background should be for pathology assistants.

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DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.

Q. Did you make any inquiries, do you recall or were you told at the time as to whether these 3 PAs who were being hired, had been hired and were being trained, met the CAP guidelines?

DR. BANERJEE:

A. I don't remember the discussion specifically, but I believe they hadn't met the guidelines, but they could achieve that through additional training.

COFFEY, Q.C.

Q. Paragraph 7, recommendation 7 is related to the Sakura processing system, you know, not been implemented yet. Was there any discussion about that, do you recall?

DR. BANERJEE:

A. No, and I didn't think that would significantly change the issue around ER/PR testing. So, it wasn't that important.

COFFEY, Q.C.

Q. Paragraph 8 refers to, recommendation 8 refers to the Ventana system and you've noted here on the right hand side, verify that ER and PR IHC

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qualities acceptable, HER2/neu staining still to be validated using FISH as the gold standard, and you just referred to that earlier.

DR. BANERJEE:

A. Right.

COFFEY, Q.C.

Q. When you say "acceptable" Doctor in relation to ER/PR IHC quality, in that context, what does the word acceptable mean?

DR. BANERJEE:

A. It means that if I was to be the reporting pathologist, I would accept the quality of those slides and be able to report on them.

COFFEY, Q.C.

Q. From your perspective at the time, did that mean that they could not be better, they were as good as they could get or -

DR. BANERJEE:

A. They could be better, but I didn't feel that we were missing anything that should have been positive.

COFFEY, Q.C.

Q. And in terms of being better, what would be required, what sorts of things, from your

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perspective, would have to be done?
DR. BANERJEE:
A. Well, I think the final step is to get that initial fixation tissue processing step optimized and that would just make everything more crisp. So, you'd get cleaner staining and easier to interpret slides.
COFFEY, Q.C.
Q. And Doctor, recommendation 9 dealt with the external quality assurance programs and you noted "implemented" and there had only been a single survey at that point. In any case, I take it, such external quality assurance programs, whether the CAP, the American one or UK NEQAS or any other for that matter would be an ongoing process, you anticipated.
DR. BANERJEE:
A. Yes. You can't do it just once in a while. It has to be done regularly.
COFFEY, Q.C.
Q. Recommendation 10, had been consideration given to an organizational chart redesign in order to provide better joint technical and medical accountability, planning and communication. You noted here "not

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implemented". Was that discussed, do you recall, this whole organization business when you were here in April?
DR. BANERJEE:
A. It was very brief discussion. So, I basically concluded they hadn't done anything about it. I wasn't clear whether they were planning to do anything about it at the time.
COFFEY, Q.C.
Q. So, the discussion was such that you couldn't tell whether they were prepared to act on it at that point?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. And you don't recall any discussion about why they might not have or what the abstinence or -
DR. BANERJEE:
A. No.
COFFEY, Q.C.
Q. Under your recommendations here which, I take it, are one to nine are your current ones in this report at the time.
DR. BANERJEE:

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A. Yes.
COFFEY, Q.C.
Q. ER and PR tests may be resumed effective immediately. You were happy, satisfied certainly to recommend that, locally. Cut-off thresholds for positivity should be based on current published consensus. So, Doctor, in relation to that, you weren't telling them or suggesting to them what that should be, I take it.
DR. BANERJEE:
A. I mentioned the fact that most labs had moved to the one percent cut-off.
COFFEY, Q.C.
Q. You told them that, but you weren't actually-- you didn't commit that to writing in the sense of you would -
DR. BANERJEE:
A. I think there was still a bit of a debate going on with the oncologists as to what the cut-off should be. So, I felt that they needed to reach that conclusion themselves.
COFFEY, Q.C.
Q. And you were recommending, look at the literature.

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DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. Recommendation three, HER2/neu testing should not be implemented until correlation of results with FISH has been verified. Other established IHC tests for diagnostic purposes may resume effect immediately. Was there some issue of concern about the other IHC tests that you were aware or are you just saying generally?
DR. BANERJEE:
A. Just generally. I think when I looked at the slides on my first visit, I would have been concerned about continuing that service without improving the technology.
COFFEY, Q.C.
Q. Continuing the IHC generally.
DR. BANERJEE:
A. That's right.
COFFEY, Q.C.
Q. Unless they actually did the optimization required?
DR. BANERJEE:
A. Right.

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COFFEY, Q.C.
Q. So, I guess, on that point then, Doctor, in terms of that, when you'd been here in September of 2005, did the 20 groupings of slides and the other thirty odd slides and based upon the other, once you saw the other thirty, if they weren't going to do anything further about it to address the concerns you raised, you would have had concerns about IHC.
DR. BANERJEE:
A. I would have, but it's not quite the same level of concern because the other tests are not stand alone tests. They're in context with the morphology and the clinical findings in individual patients and they're more of a supportive evidence for making a classification of the cancer as opposed to deciding whether or not a patient is going to get a particular drug. So, that's the difference between the two.
COFFEY, Q.C.
Q. And from your perspective, based upon what you saw in your second visit in April of '06, you thought that the improvements not only had occurred in ER, but had occurred elsewhere and

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DR. BANERJEE:
A. That's correct.
COFFEY, Q.C.
Q. - any concerns you had about the other sorts of tests in September, had been alleviated by what you saw on your return.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. Recommendation 5, external quality assurance should be continued indefinitely and you just referred to that. In particular you refer to here, NEQAS which is -
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. From your perspective, Doctor, we've referred to the CAP approach, UK NEQAS; I gather there may even be others. Is there any one or two of them that are, from your perspective superior or if it's possible, would you enrol in the whole group?
DR. BANERJEE:
A. I think either of them are acceptable. The

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NEQAS one involves many of the hospitals because it's not only United Kingdom, but all the European countries participate in that. So, the database that they have is significantly larger than the American CAP and I think the frequency of the surveys is a little higher. So, there are more tests per year that you have to participate in.
COFFEY, Q.C.
Q. And if it's possible, for an institution such as Eastern Health's General Hospital to enrol in more than one. Is it -
DR. BANERJEE:
A. Oh yes, not terribly expensive, reasonable.
COFFEY, Q.C.
Q. So, potentially, different ones have different strengths.
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. And would be useful, if you can, to avail of the strengths of all of them, that are available.
DR. BANERJEE:
A. Yes.

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COFFEY, Q.C.
Q. In terms of external proficiency testing, at the time, Doctor, between the period '97 through 2005, the General Hospital had been so enrolled in external proficiency testing, might the problem have been detected at that point because of that?
DR. BANERJEE:
A. I think it would have been detected, certainly, I do.
COFFEY, Q.C.
Q. Recommendation 6 deals with the succession plan and simply duplicates what it referred to in the chart above. Number 7, Doctor, is organizational structure design is required to provide better technical and medical accountability. So, you're reiterating your point there?
DR. BANERJEE:
A. Yes.
COFFEY, Q.C.
Q. And subspecialization for pathologists, you're continuing to urge that. And issues around qualification of pathologist assistants in training were to be discussed. Again, you're

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urging that they adopt the Canadian Association of Pathologists guidelines, if possible.

DR. BANERJEE:

A. Yes and I think, you know, it takes time for that to happen across the country. So, most centres have worked with their existing technologists and got them trained with pathologists to do that particular job, and they often do an excellent job, but I think that whole system has to evolve to more formal level of education.

COFFEY, Q.C.

Q. Exhibit P-1143. Doctor, this is two e-mails, on the bottom of the first page here is July 12th, 2006. It's to yourself, copied to--it's actually to yourself and Dr. Cook. The subject is QC for immunoperoxidase and it's from Laurette Geldenhuys.

DR. BANERJEE:

A. Geldenhuys.

COFFEY, Q.C.

Q. Geldenhuys, I apologize, who is the section head of cytopathology at the QE II in Halifax. She writes, "Diponkar and Don, I received

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these statements from Ermina Torlakovic. Since we discussed this issue in an executive meeting recently, I thought you might find these interesting. I attach". And then if we go to the next page of the exhibit. There's a document entitled "Proposal for establishment of a national external quality assurance program for clinical/diagnostic immunohistochemistry" and this thing goes on for a number of pages. And covers the topics including class one, two and three tests, methods and describes and outline, at least, or proposal for an organization that would be called CIQC. Doctor, what was this about?

DR. BANERJEE:

A. This was actually happening parallel, this initiative had been started with two pathologists, one from British Columbia and Dr. Torlakovic who had been thinking about the whole issue of quality assurance, immunohistochemistry and the lack of a national system. So, they had been working on this for a while to come up with a proposal and it was very timely because of the situation we were dealing with in Newfoundland

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and the CAP executive becoming interested in the issue of creating such a national program. So we encouraged Dr. Gilks from Vancouver General Hospital and Dr. Torlakovic, who had been working on this, have encouraged them to submit a formal proposal to us. Unfortunately, they focused on the more--the classification type of immunohistochemistry, as opposed to the predictive immunohistochemistry. So we actually advised them to change their priority because we felt that the smaller subset of breast biomarkers should be their first priority, rather than a second priority. So they have now created such a system and have actually sent out surveys to various hospital labs across the country, and the initial results are encouraging, but not all hospitals have participated. So it requires further evolution.

COFFEY, Q.C.:

Q. And Doctor, this is, I take it, this encouragement that they go with or concentrate initially on the--I think what she would refer to here as class two tests?

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DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. Originally, their proposal, as set out here, was that they would concentrate on class one tests as described here?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. I take it that you, as you just told us, they--your suggestion was "look, we have--you should concentrate initially on class two." They accepted that?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. And they've moved on it?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. Why the focus on class two, as opposed to class one tests, from your perspective? Why the need to do class two first?

DR. BANERJEE:

A. Well, the class two tests are those that

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actually trigger a specific medical decision. Based on the test result alone, regardless of everything else, and therefore class one, which is really an adjunct to morphologic diagnosis, doesn't trigger that specific medical decision. So we felt that if labs are having difficulty with immunohistochemistry, it's better to fix our efforts or focus our efforts on those tests that make the biggest difference in medical decisions. So that was why we chose class two.

COFFEY, Q.C.:

Q. And I take it that's a process of prioritization?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. Doctor, if we could look, please, at Exhibit P-2273? Now Doctor, I believe this is styled--this is a portion of a document that's styled executive meeting July 15th, I think, 2006. Items for discussion, and under--we go down through the page here, there's a reference to restructuring post graduate medical education, and I will be coming back to that with you.

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But, not this particular thing, as that subject in general, but 5.2, quality benchmarks workload, and the following is attributed to you, "Dr. Banerjee noted that CAP needs to get some standards and the time is right to set some standards" I'm sorry, "and the time is right to discuss with the provinces. A letter was sent to the provincial pathology presidents and to date, responses have been received from five provinces." I know one of them is from Paul Neil of Newfoundland and Labrador. "The purpose of the working group is to summarize all available published literature and international recommendations pertaining to pathologist's workload, manpower planning, and to develop a comprehensive national position paper on recommended pathologist workload as applied Canadian medical practice. This needs to be discussed further and we brought forward to the old and new executive meetings."

So I take it this is dealing with and trying to set some benchmarks for workload across the country?

DR. BANERJEE:

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A. That's right.

COFFEY, Q.C.:

Q. And then paragraph 5.4, titled "national standards for laboratories and immunoperox" I'm sorry, "immunohistochemistry testing. Dr. Banerjee noted that a hand-out was circulated regarding the proposal for the establishment of a national external quality assurance program for clinical diagnostic immunohistochemistry. The proposal was prepared by Dr. Torlakovic," I think you pronounced her name, "and Dr. Gilks. A quick review of the proposal brought forth a few areas of concerns, in particular last paragraph on page four regarding the class two tests and HER2. The members were asked to carefully read over the proposal and forward their comments by e-mail to Dr. Banerjee. The need to develop a working group with the medical and radiation oncologists, cancer societies, CAPCA and CCQLM is in progress."

Now Doctor, in relation to this, this was an executive CAP meeting, I take it?

DR. BANERJEE:

A. Yes, it was.

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COFFEY, Q.C.:

Q. Middle of '06, and the proposal in question that was being referred to here or being circulated, I take it that's the one we saw or one similar thereto, the one we just looked at?

DR. BANERJEE:

A. Yeah, I think it was the same proposal.

COFFEY, Q.C.:

Q. Same one, and you've referred to, or the notes here refer to "a few areas of concern, particularly the last paragraph on page four regarding class two tests and HER2."

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. And is that the concern you just referred to then?

DR. BANERJEE:

A. Yeah, I believe that was regarding which priority they had set for the national program.

COFFEY, Q.C.:

Q. Which is what you just described.

DR. BANERJEE:

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A. Yeah.
COFFEY, Q.C.:
Q. And need to develop a working group with the medical and radiation oncologists, cancer societies, CAPCA and CCQLM is in progress." How did that go, Doctor?
DR. BANERJEE:
A. Didn't go very well. There was some initial positive responses back, but I think it's the age-old problem as to who's driving the process, and somebody else should be doing the work and "we will be happy to help out," that sort of response. So it's very difficult to get people to look beyond their own particular domain and look at the bigger picture. There's a lot of inertia and I would say that we have not yet developed an effective working group, but there's still comments made whenever I talk to people or call them up or meet them at meetings that "yes, yes, this is an important issue. We need to get to it," but there's a lot of inertia.
COFFEY, Q.C.:
Q. Doctor, here, if we could, CAPCA is what? CACP--CAPCA is what?

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DR. BANERJEE:
A. I believe that's the Canadian Association of Provincial Cancer Agencies.
COFFEY, Q.C.:
Q. And the CCQLM?
DR. BANERJEE:
A. I can't quite remember what that stands for.
COFFEY, Q.C.:
Q. Okay, and Doctor, here in the paragraph 5.5, just a point for the Commissioner, to bring to her attention, there's a membership update and pathology assistants are referenced and "Dr. Banerjee noted that there are 26 PAs who have joined CAP as associate members and indicated that it is encouraging to see that so many joined." So in terms of the pathology assistants and where they are in the medical world, they are invited to join the Canadian Association of Pathologists?
DR. BANERJEE:
A. Yes, we felt that they needed to be invited to join so they could feel that they're part of the team, and not, you know, off on their own, and there was a lot of enthusiasm, so lots of people joined up, and we have special programs

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for them at the annual meetings.
COFFEY, Q.C.:
Q. Exhibit P-2432.
THE COMMISSIONER:
Q. Mr. Coffey, we'll take the afternoon break after you deal with this one.
COFFEY, Q.C.:
Q. Thank you, Commissioner. This is a letter, Doctor, from the Canadian Cancer Society of August 25th, 2006. Actually, perhaps if I could, because I could deal with these both together, Exhibit P-2433? Doctor, this is a letter--it appears to be a form letter, September 18th, 2006. It's for your signature. It's addressed to a number of different agencies, Canadian Strategy for Cancer Control and so on. They're all listed here at the bottom of the page, cc'ed to, and it's regarding the establishment of national standards for laboratories immunohistochemistry testing. And if we could go back then to Exhibit P-2432? About three weeks before that, you had received this--or letter dated three weeks before that, August 25th 2006, from the Canadian Cancer Society.

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The subject is the establishment of national standards for laboratories immunohistochemistry testing and they thank you for your letter about your interest in collaborating with the Canadian Cancer Society and it's stated here that they "agree that national standards are important for laboratories. Please feel free to contact Paul Lapierre, who's the director of public affairs and cancer control," and there's a note here "Diponkar has only heard from CSC and Dr. Bert Schacter"
DR. BANERJEE:
A. Brent.
COFFEY, Q.C.:
Q. Brent, I apologize, Brent Schacter.
DR. BANERJEE:
A. Yeah.
COFFEY, Q.C.:
Q. Of CAPCA, and these are Dr. Cook's notes, I believe.
DR. BANERJEE:
A. Yes, yes.
COFFEY, Q.C.:
Q. So Doctor, I'm just going to bring those to

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your attention and we'll come back then and I want to take this up then to ask you a final set of questions.

DR. BANERJEE:

A. Thank you.

THE COMMISSIONER:

Q. Afternoon break.

COFFEY, Q.C.:

Q. Thank you, Commissioner.

THE COMMISSIONER:

Q. Thank you.

(BREAK)

THE COMMISSIONER:

Q. Please be seated. Mr. Coffey.

COFFEY, Q.C.:

Q. Thank you, Commissioner. Doctor, I wanted to ask you then, if I could, Doctor, about really the subject matter of the caption of these two letters we just looked at before the break, establishment of national standards for laboratories and immunohistochemistry testing. In particular, if we could look at Exhibit P-2433? Here, Doctor, and I take it, did you send this letter on actually afterward, Doctor?

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DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. And to the bodies listed at the bottom here?

DR. BANERJEE:

A. That is correct.

COFFEY, Q.C.:

Q. I take it that this grouping listed under the cc here are in effect, in one sense, a who's who of cancer treatment throughout the country?

DR. BANERJEE:

A. That is correct.

COFFEY, Q.C.:

Q. Not necessarily exhaustive, but certainly a who's who.

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. You've written then, Doctor, that "the Canadian Association of Pathologists, representing over 940 pathologists, wishes to develop a national external quality assurance policy in laboratory medicine immunohistochemistry and would welcome the

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opportunity of working collectively with you on these national standards." Now just before I go on, Doctor, 940 pathologists, Canadian Association of Pathologists, are all Canadian pathologists members of that association?

DR. BANERJEE:

A. No, they're not.

COFFEY, Q.C.:

Q. So approximately how--what proportion would be?

DR. BANERJEE:

A. I think probably just over half.

COFFEY, Q.C.:

Q. So that would mean that there, at least in '06, probably were under 2,000 pathologists in Canada?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. You go on to say then, went on to say, "at the moment, there are different tests, systems and applications used across the country with little or no consensus on quality assurance, inconsistent protocols, valuable criteria"--I'm sorry, "variable criteria for

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interpretation. This is a very high risk area and by not having national standards on quality assurance, we will be looking at high costs down the road. We strongly feel that the government needs to be made aware of the importance of having national quality assurance of laboratories, laboratory tests and the interpretation of the results. Our plan is to form a coalition working group to develop national standards for laboratories, particularly for immunohistochemistry testing. This group consists of several stakeholders" and you've listed them below, "would then prepare a business plan and present this to the government as a group. We believe by working together, our voice will be heard and acted upon by government. An additional item for discussion is the timely introduction of biomarker tests in order to facilitate patient selection for targeted therapies across the nation with a clear national process for evidence based decision making and a consistent mechanism of credentialling and funding laboratories to perform these medically necessary tests. Failure to address

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this will lead to inconsistent access to targeted therapies and inappropriate therapy or denial of therapy triggered by false positive or false negative tests respectively. I will follow this up with a phone call to discuss the possibility of collaboration. In the meantime, please feel free to contact me" at your e-mail address "with any questions and comments. The Canadian Association of Pathologists looks forward to working with you on this important and much needed policy. Sincerely yours."

Now Doctor, I'm going to ask you a question and then I'm going to let you answer, continue as--and I would ask you in as full a manner as you can possible, how had these state of affairs come about? How had we come to this point in the middle of 2006?

DR. BANERJEE:

A. Well, I think partly it's related to how knowledge is generated, how knowledge is applied to clinical care and how different specialty groups, professional groups look after cancer patients and how they interact. So in general I would say that medical

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discoveries come at us at a rate beyond our capacity to implement because there is no formal process by which we review the evidence for changing practice, whether it's radiation oncology, medical oncology, all of them face the same problem, pathologists face the same problem. It's the rate at which basic science discoveries are going to impact clinical care has reached a point where the application of discoveries is going to be the biggest bottleneck we have, and that is largely historically related to how research is funded, how clinical care is funded and the validation process in between the research discovery and the application to clinical care is funded. And this is true world wide; I'm not blaming Canadian granting agencies, but Canadian granting agencies fund basic research and they fund clinical trials which are, in essence, testing new drugs against standard therapy to see if they're any better. What's happening now is because of the human geno project. The knowledge of human genomics and the fallout of that is such that we know that our current practice in making medical

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decisions about individual patients requires a complete redesign. In the cancer field, if you look at drug-based therapies in general, not just in oncology, it is known that about 40 percent of drugs don't actually work. If you look at oncology across the spectrum of cancer types, 75 percent of drugs don't work. In other words, there is no clinical benefit. And the problem is due to the fact that drugs are approved on the basis of clinical trials and the outcome of that clinical trial may show a benefit to a group of patients. But what human genomics had taught us is that each individual has his or her own characteristics on top of what the cancer genes tell you so that even if a drug works on, say, 25 percent of patients in a particular category, we don't know exactly why it worked and why the 75 percent that didn't respond did not respond. But there's clearly evidence coming out that there's something about the genetics of the tumour itself and the patient that actually influences how they respond to a particular drug. So the industry in terms of the pharmaceutical industry is moving towards

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targeted therapies, ie, they target a particular gene or the product of that gene with the hope of having more effective therapies. At the same time they realize that that therapy cannot work for everyone unless they express the target in the tumour, and they don't all express the target, so what you need is some process by which we identify those patients that express the appropriate target and therefore would be eligible for therapy using those targeted therapies. That means you have to then design a test that looks at the target to make sure it accurately reflects the presence of that target in the tissue and it withstands formalin fixation, all of that sort of stuff. So that process by which we validate a research finding and make it a practical kind of test for clinicials to make decisions on is not funded by anyone, nobody funds it, not the granting agencies, not the health care systems. It's a completely neglected area of development. So what we try and do is, again, using evidence-based decision making, look at options whereby we can introduce those tests without a clear

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funding mechanism for it. So we might say we're going to replace this old test with a new one and hopefully can do it for the same money or less, automated, etcetera. It's a hit or miss game; and there is no process in any province that actually has a logical step wise decision-making process that says if the medical oncologists now want to bring in another targeted therapy against whatever cancer, that that process by which the government decides to approve that therapy and fund it has to be packaged with a patient-selection testing process. Right now it isn't packaged that way, so they might approve the drug, but when the labs ask for the funding for the test, they say, sorry, we don't have any money for you guys, just figure it out yourselves. Well, that may have worked in the past because of, you know, getting rid of obsolete tests and improving efficiencies, but labs across the country have gone through all the efficiency gains, they've down sized, etcetera, etcetera, so that buffer zone is no longer available. So I keep arguing with our oncologists saying that the next time you ask

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for a new drug and it requires a predictive test, you should package your request appropriately so the test is also funded, which is a very, very small fraction of the total cost of that particular therapy.

COFFEY, Q.C.:

Q. Doctor, just in a concrete way here on this, as an example, Herceptin.

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. Targeted therapy and the HER2/neu.

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. Herceptin being approved and I think -

DR. BANERJEE:

A. And the test -

COFFEY, Q.C.:

Q. - we've seen some evidence that it happened in Newfoundland, for example, at one point in this scenario that we've heard. And you're saying that, well,, okay, it's all very well and good to fund Herceptin, to agree to make, accept the oncologists' proposal that that be

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done?

DR. BANERJEE:

A. Um-hm.

COFFEY, Q.C.:

Q. But what about the HER2, funding the HER2/neu tests required to decide whether the individual patients should, or it's appropriate to give them?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. Herceptin?

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. Is that an example of -

DR. BANERJEE:

A. That is the, that's the primary example, that's the prototype of what's to come.

COFFEY, Q.C.:

Q. Okay. I apologize -

DR. BANERJEE:

A. And governments have not understood the issue. So a $45,000 drug is funded which you multiply by the number of patients available for the

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drug, it's in the millions of dollars. The test itself may cost less than $100 per patient and that doesn't get funded. So what's the logic in that?

COFFEY, Q.C.:

Q. I'm sorry, Doctor, I interrupted you.

DR. BANERJEE:

A. So since health care is a provincial jurisdiction that there's variability in how provincial ministries of health deal with these kinds of issues, I would say that it has been not a systems approach but more like an ad hoc approach, so if you make a case, you might get the money, the drug gets funded but the test is not funded. Some provinces have funded the test. In British Columbia it is not funded, so we have had to find resources from within the budget to do it. That means probably denying something else that we could be doing for other patients' benefits. So this has to be addressed across the country and there has to be an understanding of the future of cancer therapy is going to be more and more targeted. There are approximately 2600, probably more than that by now, new

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drugs in the pipeline in development which is all targeted types of therapies, so each one of them will need a test for patient selection. Now, who's going to do that and how well is it going to be done? And if the patients know that, you know, they're all desperate for something that'll work, and if they know that is the test result that influences the decision whether or not they get the drug and there's no quality assurance in the system -

COFFEY, Q.C.:

Q. In relation to the test?

DR. BANERJEE:

A. - they'll go shopping for a lab that can produce a positive result. And who knows whether that's a real positive, you know. So I think it's, it's a huge risk to patients in not addressing this problem.

COFFEY, Q.C.:

Q. And how has it come about, Doctor, that from your perspective there have been at least not the appropriate efforts to address it at least -

DR. BANERJEE:

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A. Yeah, I think it's because although we have organized cancer systems in various provinces that the individual specialties within a cancer care delivery system tend to focus on their particular subspeciality. They don't necessarily wish to address the system approach and the way they are funded influences that. So if a medical oncology department needs funding for a new drug, there is a process for them to fight for funding, and they will do it regardless of whether or not the tests required for that drug is required to be established in the lab. So Herceptin got approved in British Columbia before we had any funding for the test. So the next drug that they'll go after will have the same problem and then what will happen is we will say, well, we don't have the test established, it's not funded, we can't offer it to you, so then they'll have to send all that stuff to the United States to some other lab that has the test set up and that's going to cost us probably three times what it would cost us to provide the test locally. So all of this is going to come to a head unless

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people are willing to look at the entire system in some kind of logical manner and ministries have to fund patient care in a more holistic manner as opposed to, well, we have only so much money, we'll give you this amount of money for the drugs and you worry about, you know, how you're going to pay for the pharmacists, the nurses to deliver the drugs, that's your problem and for the labs to provide the test, that's your problem. Well, you know, there isn't enough money in the system for us to keep adding to the burden of the lab without giving something else up. And we have reached a point where we can't give anything up without affecting other patients in their care.

COFFEY, Q.C.:

Q. Doctor, other than--just looking at the second-last paragraph of your letter and, of course, even thinking about Herceptin and the HER2/neu test, testing process, in principle really is there any difference between the target therapy of Tamoxifen or any Aromatase inhibitor -

DR. BANERJEE:

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A. No, it's the same principle -
COFFEY, Q.C.:
Q. - and ER/PR, the ER/PR in that world function is the correspondence to the HER2/neu test and the Tamoxifen corresponds to the Herceptin in terms of the targeted -
DR. BANERJEE:
A. Yes, it's the same principle.
COFFEY, Q.C.:
Q. Same principle.
DR. BANERJEE:
A. One could ask why was this not an issue when Tamoxifen and ER became relevant in breast cancer and part of it is that it happened during an era where budgets were reasonable and annually the increments were reasonable, but that's no longer the case. Also, the drug costs were quite low. Tamoxifen is not an expensive drug compared to Herceptin or the new targeted therapies. Those are in the tens of thousands per patient. So that, you know, the economics of the argument are significantly different now.
COFFEY, Q.C.:
Q. Doctor, in respect of the ER and PR testing,

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you pointed out there are different test systems and applications, I take it, with little or no consensus on quality assurance, inconsistent protocols and variable criteria for interpretation. Would that apply in Canada to ER and PR?
DR. BANERJEE:
A. Oh, yes, yes.
COFFEY, Q.C.:
Q. And how can, again, looking back on it from your perspective having worked in pathology in Canada for decades, how had that come about in an era when even at times going back at one point there was money, perhaps going back to the '80s, how could there be a situation where IHC, ER/PR testing gets introduced, utilized, but it varies, as it does, I gather, across the country, different approaches, you know, no requirement for quality assurance, external proficiency testing, how could that come about?
DR. BANERJEE:
A. Because no one takes responsibility for any of those issues and the, if you look across the country how labs are funded, that's variable

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too. So if I was running a private sector lab, I would bill the government for the work I would do and I would get paid, so it's volume sensitive funding. If I work in a public sector hospital lab, then, particularly the cancer agency, everything we do is not billable to the government, it's block funding and the block funding was based on when the cancer agency was first created in 1935 or something like that, and then there was some incremental funding on an annual basis out of which administrators would decide how much the lab got and how much everybody else got, et cetera, et cetera. So the basic problem is there is no volume sensitive funding mechanism, there is no process by which you add new tests to the fee schedule. In some provinces, there is no fee schedule; other provinces there are. In British Columbia there's a fee schedule for certain tasks, but not others, so it's a hodge-podge of things. Compare that with the American system, everything is billable and everything is listed and there is a consensus on the cost of every test because there's a daily or at least

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annual battle between insurance companies and the health care providers, but at least there is some volume sensitivity. We don't have that in Canada.
COFFEY, Q.C.:
Q. Doctor, I want to ask you about the matter of the Royal College of Physicians in Canada, okay, in terms of whether or not they are involved, at least from your perspective or have been to date involved in the concerns or trying to address the concerns for example raised in the letter which is on the screen here.
DR. BANERJEE:
A. Absolutely not, the Royal College has not been interested in the practise of subspeciality or the speciality groups, other than their certification and now continuing education towards maintenance of certification; however, they have not been involved in manpower planning. They have not been involved in creating a more dynamic curriculum for training of pathologists. There is still training in the mode that we train people in the early 60's and 70's and the newer

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technologies are considered, new technologies that require maybe some elective time during training and perhaps some of them have matured to the point of being mandatory, but they are fairly short training periods and it's insufficient for these programs to actually generate trained pathologists who are fully versed in these technologies, that is something they have to learn after their Royal College certification, so that they do through informal connections with reference laboratories or fellowship training beyond the Royal College training et cetera. It's not an organized system. The Royal College and the Canadian Association of Pathologists have over the years had significant differences of opinion on the future of pathology and we continue to have those discussions. There's been a trend recently to go against the whole evolution of subspecialization, the Royal College feeling that they need fewer specialities and fewer subspecialties and we feel the opposite, that for good patient care, we actually need to specialize even more because the knowledge base required for

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generalists is so huge that they cannot keep up with everything, so that's something we've challenged the Royal College on on a number of occasions and we've had some positive response from them. They reversed some decisions recently, but they still haven't grasped the whole issue of quality assurance and lab medicine as their responsibility, unlike the British Royal College of Pathology and the Australian College of Pathology who are not just involved in education, but they actually have significant programs in quality assurance across the country.

COFFEY, Q.C.:

Q. I was going to ask you about that point, Doctor, because what the situation is to your knowledge or your understanding in, for example, the UK and Australia in that regard, in terms of the colleges. For example in the UK, the pathologists in the UK, are they part of the college at large or do they have their own college?

DR. BANERJEE:

A. They have their own college, as do the Australians.

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COFFEY, Q.C.:

Q. As do the Australians.

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. And your understanding is what then in terms of what sorts of activities are those colleges involved in, in comparison to the situation in Canada for pathologists.

DR. BANERJEE:

A. Well those colleges are involved in setting the curriculum for training programs, they're involved in setting the examinations, certification of pathologists and also running quality assurance programs which are mandatory, particularly in Australia. In the United Kingdom, I'm not sure whether it's entirely the role of the Royal College or their other NEQAS group is probably an independent, but same faculty involved in that effort. In the Australian Royal College, they do all of the quality assurance, licensing of laboratories across the country, so they are very much involved in that and that's mandatory. Americans have a similar system,

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the College of American Pathologists are involved in accrediting labs and inspecting labs, et cetera, so it's a national process which works very well.

COFFEY, Q.C.:

Q. In those three other countries.

DR. BANERJEE:

A. That's right.

COFFEY, Q.C.:

Q. And that's not true in Canada?

DR. BANERJEE:

A. No.

COFFEY, Q.C.:

Q. Now, Doctor, having sent out your letter, what happened?

DR. BANERJEE:

A. I got a few responses, some, I think just one in writing, a couple by telephone indicating an interest in the issue. There were quite a few that did not respond.

COFFEY, Q.C.:

Q. Doctor, I wanted to ask you about, perhaps if you could give a brief overview to the Commissioner of how the BC Cancer Agency operates in terms of its involvement

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throughout British Columbia, and particularly in relation to pathologists and pathologists' work, not only in the urban areas, but in the more rural or less urbanized areas, how does that work?

DR. BANERJEE:

A. So as you know, the British Columbia Cancer Agency is a provincial entity, it provides cancer care for patients throughout the province. They are predominantly designed as treatment centres, so radiation therapy, medical oncology, chemotherapy or systemic therapy as they call it, they are not really involved in the initial diagnosis or surgical procedures, those are done outside of the cancer agency. They don't have any jurisdiction over that, so they don't have any jurisdiction over the pathology quality in the various hospitals where the surgery is being done. However, as we have discussed earlier, the oncologists over a number of years have realized that there are significant problems with some of the reports and it's hard to predict which report has a problem by reading the report, by looking at the slide, so we now

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have a policy that requires some central review or review, not necessarily centrally, but by pathologists who are credentialed as consultants to the cancer agency that may be working out of other hospitals, like Vancouver General Hospital, et cetera. So those individuals are specifically credentialed and I have a role in selecting those individuals and credentialling them through the Medical Advisory Committee and the hospital board, et cetera. That means that we have jurisdiction over their practice, in terms of the review of pathology or signing out of pathology for cancer patients; however, we don't have any jurisdiction over pathologists in other hospitals and therefore, we have this policy of second opinion type review, take another look at the slides, the original slides from various hospitals and issue a review report which may or may not change the interpretation of a particular case or change the medical management of a particular case. Now we don't review every cancer patient in the province because, as I said, if they're presenting in fairly late stages, the initial diagnosis of

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it, at a stage where they already have metastatic diseased, then we don't believe that we would provide any value to the management of that patient through the review process. So each tumour group, so there are I believe 14 different tumour groups in the cancer agency dealing with particular organ sites where cancers occur, and through those tumour groups, guidelines have been developed in terms of what happens when a patient is referred to a cancer centre for therapy and whether or not a pathology review is required and those are all posted on the website, it's publicly available. So for breast cancer they have particular rules; for lymphoma there are particular rules, et cetera.

COFFEY, Q.C.:

Q. So the cancer agency of which you're the head, you're involved in accrediting, did you use the word "accrediting" of certain pathologists?

DR. BANERJEE:

A. Credentialling.

COFFEY, Q.C.:

Q. I apologize, credentialling is the word, I

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thought I had it wrong.

DR. BANERJEE:

A. We don't accredit the labs.

COFFEY, Q.C.:

Q. No, I appreciate--so the credentialling of individual pathologists who--and the effect then of you credentialling them is what?

DR. BANERJEE:

A. Number one, that they are accountable to the cancer agency and if they are the primary pathologist who signs out a report after a surgical procedure, then we would accept that report without further review, unless an oncologist wishes to have it reviewed, for whatever reason and it's their right to ask for that review.

COFFEY, Q.C.:

Q. And if you receive a report from a pathologist that is not credentialed by your organization, then there is a second look -

DR. BANERJEE:

A. A second look as long as it follows the guidelines for that (unintelligible) group, we don't look at everything.

COFFEY, Q.C.:

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Q. And this is pursuant to an understanding or an agreement you had with the oncologist groups.

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. Doctor, I have one other actual question I wanted to ask you about, one other topic, you did indicate to us that, and certainly while you were involved in St. John's in 2005 and 2006, you weren't aware of Ms. Wegrynowski's involvement.

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. And I understand that yesterday, I believe you had the opportunity to receive a copy of her reports?

DR. BANERJEE:

A. That's correct.

COFFEY, Q.C.:

Q. And you have reviewed them?

DR. BANERJEE:

A. Yes.

COFFEY, Q.C.:

Q. I appreciate at times it may be difficult to

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tell what one might have done in hindsight, but if you had been provided with copies of those reports back in 2005 and 2006, would it have made any difference to your approach?

DR. BANERJEE:

A. I don't think it would have made a difference to my conclusions, but I think I would certainly have preferred to have seen that report because perhaps some of my recommendations would have been in greater detail, particularly on the technical side. So it would have helped, but the overall impression of the problem would not have changed.

COFFEY, Q.C.:

Q. Would not have changed. Fixation, better education, internal controls -

DR. BANERJEE:

A. Right.

COFFEY, Q.C.:

Q. Optimization of stains.

DR. BANERJEE:

A. That is correct.

COFFEY, Q.C.:

Q. That whole approach. Commissioner, they are

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the questions I have.

THE COMMISSIONER:

Q. Thank you. Mr. Pritchett.

MR. PRITCHETT:

Q. Thank you, Commissioner, I don't have any questions for this witness.

THE COMMISSIONER:

Q. Mr. Simmons.

MR. SIMMONS:

COFFEY, Q.C.:

Q. Thank you, Commissioner.

DR. DIPONKAR BANERJEE, EXAMINATION BY DAN SIMMONS

MR. SIMMONS:

Q. Good afternoon, Dr. Banerjee. We met yesterday. I'm Dan Simmons, I'm the lawyer here for Eastern Health. I have a few specific things I want to follow up with you, but first I want to thank you for your detailed and thoughtful evidence that you have given so far, because I'm sure it's going to be of quite a bit of assistance to the Commission. When you came here for the first visit in the fall of 2005, you've told us how you reviewed about 20 of the slides or cases that had originally been tested using the DAKO

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autostain or technology and before your arrival had been retested on the Ventana technology. And I understand that you had the opportunity, went to explain to look at the original slide from the first test and then the subsequent slide.

DR. BANERJEE:

A. That's correct.

MR. SIMMONS:

Q. And the H&E slides also?

DR. BANERJEE:

A. Yes.

MR. SIMMONS:

Q. And from looking at your report, what you described in your report is that you were of the understanding that those cases originated in 2002, that the initial tests were done in the year 2002 and had then retested prior to your visit?

DR. BANERJEE:

A. I wasn't quite sure of the date of the original testing for some of those cases. I did look at the numbers or recorded the numbers.

MR. SIMMONS:

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Q. Right, and we've seen other evidence here at the Commission to know which cases had been retested by the time of your arrival and the majority of them were in 2002, there were a small number that were from some other years.

DR. BANERJEE:

A. Uh-hm.

MR. SIMMONS:

Q. We also know that the time period for which retesting was later done at Mount Sinai covered from 1997 all the way up to 2005 and I'm just wondering if when you were here, if you made any effort or if you were asked to make any effort to review any larger time period other than that?

DR. BANERJEE:

A. No.

MR. SIMMONS:

Q. Okay. So that the conclusions that you drew regarding the reasons for the failure of the original test, would it be fair to say that those would be based on what you saw for the time period from which those particular 20 cases came?

DR. BANERJEE:

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A. That's correct.

MR. SIMMONS:

Q. And you've described for us how you were able to tell by looking at those cases that there were issues with the fixation of the tissue that had been used in the testing process that you were able to see when you reviewed those slides.

DR. BANERJEE:

A. That's correct.

MR. SIMMONS:

Q. So that tissue would have originated then at the time that the original tests were done in, largely in 2002 and if I understand correctly that same tissue was then used for the retests in 2005, that was your understanding as well?

DR. BANERJEE:

A. That is correct, yes.

MR. SIMMONS:

Q. And you also told us that aside from recognizing, from looking at the slides that there was issues with the fixation, you also determined that there was likely issues with the antigen retrieval and the optimization of the antibodies for the original tests done on

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the DAKO technology.

DR. BANERJEE:

A. That's correct.

MR. SIMMONS:

Q. And do I understand correctly that that was a conclusion you were able to make because there had been a change in test results when those same blocks were retested on the Ventana system?

DR. BANERJEE:

A. That's correct.

MR. SIMMONS:

Q. And so that was not--you couldn't look at a slide and say there was bad antigen retrieval here, you had to deduce that from the change in the results?

DR. BANERJEE:

A. Not entirely correct as a statement, because the fact that the internal control, benign epithelium of the breast were, the results were negative which would tell you that potentially two explanations or combinations, fixation, antigen retrieval or both.

MR. SIMMONS:

Q. Right.

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DR. BANERJEE:

A. And when you switched platforms, it became clear that the staining protocol optimization was a significant factor because the Ventana machine could create a positive result and something was negative earlier on the other platform.

MR. SIMMONS:

Q. Would it be a fair inference to draw from your observations that either the antigen retrieval or the staining optimization or both in use when the tests were done on the Ventana, must have been improved or better in some way than the antigen retrieval and/or the staining that was used on the DAKO.

DR. BANERJEE:

A. Yes, yes, that's correct.

MR. SIMMONS:

Q. So we can conclude that whether it was the technology itself or the process that was used to implement and validate the newer system, something had made the test results better and more reliable?

DR. BANERJEE:

A. That's correct.

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MR. SIMMONS:
Q. I believe you mentioned that there are different antigen retrieval methods that can be used and that are in use in semi-automated staining systems, like the DAKO autostainer that's in use in your lab?
DR. BANERJEE:
A. Yes.
MR. SIMMONS:
Q. And I believe you mentioned microwave heating in water or in liquids, I believe, we've heard that boiling the tissue or different varieties.
DR. BANERJEE:
A. Yes.
MR. SIMMONS:
Q. For that type of system, is there any single antigen retrieval method that's regarded as preferable or the best system to use?
DR. BANERJEE:
A. I think the microwave heating system has become a preferred technology, but there are still certain antigens that require enzymatic treatment, even if you're using the Ventana system. By the way, we have switched to

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Ventana not because it's a better system, but because for economic reasons and workflow redesign.
MR. SIMMONS:
Q. And we've heard as well that with the Ventana benchmark system, which is the one that's here, that the antigen retrieval is now done as part of the automated part of the process -
DR. BANERJEE:
A. That's correct.
MR. SIMMONS:
Q. Instead of being done separately as a manual step in the process.
DR. BANERJEE:
A. Yes, the variability has been removed in that process.
MR. SIMMONS:
Q. And that was going to be my next question, by automating it, that reduces the opportunity for variability in the performance of that step?
DR. BANERJEE:
A. That's correct.
MR. SIMMONS:
Q. You've told us about the different antibodies

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that have been used for ER testing, 1D5, 6F11 and now SP1, over time have there been changes with the other reagents used in the test? As I understand there are buffers and in particular, there are what they referred to as detection kits, which are the chemicals used, I gather, to actually stain the antibodies and make them visible under the microscope?
DR. BANERJEE:
A. That's correct.
MR. SIMMONS:
Q. Have there been changes over time in the detection kits which may have enhanced the effectiveness of the testing?
DR. BANERJEE:
A. Oh definitely yes, major changes in the detection kits, they've become more sensitive, the background problem has been reduced, et cetera, so there's continuous improvement in that area.
MR. SIMMONS:
Q. You told us of your observations regarding the external control slides associated with the DAKO tests for those 20 cases that you reviewed and that you observed generally that

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you thought the intensity of the staining was weak, compared to what you would expect for a positive control?
DR. BANERJEE:
A. That's correct.
MR. SIMMONS:
Q. The slides that you looked at as part of those testing sets that have been run on the Ventana system, we know that at some point there was a step taken here which saw the control tissue being placed on the same slide as the patient tissue and I wonder if you observed any of those slides among the many cases that you did?
DR. BANERJEE:
A. Yes, I did.
MR. SIMMONS:
Q. And did you make any observations about the intensity of the staining of the positive controls on those slides that had been run using the Ventana system?
DR. BANERJEE:
A. Well on the Ventana system, clearly there was higher intensity of staining in the positive controls, as well as the test tissue.

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MR. SIMMONS:
Q. Okay. Now you've commented on the idea of the reading of both external and internal controls by technologists and I believe you've told us that it's not a universal standard in Canada that technologists would read, read those controls?
DR. BANERJEE:
A. That is correct.
MR. SIMMONS:
Q. Where the technologists have received the training and acquired the knowledge and ability to be able to read those controls, I wonder can you tell me what effect that has then on the pathologist's responsibility in relation to both the internal and the external controls? Does it displace it or -
DR. BANERJEE:
A. No, it doesn't, it just--the pathologist is still ultimately responsible for signing out a particular case, so they have to accept their responsibility.
MR. SIMMONS:
Q. You've told us about how you would deal with a case where the internal control on an ER/PR

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test is negative and the tumour is negative and that that's one where it would be called into question and you would consider that a case where you could report a result?
DR. BANERJEE:
A. That's correct. We would report the case if there was no other tissue available to stain and there was--if there was tissue available and still was negative internal controls, we would issue a report that says this is uninterpretable, so no conclusions could be drawn, but you'd still have a report.
MR. SIMMONS:
Q. Yes, so in your laboratory with the level of optimization of staining and quality control that you have, do you still at times encounter cases where the internal controls do not stain?
DR. BANERJEE:
A. No.
MR. SIMMONS:
Q. No. Earlier this afternoon, when you were asked by Mr. Coffey some questions about what opportunities there might have been to have detected this issue with the ER/PR testing

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here earlier, one of the things you mentioned was the transition from the bioassay testing method to the IHC testing method. On your visits here, either first or second visit, did you do anything to investigate or determine what had been done here when that transition was made back in 1997?
DR. BANERJEE:
A. No.
MR. SIMMONS:
Q. You haven't seen any documentation or spoken to anyone about that?
DR. BANERJEE:
A. No documentation or correlation data, no.
MR. SIMMONS:
Q. So you don't know what kind of correlation was done?
DR. BANERJEE:
A. No.
MR. SIMMONS:
Q. My final question, you had made a recommendation regarding dedication of technologists to the IHC service so that they would not have other duties outside that, and you'd observed that there had been a rotation

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system in place here. In your experience with other laboratories that you've been involved with or know of, was that something that was unique to here or is it something that you find in other -
DR. BANERJEE:
A. No, it's a very common sort of process of rotation, cross-training people between different lab sections.
MR. SIMMONS:
Q. Yes.
DR. BANERJEE:
A. Which makes sense in certain lab sections, but this is an area that requires such detailed attention to the work that I think it's not a good idea.
MR. SIMMONS:
Q. Right. I believe you -
DR. BANERJEE:
A. But not everyone can achieve that, given the resources.
MR. SIMMONS:
Q. Right, and I believe you'd said this is a recommendation you would make to any lab, to achieve that?

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DR. BANERJEE:
A. Yes.
MR. SIMMONS:
Q. Okay, good. Thank you very much. Those are all the questions I have.
DR. BANERJEE:
A. Thank you.
THE COMMISSIONER:
Q. Thank you, Mr. Simmons. Mr. Browne?
MR. BROWNE:
Q. Thank you, Commissioner. I have no questions for Dr. Banerjee. Thank you for your evidence, Dr. Banerjee.
DR. BANERJEE:
A. Thank you.
THE COMMISSIONER:
Q. Mr. Pritchett? Sorry, Mr. Eaton, you're here.
EATON, Q.C.:
Q. Don't sound so surprised. We have no questions.
THE COMMISSIONER:
Q. You are hiding behind Mr. Pike. That was what my problem was.
EATON, Q.C.:
Q. I'm glad I (unintelligible).

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THE COMMISSIONER:
Q. Ms. Newbury?
DR. DIPONKAR BANERJEE, EXAMINATION BY MS. JENNIFER NEWBURY
MS. NEWBURY:
Q. Good afternoon, Dr. Banerjee. My name is Jennifer Newbury and I represent the Canadian Cancer Society, Newfoundland and Labrador division, and I have just a couple of questions for you today. If we could bring up your report, P-0046, please, and turn to page five of the exhibit? Okay, recommendation number one, which I think is a bit lower there, you've indicated that "pathologists should subspecialize, if possible, covering two or more sites each with one designated leader for each major tumour site." And I'm wondering what your views are, if there are obstacles for a lab in implementing this, maybe on a temporary basis due to financial resources or pathologists are on leave, in that event, what are your views as to what the lab should do in terms of testing in a subspecialty area?
DR. BANERJEE:

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A. I think obviously you can't do it overnight, shift from the generalist approach to subspecialization approach, so this requires planning and you have to work with the staff you have. If you have vacant positions, then you would recruit strategically into those positions. With the existing staff, you should have a plan to send individuals to very busy pure cancer pathology service to really bring them up to speed on and, you know, become comfortable with the content that is required in the reports for specific cancer types and you keep doing that until everyone has been trained and has one or two or even three different sites that they cover. You can't have one for each site because you need too many pathologists and of course, you have to cover the service when somebody is on vacation, etcetera. So there has to be cross coverage. So it takes time to build a system like that.
MS. NEWBURY:
Q. And once that's done, I guess, the concern is with problems that may be experienced with turnover of pathologists. Is the only option

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at that point for the lab to refer tests out to another laboratory?
DR. BANERJEE:
A. For--and this is what requires discussion with the oncology departments to set some priorities as to what types of cases need to be sent out to a reference lab or service and what could be handled in house, and you know, there's different levels of complexity so you can make that sort of judgment.
MS. NEWBURY:
Q. So it's something that you think should be thought out in advance?
DR. BANERJEE:
A. Yes.
MS. NEWBURY:
Q. To have a plan in place and how to deal with it, in the event that you have subspecialists on staff, but for some reason maybe -
DR. BANERJEE:
A. Yeah.
MS. NEWBURY:
Q. - not able to avail of their services for a particular period of time?
DR. BANERJEE:

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A. Right. You sort of allow them to buy some time when they're getting into the strategic recruitment or expanding their program, they get funding and so on.

MS. NEWBURY:

Q. Okay, and are there any circumstances, I guess, if other labs--you know, we hear from time to time that other labs are also operating at maximum capacity and if other labs are not able to respond quickly enough to the needs of a lab here, for example, who need some temporary services, is there a way that a general pathologist, general anatomic pathologist could safely sign out cases in a subspecialty area? Are there any extra mechanisms that could be in place, such as additional quality assurance or additional quality control to facilitate that?

DR. BANERJEE:

A. Again, yes. The answer is yes, but it will take major effort in setting up the quality assurance processes to make sure inter observer variability is minimized, and since we know what the discrepancy rates are out there, it will be difficult to recommend that,

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that you just send it out to whoever is available. I think that would be a mistake. It's also true that across the country that capacity is saturated. So if, for instance, tomorrow you decided to send all the breast cancer cases to say the B.C. Cancer Agency, we would probably say no, because we can't handle any more work.

MS. NEWBURY:

Q. Okay, and on page four of this report, it's actually four of the exhibit, under conclusions about the reasons for test failure, item number two, "Is the Ventana system too sensitive? There's no evidence that the Ventana system creates false positive results. However, the system still requires optimization to avoid non-specific cytoplasmic staining" and you've explained that in some detail this morning.

DR. BANERJEE:

A. Um-hm.

MS. NEWBURY:

Q. Did your review of slides, when you were here in October of 2005 and on your subsequent visit, did it include any positive test

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results or were they all negative?

DR. BANERJEE:

A. No, they included samples that were positive, and in the first visit, we're comparing the two different platforms, so the same cases stained by the two different systems. So there were obviously those that had converted were definitely positive on the Ventana system. And the second visit, we essentially looked at the Ventana output, in terms of further optimization and they had done a very good job.

MS. NEWBURY:

Q. So the test results that you looked at, they were all--were they all of the same category, initially ER negative -

DR. BANERJEE:

A. Yes, that's right.

MS. NEWBURY:

Q. - on DAKO and then converted to Ventana.

DR. BANERJEE:

A. That's correct.

MS. NEWBURY:

Q. Were any of the DAKO tested slides positive?

DR. BANERJEE:

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A. Oh yes, there were.

MS. NEWBURY:

Q. Initially reported as positive?

DR. BANERJEE:

A. Yes.

MS. NEWBURY:

Q. You had a random sampling of both?

DR. BANERJEE:

A. Yes, we had a random sample.

MS. NEWBURY:

Q. Okay, and on either of the platforms for the slides that you looked at, and taking into account your observations, particularly with the Ventana there might have been some non-specific cytoplasmic staining, and also considering that there appears to have been no quality assurance in place at the time, do you have any concerns about the possibility of false positive results?

DR. BANERJEE:

A. Not for estrogen receptors.

MS. NEWBURY:

Q. And why is that?

DR. BANERJEE:

A. It's highly unlikely. But for HER2, there's

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definitely risk of false positive stain.

MS. NEWBURY:

Q. And why would you not have any concern about false positive results, given the issue that you observed about the non-specific cytoplasmic staining?

DR. BANERJEE:

A. Because if you see the staining in the cytoplasm, you disregard that in your assessment. It has to be nuclear stain.

MS. NEWBURY:

Q. Okay. So in your view then, if the pathologist who reported various tests during the time period, either on the DAKO platform or the Ventana platform, was aware that you've got to be careful, you shouldn't interpret non-specific cytoplasmic staining to be a positive test, then you shouldn't have false positive results?

DR. BANERJEE:

A. That's correct.

MS. NEWBURY:

Q. What if that was not well known to the pathologists?

DR. BANERJEE:

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A. I would be surprised if they didn't know that.

MS. NEWBURY:

Q. Okay.

DR. BANERJEE:

A. So it's more about optimization of the technique, as opposed to interpretation I was concerned about.

MS. NEWBURY:

Q. So your concern then, when you saw evidence of non-specific cytoplasmic staining, is that it's an indication that the test hasn't been optimized?

DR. BANERJEE:

A. Right.

MS. NEWBURY:

Q. As opposed to it being an indication that there might be false positive results?

DR. BANERJEE:

A. If there was a case, and I don't recall seeing such a case, that the nuclear staining intensity was the same as the cytoplasm, then I would definitely question that because then you don't know whether it's all non-specific staining.

MS. NEWBURY:

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Q. Okay, right.

DR. BANERJEE:

A. It's the pattern of staining that's also important.

MS. NEWBURY:

Q. Okay, and there's nothing that caused you concern in the 20 slides, I guess, that you looked at?

DR. BANERJEE:

A. No.

MS. NEWBURY:

Q. About false positive results?

DR. BANERJEE:

A. No.

MS. NEWBURY:

Q. And to rule that out as a possibility, do you think that a larger review would be required of tests that had been initially reported as positive? Because you were focusing on those that had converted from negative to positive.

DR. BANERJEE:

A. Well, if they were reported as positive using the appropriate cutoffs, so anything that they were using maybe ten percent or 30 percent, would be in the upper range anyway, so in

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terms of the decision making about the individual patients that would have been appropriate, so I'm not concerned about that. I'm more concerned about the ones in the lower end of the scale that were called negative and didn't receive the therapy.

MS. NEWBURY:

Q. Right. In terms of the external quality programs, you've referenced this on page six of your report, page six of the exhibit. You said that "the laboratory should subscribe to external quality assurance programs, such as CAP or NEQAS, and should continue to monitor performance by interlaboratory comparisons with large--with appropriate large volume teaching hospital laboratories in Canada or the U.S." What do each of those three types of quality assurance programs, the CAP, the NEQAS and the interlaboratory comparisons, what do they assess and I guess, specifically, what do they each capture in terms of technical versus clinical skills or results, and in terms of pre-analytic, analytic and post analytic issues?

DR. BANERJEE:

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A. Right. So the CAP is organized in that they will send out some unknown cases for the labs to stain and interpret, and then what they look at is the entire range of responses and see where the majority fell, and whether your lab was an outlier or not. So it's more like a consensus approach, as opposed to just saying that we're using one reference lab as the gold, you know, standard and then comparing everyone else against that. They don't do it that way.

MS. NEWBURY:

Q. Right.

DR. BANERJEE:

A. Now, the United Kingdom one is a bit of a hybrid in that they will do the same thing, but they actually look at your slides. So you have to submit your slides as well.

MS. NEWBURY:

Q. Yes.

DR. BANERJEE:

A. And also, they have, I think they have six teaching hospital labs that are their reference labs. So those are kind of the gold standard for them. So it's a different

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process, so that's why I think both have some value, but they're not equal. In terms of interlab comparisons, it's a sort of good habit for technologists and pathologists to get into, particularly when they're establishing a new assay with a new antibody, just to make sure that it's functioning as expected, to have another lab get additional slides from you from the same case and do their stain on that, and then you compare the two.

MS. NEWBURY:

Q. Okay, and so that, what you've described, it would be good practice for technologists and pathologists, how long has that been something, a technique utilized by labs, by pathologists and technologists?

DR. BANERJEE:

A. Some labs, it's always been done from the very beginning. Others, don't do it. It's not mandated by anyone, so it's really a voluntary thing.

MS. NEWBURY:

Q. Okay, and are there any guidelines in terms of percentages? For example, if you're going to

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do interlaboratory lab comparisons on an ongoing basis versus if you're doing it at the time that you're implementing a new assay? For example, are there any percentages of tests that you might send out for comparison at those two different stages?

DR. BANERJEE:

A. When you're first establishing a new assay, you should send every slide and additional slides for the other lab to stain and then look at both sets, and it's more for fine tuning. So if you're, you know, missing something or over staining, not staining issues, it would correct it. That's important. And also, if you were being reviewed because there was a central review process like we have in British Columbia, then all of that is automatically part of the review process, you look at the immunohistochemistry preparations. But in a situation like this when you are the reference centre in the province, then I think you have to look for some external reference point as well, because if you do everything just internally, your benchmark may be drifting and

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you wouldn't even know about it.

MS. NEWBURY:

Q. Right. So on an annual basis even though you're not doing anything new in that particular year, you would still send out a certain percentage -

DR. BANERJEE:

A. I think it's a good idea.

MS. NEWBURY:

Q. And is there a figure that you would have, you know, is it two percent or ten percent?

DR. BANERJEE:

A. No, I don't. But, you know, normally, you know, in audit systems they look at a ten percent retesting or review. In the United States they may be more specific sort of percentages that they would use. We don't have that in Canada, but I would say about ten percent random.

MS. NEWBURY:

Q. Ten percent random audit?

DR. BANERJEE:

A. Um-hm.

MS. NEWBURY:

Q. And 100 percent when you're setting up a new

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procedure?
DR. BANERJEE:
A. That's right.
MS. NEWBURY:
Q. And again, back to the CAP and the NEQAS, do they both capture but the technical and the clinical aspects of testing, laboratory testing?
DR. BANERJEE:
A. I think CAP is they look at the end result.
MS. NEWBURY:
Q. Okay.
DR. BANERJEE:
A. So what are you saying, is the report. Whereas NEQAS actually needs your slides and they will look at it -
MS. NEWBURY:
Q. So they can more -
DR. BANERJEE:
A. - and evaluate it.
MS. NEWBURY:
Q. - likely get into the technical issues -
DR. BANERJEE:
A. Technical as well as the professional interpretation.

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MS. NEWBURY:
Q. And the CAP is more the professional interpretation?
DR. BANERJEE:
A. That's right.
MS. NEWBURY:
Q. Now, on page 3 of your report there's a reference there to the incident problem case and I won't read through that again. But you'd indicated that it, that the incident case was invasive lobular carcinoma?
DR. BANERJEE:
A. Um-hm.
MS. NEWBURY:
Q. Which are frequently ER positive and the initial negative result should have been questioned. And you've indicated this morning, I believe, that both oncologists and pathologists probably ought have been alerted to this. Are there any basic programs for monitoring these types of trends that should be in place to look at, you know, what are we producing and does it match up with what we might expect in terms of the patient population? And perhaps you can give us an

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example by -
DR. BANERJEE:
A. No, I don't think there is such a process. And one could argue that in particular situations when we have perhaps less genetic variation of the population, you know, like small island populations, that you might see a difference skew. But I am not aware of such studies that have shown that there's some natural sort of difference in protein expression for estrogen receptors.
MS. NEWBURY:
Q. I guess -
DR. BANERJEE:
A. Population based.
MS. NEWBURY:
Q. I guess the question is there you've got a patient that's determined to be ER negative but the patient has invasive lobular carcinoma, so I guess there's still a chance, based on your statistics, that that's an accurate result for the patient because 92 percent are positive, but eight percent are negative?
DR. BANERJEE:

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A. Right. I think that the publication I've quoted has that number, but I would suspect that the eight percent that were negative were related to some technical issues.
MS. NEWBURY:
Q. Okay. So they might, in fact -
DR. BANERJEE:
A. It's not a true negative.
MS. NEWBURY:
Q. - truly have been positive?
DR. BANERJEE:
A. That's right.
MS. NEWBURY:
Q. Okay. And I think you've said earlier that from a clinical perspective it's 100 percent?
DR. BANERJEE:
A. We always see every case positive.
MS. NEWBURY:
Q. Okay. Are there any other types of cancers that might not be as strongly expected to be positive where keeping a look at what's being produced in your lab either by the oncologists or the pathologists or perhaps a cancer registry might be appropriate?
DR. BANERJEE:

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A. Yeah, it would be hard to detect those patterns unless you deliberately sort of retrospectively reviewed, at the end of the year, what you've got and what is to be expected and so on.

MS. NEWBURY:

Q. And does the BC Cancer Agency have any sort of program in place where they -

DR. BANERJEE:

A. Not on an annual basis but once the question comes up, we do review that and we certainly keep an eye on the positivity rates and where it is and what's in the literature as an expected rate and so on. In some research protocols, like the papers published by Dr. Huntsman (phonetic), they've gone back and looked at 4000 patients and, you know, the immunohistochemistry procedures seem to correlate extremely well with the biochemical data, so we're very happy with that.

MS. NEWBURY:

Q. And that's more for research purposes or is that -

DR. BANERJEE:

A. Yes.

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MS. NEWBURY:

Q. Yes, okay. Thank you very much, Dr. Banerjee.

DR. BANERJEE:

A. Thank you.

MS. NEWBURY:

Q. Those are my questions.

COMMISSIONER:

Q. Thank you. Yes, no questions, Ms. Russell? Mr. Pike?

MR. PIKE:

Q. No questions, thank you.

COMMISSIONER:

Q. Mr. Clark?

MR. CLARK:

Q. No questions.

COMMISSIONER:

Q. Anything arising, Mr. Coffey?

COFFEY, Q.C.:

Q. No, Commissioner.

DR. DIPONKAR BANERJEE, EXAMINATION BY MADAM COMMISSIONER

COMMISSIONER:

Q. Dr. Banerjee, I have one or two small things.

DR. BANERJEE:

A. Certainly.

COMMISSIONER:

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Q. If you, you might be able to help me with. And I think most of them you've addressed. But when you were discussing the role of the Royal College in standards and a role which your organization has, if you will, tried to assume, is it in your view the role of, the appropriate role for the Royal College and your organization has come in because there has been a vacuum or do you think that really is the role for the Canadian Association for Pathologists, it's the proper place for it to lie?

DR. BANERJEE:

A. Right. First of all, the Canadian Association of Pathologists is a voluntary organization. Pathologists are not obliged to be members.

COMMISSIONER:

Q. Um-hm.

DR. BANERJEE:

A. It's designed to provide some kind of annual educational experience for pathologists. It has not had the mandate to set policies, however it does set guidelines of practice. Over the years we have discussed and threatened to create our own college, royal

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college of pathologists, but that's a daunting task for most pathologists because it's a significant effort required given our fairly small membership, there won't be enough resources to do that. So one of our visiting professors from Australia was a member of the Royal College of Australia's accrediting process and I asked him how, they being the same kind of size population as Canada, how did they afford to have their own college of pathology, and he basically said all of the revenue that is generated from quality assurance and accreditation, on-site inspections is what drives the Royal College there. So it is possible to generate enough revenue to actually create a system whereby the Canadian Association of Pathologists could create their own royal college, but I think the energy levels amongst the profession right now are so low that they will probably not be galvanized into creating that process, so we are looking at alternatives. I think the Royal College has not responded to the pathology issues very well in the past and have not currently understood what needs to

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happen, so I'm not confident that they will take up this challenge and do something of value added. So we are stuck with either getting our Canadian Association of Pathology to another level of activity and require some kind of, some kind of authority to be the national body for quality assurance for laboratories and that's going to be a major battle. I mean, where is the money going to come from, who's responsible? If we look at how health care is delivered in the country, it's largely a provincial jurisdiction. There isn't really a national body that looks at funding health care activities in an organized sense. So we have some challenges because of the structure of how health care is provided in this country, how labs are funded in this country and how quality assurance activities are recognized by hospital administrators as important activities and therefore should be funded appropriately. Those are all of the challenges we are facing, so I'm not sure what the final answer is going to be. But I was hoping that the other societies that are involved in cancer patient care would see that

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this is a significant issue for them to address, as well, because, after all, they are dependent on what pathologists say for the individual patient in order to make a treatment decision, so if we are not doing a good job, then they are not doing a good job by default. And so have they truly understood that? And I'll take this moment to actually talk about something else that I feel very strongly about. There have been two major studies of the health care system in Canada, that was the Romano Report and the Kirby Report. I happened to read through those reports in great detail and did a word search for the word "pathology" in the two reports. In the Romano Report there was not a single hit; in the Kirby Report there were six hits, they're all related to speech pathology. Not a single word about labs in either document. So we are invisible to politicians, we are invisible to hospital administrators and we are invisible to the public until there's a scandal.

COMMISSIONER:

Q. To go back to the reality of your profession

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in rural areas and to bring it down to the level of ER and PR, one thing that's kind of puzzled me along the way is whether or not there is a place whereby a pathologist will see so little of a particular type of IHC test, in particular, that he or she should just not be doing it.

DR. BANERJEE:

A. I do believe that to be true. If you're asking me whether I can come up with a number, that is not possible. But I would say that there's no need for immunohistochemistry to be provided at every hospital because, number one, the turn around time requirements is such that it could easily be sent to a central lab within any province, secondly, you need that critical mass of not only pathologists who can interpret correctly, you need the technologists to understand how to troubleshoot this whole procedure, and in a small hospital lab that is not going to be possible. They'll have very limited menus, they won't have the experience to judge whether this is -

COMMISSIONER:

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Q. Well what happened in our province was that they would be sent to a central location for the purpose of processing and then sent back to a rural location for reading and -

DR. BANERJEE:

A. Reading the slides?

THE COMMISSIONER:

Q. Reading the slides by the local pathologist who might see one or two a month.

DR. BANERJEE:

A. So, even the immunohistochemistry slides were being sent -

THE COMMISSIONER:

Q. ER/PR.

DR. BANERJEE:

A. Oh, I think that's inappropriate. It should be read at the lab that's doing the staining because they know what to look for. They should be able to troubleshoot.

THE COMMISSIONER:

Q. Okay. And then there's one final thing, in your report, you referred to the business of the reporting nature within the lab.

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DR. BANERJEE:
A. Yes.
THE COMMISSIONER:
Q. And in our case, really the two divisions the lab did not meet until they got to the level of Dr. Williams, who, as you said today, that effectively made him the lab manager.
DR. BANERJEE:
A. Lab director.
THE COMMISSIONER:
Q. Lab director, thank you. So, do I assume your concern is that the place where these, if we do have this dual system, the place where they meet would be at a level where the person is a pathologist because the pathologist understands the working of the lab.
DR. BANERJEE:
A. That is correct.
THE COMMISSIONER:
Q. That's the basic principle.
DR. BANERJEE:
A. Yes, and that pathologist can report to the vice president.
THE COMMISSIONER:
Q. Because if you just leave it to the vice

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president level, the decisions are made by people who are really divorced from labs themselves.
DR. BANERJEE:
A. That's correct.
THE COMMISSIONER:
Q. And the many technical things that go on in labs that other physicians have come here and said they didn't really quite necessarily understand what was going on in the lab. It was that mystery behind the door that they were willing to leave to those who could go in -
DR. BANERJEE:
A. Well, having said that I would also have to say that that's not a unique situation. This is a model that's evolved across the country, dual management, separation of management from the medical staff. I personally think it's the wrong one, but I'm a minority as far as saying that publicly, I guess.
THE COMMISSIONER:
Q. Well, my thought process is whether it's that restructure that's required or whether it is the kind of relationship that's been developed

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with either model where due respect is given to the reviews of the other group or do you feel that it's just necessary that the final-- if it comes to that point where a consensus could not be achieved and somebody has to make a recommendation within the system -
DR. BANERJEE:
A. That's exactly right.
THE COMMISSIONER:
Q. - it should be a pathologist.
DR. BANERJEE:
A. The structure should be independent of the personalities. So, if you have a have dual management model where the lab director and the program or lab manager gets along very well, then it works. But if they don't get along very well, the structure doesn't help the situation because when things go wrong, nobody is actually accountable because they'll say, well, it wasn't my problem; it was that person's problem.
THE COMMISSIONER:
Q. Okay. Well, thank you very much.
DR. BANERJEE:
A. Thank you.

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THE COMMISSIONER:
Q. For me, I must tell you, it's been a really interesting day which I've enjoyed very much.
DR. BANERJEE:
A. Thank you very much, I really appreciate the comment.
THE COMMISSIONER:
Q. Thank you all. I'll see you at 9:30 in the morning. Oh, I think you've already been delivered of envelopes. If you haven't gotten one, there is one available for you. Thank you.
Upon conclusion.

CERTIFICATE

I, Judy Moss, hereby certify that the foregoing is a true and correct transcript in the matter of the Commission of Inquiry on Hormone Receptor Testing, heard on the 30th day of July, A.D., 2008 before the Honourable Justice Margaret A. Cameron, Commissioner, at the Commission of Inquiry, St. John's, Newfoundland and Labrador and was transcribed by me to the best of my ability by means of a sound apparatus.

Dated at St. John's, Newfoundland and Labrador this 30th day of July, A.D., 2008

Judy Moss

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