

<p style="text-align: center;">COMMISSION OF INQUIRY ON HORMONE RECEPTOR TESTING</p> <p style="text-align: center;">BEFORE THE HONOURABLE JUSTICE CAMERON - COMMISSIONER</p> <p style="text-align: center;">September 16, 2008</p> <p>Appearances:</p> <p>Bernard Coffey, Q.C. . . . . Commission Co-counsel Sandra Chaytor, Q.C. . . . . Commission Co-counsel</p> <p>Rolf Pritchard/Jackie Brazil . . . . Her Majesty in Right of NL</p> <p>Peter Browne/Jane Hennebury . . . . . Doctors Kara Laing et al</p> <p>Daniel Simmons . . . . . Eastern Regional Integrated . . . . . Health Authority</p> <p>Chesley Crosbie, Q.C.. . . . . Members of the Breast Cancer . . . . . Testing Class Action</p> <p>Mark Pike . . . . . NL Medical Association Jennifer Newbury . . . . . Canadian Cancer Society (NL Division) Blair Pritchett. . . . . Central, Western and Labrador-Grenfell Regional Integrated Health Authorities</p>	<p>THIS PAGE ONLY REVISED NOVEMBER 18, 2008</p> <p style="text-align: center;">LIST OF EXHIBITS</p> <p>EXHIBIT P-2619 . . . . . Pg. 183</p> <p>EXHIBIT P-2617 . . . . . Pg. 252</p> <p>EXHIBIT P-2618 . . . . . Pg. 253</p> <p>EXHIBITS P-2631 THROUGH 2634, INCLUSIVE . . . . . Pg. 253</p>
<p style="text-align: center;">TABLE OF CONTENTS</p> <p>DR. DAVID DABBS - RESUMES THE STAND</p> <p>Examination by Bernard Coffey, Q.C. . . . . Pgs. 1 - 74 Examination by Mr. Daniel Simmons . . . . . Pgs. 74 - 165 Examination by Peter Browne . . . . . Pgs. 165 - 200 Examination by Jennifer Newbury . . . . . Pgs. 200 - 229 Examination by Chesley Crosbie, Q.C. . . . . Pgs. 229 - 253</p> <p>DR. KARA LAING - RESUMES THE STAND</p> <p>Examination by Sandra Chaytor, Q.C. (Continued) . Pgs. 253 334</p> <p>Certificate</p>	<p style="text-align: right;">Page 4</p> <p>1 THE COMMISSIONER: 2 Q. Please be seated. Now, Mr. Coffey, we'll try 3 again. 4 COFFEY, Q.C.: 5 Q. Thank you, Commissioner. Yes, we have the 6 signal, I believe, the recording is good. 7 DR. DAVID DABBS, EXAMINATION BY BERNARD COFFEY, Q.C. 8 (CONTINUED) 9 COFFEY, Q.C.: 10 Q. Doctor, looking at P-0046 yesterday. And I 11 think at page 5 of the exhibit. And, Doctor, 12 we'd spoken of subspecialization, I believe. 13 At paragraph 5 of Dr. Banerjee's report, this 14 page refers to what he calls a disconnect 15 between the laboratory program director, 16 division manager, the clinical site chief and 17 laboratory director in decision making and 18 talks about the organizational chart 19 indicating a complete separation of reporting 20 structures in technical and clinical streams 21 with no matrices--matrix, I'm sorry, cross 22 reporting between technical and medical 23 leadership. He talks about what he viewed as 24 frustration and resentment on both sides, lack 25 of communication, lack of accountability and</p>

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1 lack of buy in. Doctor, I appreciate you, of  
 2 course, haven't visited that lab. But I'm  
 3 going to ask you about from your perspective  
 4 the importance of communication and  
 5 organization in relation to  
 6 immunohistochemistry, pathology in general and  
 7 IHC in particular.

8 DR. DABBS:  
 9 A. Yes. It's just in other areas of complex  
 10 testing, it's critically important that the  
 11 medical director knows what's going on in the  
 12 laboratory and is able to communicate  
 13 effectively among pathologists colleagues, as  
 14 well as to the laboratory administrator, the  
 15 person who is responsible for the technical  
 16 staff in the hospital to assure that whenever  
 17 issues or problems arise, that person inform--  
 18 they're brought to the attention of the  
 19 medical director who can then act on them in  
 20 communicating with the laboratory  
 21 administrator so that that person can  
 22 effectively find out what the specific issues  
 23 are with technical procedures and the  
 24 technical staff that are responsible for  
 25 performing.

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1 COFFEY, Q.C.:  
 2 Q. And I believe yesterday you indicated that, at  
 3 least in your institution, the  
 4 immunohistochemistry, the person who's on the  
 5 ground primarily responsible for it is a  
 6 pathologist?

7 DR. DABBS:  
 8 A. Yes.

9 COFFEY, Q.C.:  
 10 Q. A medical -

11 DR. DABBS:  
 12 A. Yes.

13 COFFEY, Q.C.:  
 14 Q. - (unintelligible) a doctor. Doctor, while  
 15 it's there on the screen in front of us,  
 16 there's a reference to the Sakura Express.  
 17 And Dr. Banerjee noted that in his view the  
 18 implementation of it here locally had failed  
 19 due to a lack of planning of work flow  
 20 changes. The Commissioner has heard evidence  
 21 on that. I just wanted to ask you about the  
 22 Sakura Express itself. Have you had any  
 23 experience with it?

24 DR. DABBS:  
 25 A. Yes, I did.

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1 COFFEY, Q.C.:  
 2 Q. And could you tell us, please, at least give  
 3 the Commissioner the benefit of what your own  
 4 thoughts on the Sakura Express?

5 DR. DABBS:  
 6 A. Sure. What I know about the Sakura express is  
 7 twofold. I spent a few days in Miami where  
 8 this device was actually put together and the  
 9 prototype was, and I observed their work flow  
 10 with this device. It's a microwave enhanced  
 11 tissue processor and slides can be generated  
 12 in under three hours from the time the  
 13 specimen is received. It requires a great  
 14 deal of special grossing techniques up front  
 15 with tissues cut very, very thin, and that  
 16 requires special tools. The second part is  
 17 that I had the device actually at our  
 18 institution for approximately two months. My  
 19 main interest in this was if tissues could be  
 20 processed with the molecular friendly fixative  
 21 that is marketed along with this device. And  
 22 what I did was I operated this device for  
 23 approximately five weeks, comparing specimens  
 24 that were fixed in formalin in the  
 25 conventional fashion, along with this new

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1 fixative, specifically for hormone receptors  
 2 and for HER2, analysis and I was not confident  
 3 in the outcome, the results using this special  
 4 fixative. So while that was my main interest  
 5 in exploring the Sakura, I decided that this  
 6 was not a device that could be used in that  
 7 fashion because of the unreliable results that  
 8 was given with this special fixative that was  
 9 marketed by Sakura, so I had the device  
 10 removed.

11 COFFEY, Q.C.:  
 12 Q. And when was that, Doctor, that experience?

13 DR. DABBS:  
 14 A. I don't remember the exact date, but it was  
 15 more than two years ago.

16 COFFEY, Q.C.:  
 17 Q. Dr. Banerjee in paragraph 6 here notes,  
 18 "Attendance by both medical and technical  
 19 staff at various conferences with a focus on  
 20 new technology should be encouraged.  
 21 Consensus driven innovation should be the  
 22 goal." Doctor, in the field of  
 23 immunohistochemistry, in your view is it  
 24 necessary that the medical and technical staff  
 25 that are involved in immunohistochemistry

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1 would find it necessary to continuously  
 2 upgrade their skills and their knowledge?  
 3 DR. DABBS:  
 4 A. Yes, it always is. Immunohistochemistry, like  
 5 many other areas in medicine, is a constantly  
 6 evolving discipline and there are a fair  
 7 number of conferences that are available for  
 8 medical and technical staff to attend. And in  
 9 fact, the day that I flew up here, I had just  
 10 given a small seminar at the National Society  
 11 of Histotechnologists which has a great deal  
 12 to do with immunohistochemistry, it happens to  
 13 be held in Pittsburg this year.  
 14 COFFEY, Q.C.:  
 15 Q. Doctor, now there's a reference here to  
 16 pathology assistants. Are they utilized in  
 17 the States now?  
 18 DR. DABBS:  
 19 A. Yes, to a great degree, especially at our  
 20 institution.  
 21 COFFEY, Q.C.:  
 22 Q. Yes, okay. And their role there is what?  
 23 DR. DABBS:  
 24 A. Their role there is largely to oversee  
 25 accessioning and grossing of the specimens and

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1 specimen preparation so that slides can be  
 2 prepared from tissues. Some of the  
 3 pathologist assistance are on the job trained,  
 4 many of them are also school trained, they  
 5 take masters degrees at various institutions,  
 6 and they work together to assist the  
 7 pathologists in preparing specimens to make  
 8 slides.  
 9 COFFEY, Q.C.:  
 10 Q. Doctor, there are--we looked under  
 11 "Recommendations", I'm not going to take you  
 12 through all of those, but on the paragraph 3  
 13 on page 6 of the exhibit, Dr. Banerjee's noted  
 14 that "Consideration should be given to  
 15 switching into the rapid monoclonal antibody  
 16 SP1 for ER IHC." Doctor, in terms of ER, the  
 17 ER antibodies, I think you referred to this  
 18 yesterday, you referred to the SF11, 1D5 and  
 19 SP1?  
 20 DR. DABBS:  
 21 A. Yes.  
 22 COFFEY, Q.C.:  
 23 Q. Okay. Doctor, in your view, are either one or  
 24 more of those acceptable or all of them?  
 25 DR. DABBS:

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1 A. Yes, they are.  
 2 COFFEY, Q.C.:  
 3 Q. They're all acceptable?  
 4 DR. DABBS:  
 5 A. They're all acceptable, yes.  
 6 COFFEY, Q.C.:  
 7 Q. I take it that whichever one a laboratory  
 8 chooses to utilize, that they have to optimize  
 9 for that?  
 10 DR. DABBS:  
 11 A. Correct.  
 12 COFFEY, Q.C.:  
 13 Q. Doctor, while we're on the subject, I'm going  
 14 to go back to page 4 of the exhibit, which is  
 15 under the heading, "Conclusions About the  
 16 Reasons For Test Failure," paragraph 1 and 2.  
 17 One refers to the DAKO system and two to the  
 18 Ventana system. Now, we understand, from  
 19 evidence the Commissioner has heard that the  
 20 DAKO system is what--the DAKO autostainer is  
 21 referred to, has been referred to here as a  
 22 semi-automated platform and the Ventana is,  
 23 that was being referred to here as an  
 24 automated platform. I appreciate that they  
 25 are relative terms. Doctor, do you have any

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1 views on the advantages or disadvantages of  
 2 one, like a relatively semi-automated system  
 3 such as the DAKO autostainer versus the  
 4 Ventana system?  
 5 DR. DABBS:  
 6 A. I think the only significant difference is  
 7 that the DAKO is not fully automated, and  
 8 that's not an issue. That device is used  
 9 throughout the States. It's a very robust  
 10 device. I just obtained the new version,  
 11 actually, of this device for my research  
 12 laboratory. It's a totally open system so it  
 13 has significant advantages over the Ventana  
 14 system, which is really a closed system, the  
 15 software for the Ventana system is a closed  
 16 system. So in that regard if one wants to  
 17 work up a variety of basically any antibody  
 18 from scratch, the DAKO system would have an  
 19 advantage because it's an open system and  
 20 you're able to do that, whereas you're not  
 21 able to do that with a Ventana system. But on  
 22 the other hand, if you're doing predominantly  
 23 clinical work and you want to have minimal  
 24 technical input to it, it becomes useful in  
 25 that regard because it's basically fully

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1 automated, and with ready to use reagents and  
2 has a, you know, a slight advantage in that  
3 regard. So they're both robust, excellent  
4 systems. It's a matter of how are you going  
5 to use it.

6 COFFEY, Q.C.:

7 Q. Look, please, at--just a moment, please? It's  
8 Exhibit P-1850, I believe. No, sorry. It's  
9 Dr. Mullen's report. The copy I happen to  
10 have in front of me happens to be unnumbered,  
11 as it turns out. It's the April 14th report,  
12 1840, maybe? I apologize, Commissioner. I'm  
13 just--I hadn't noticed it.

14 THE COMMISSIONER:

15 Q. I'm sure we'll find it.

16 COFFEY, Q.C.:

17 Q. Okay, it's dated April, 2008. It's 1840.

18 REGISTRAR:

19 Q. 1840?

20 COFFEY, Q.C.:

21 Q. I was right. Yes, thank you, Registrar.  
22 Doctor, this is a report dated April 14th,  
23 2008. It was prepared by Dr. Brendan Mullen,  
24 who is the pathologist from Mount Sinai  
25 Hospital in Toronto, Canada. Doctor, have you

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1 had a chance to have a look this report?

2 DR. DABBS:

3 A. Yes, I have.

4 COFFEY, Q.C.:

5 Q. And again, without kind of reading it out to  
6 you, I'm going to ask you perhaps using the  
7 mouse and the cursor on the screen, are there  
8 any things that you'd like to--or think are  
9 noteworthy, looking at it, in the context of  
10 what the Commissioner is dealing with here?

11 DR. DABBS:

12 A. Well, I was struck particularly by the  
13 "Summary of Observations." In fact, point No.  
14 1 where Dr. Mullen describes poor fixation and  
15 processing that resulted, at least in part, in  
16 incomplete tissue sections. And some of that  
17 can result, as I mentioned before, from tissue  
18 that contains water, isn't properly dried off  
19 before the actual slide goes to  
20 immunohistochemistry. That's a risk for  
21 losing tissue during the process. The loss of  
22 internal structure of the nucleus in staining  
23 restricted to the periphery of the slide  
24 sounds like he's describing poor fixation  
25 whenever the nuclei don't look like they

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1 should. It suggests that the fixation is  
2 responsible for that. And again, what he  
3 refers to as exploding sections resulting in  
4 loss of sections of the tissue, which in some  
5 instances apparently lost pieces of, portions  
6 of the actual tumour tissue that was to be  
7 assayed, again likely a result of  
8 inappropriate adherence to the slide,  
9 inappropriate drying that lead to that. And  
10 he refers to these hollow nuclei again. So it  
11 sounds like poor fixation and technique in  
12 preparing the slide for immunohistochemistry,  
13 at least in that part. The second, the  
14 absence of internal controls, he noted that  
15 many cases had no normal epithelium to be used  
16 as an internal control and where it--some was  
17 present, some of it apparently was lost  
18 because of this what he refers to as exploding  
19 tissue sections or loss of tissue due to  
20 inappropriate drying. Negative internal  
21 controls, he describes in many cases the  
22 internal control either did not stain or  
23 stained very weakly. Also, with the exception  
24 of a small minority of cases the ER internal  
25 control was significantly weaker. Again,

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1 these are major red flags for improper  
2 technique that may be related to fixation,  
3 antibody concentration or even improper  
4 antigen retrieval leading all to, potentially  
5 point No. 3 there.

6 COFFEY, Q.C.:

7 Q. Doctor, he notice the difference, a difference  
8 in his view, looking at the original slides,  
9 at least quite a number of them, between the  
10 ER internal control and the PR internal  
11 control where it was there, the PR control  
12 generally stained better. Can you account for  
13 that?

14 DR. DABBS:

15 A. Well, it's difficult to account for that  
16 specifically. But again, we're dealing with  
17 two different titres, two different  
18 antibodies.

19 COFFEY, Q.C.:

20 Q. Okay.

21 DR. DABBS:

22 A. So again, a fair amount of the things that  
23 I've observed and what people have written  
24 seems to be related to perhaps proper antibody  
25 dilutions, at least in part. The stain

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1 deposit obscuring morphology, in many cases  
 2 excess stain was present either on the surface  
 3 or beneath the section, those are artifacts  
 4 that can be associated with overheating or  
 5 improper development of the chromogen  
 6 solution. External controls he describes as  
 7 being inconsistent, both between slides or  
 8 within slides, in some cases positive cells  
 9 were barely stained. Again, that's a hallmark  
 10 that there's definitely something systemically  
 11 wrong with the staining apparatus if your  
 12 expected positive results are weak or not  
 13 staining at all. And then lastly, the  
 14 discrepancy between internal and external  
 15 controls in only one of the two--in only one  
 16 or two of the 539 cases he looked at was the  
 17 staining of the internal control as strong as  
 18 the corresponding external control. So again,  
 19 there are multiple points here that all  
 20 substantiate that the process was uneven and  
 21 erratic and fraught with technical  
 22 difficulties.  
 23 COFFEY, Q.C.:  
 24 Q. Doctor, the final point he makes is he says,  
 25 "There were few cases," I'm sorry, there were

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1 very few cases in which there was a  
 2 significant difference in my" he calls it "my  
 3 observation compared to that recorded on the  
 4 original report," which is a percentage, okay,  
 5 on the original reports. "Some of my  
 6 observations were higher than those recorded  
 7 and some lower." I understand from the  
 8 evidence he's given here is that, well, you  
 9 know, he might have called something 20 and  
 10 somebody else originally had called it 30 or  
 11 vice versa.  
 12 DR. DABBS:  
 13 A. Yes.  
 14 COFFEY, Q.C.:  
 15 Q. Or 60 versus 70.  
 16 DR. DABBS:  
 17 A. Yes.  
 18 COFFEY, Q.C.:  
 19 Q. That sort of thing, 60 versus 65. Doctor,  
 20 that sort of, you know, leaving aside the  
 21 issue of whether or not the original slides  
 22 should have been interpreted at all, okay,  
 23 leave that aside for the moment, in relation  
 24 to the issue, or this particular aspect of the  
 25 matter which is an estimation of the portion

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1 of cells that have nuclei staining.  
 2 DR. DABBS:  
 3 A. Yes.  
 4 COFFEY, Q.C.:  
 5 Q. And Dr. Mullen said there was some difference  
 6 but only a couple of cases, I said a couple,  
 7 very few that there was significant  
 8 difference. I wanted to ask you about that.  
 9 The fact that he wouldn't come up with a whole  
 10 lot of different figures for the proportions  
 11 or percentage figures, does that surprise you  
 12 or would you--and what I want to ask you about  
 13 is, I suppose, inter-observer variability in  
 14 that regard.  
 15 DR. DABBS:  
 16 A. Um-hm.  
 17 COFFEY, Q.C.:  
 18 Q. And, in fact, intra-observer variability and  
 19 just generally what you know about variability  
 20 in terms of interpretation, the interpretation  
 21 end of this?  
 22 DR. DABBS:  
 23 A. Sure. When examining for proportion of number  
 24 of cells that are present, the inter-observer  
 25 variability tends to be lower than when one is

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1 looking at both percent of cells and the  
 2 staining intensity. So it's not really  
 3 surprising here that apparently what he's  
 4 describing is that there is a low variability  
 5 between what he observed and what the original  
 6 observer catalogued in the report. And there  
 7 were only just a very few or a handful of  
 8 cases where there was a significant  
 9 difference. And I think that's probably to be  
 10 expected within acceptable parameters, so I  
 11 think what he's describing here is that the  
 12 interpretation was not an issue.  
 13 COFFEY, Q.C.:  
 14 Q. Now, whether or not it should have been  
 15 interpreted and what should have or might have  
 16 been done, having observed these kind of  
 17 problems he's noted in the slides, that's a  
 18 different issue.  
 19 DR. DABBS:  
 20 A. Yes.  
 21 COFFEY, Q.C.:  
 22 Q. But in terms of the actual percentage call,  
 23 the fact that in 539, approximately 539 cases  
 24 there would be a few cases in which there  
 25 would be a significant difference in

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<p>1 interpretation, you wouldn't find that 2 unusual?</p> <p>3 DR. DABBS:</p> <p>4 A. No, I wouldn't find that to be unusual. The 5 only--the key item there, in my opinion, would 6 be if something was interpreted as negative 7 and in fact it was positive, but he's not 8 describing that.</p> <p>9 COFFEY, Q.C.:</p> <p>10 Q. And in this context negative means zero, I 11 take it?</p> <p>12 DR. DABBS:</p> <p>13 A. Negative means zero, yes.</p> <p>14 COFFEY, Q.C.:</p> <p>15 Q. Yeah, okay. And positive is anything, any 16 percentage staining?</p> <p>17 DR. DABBS:</p> <p>18 A. Yes.</p> <p>19 COFFEY, Q.C.:</p> <p>20 Q. Doctor, there are some other subject matters 21 that I wanted to ask you about, discreet onto 22 themselves. One is the effect of--your 23 understanding of the current view within 24 pathology of the effect, if any, of 25 refrigeration of--refrigeration of tumour</p>	<p>1 COFFEY, Q.C.:</p> <p>2 Q. Does that have--do you know if there's any 3 studies at least that you're aware of in 4 relation to that?</p> <p>5 DR. DABBS:</p> <p>6 A. I'm not aware of chilled formalin, but we do 7 know that warm formalin will penetrate tissues 8 better than room temperature formalin, and 9 that's been the idea behind enhanced heating 10 for tissue processors, enhancing the fixation 11 process.</p> <p>12 COFFEY, Q.C.:</p> <p>13 Q. Doctor, so ideally then, from your perspective 14 in terms of a tissue sample when it's either 15 taken out using a needle or excised with a 16 scalpel, what should be done with it, a breast 17 tissue sample in this context?</p> <p>18 DR. DABBS:</p> <p>19 A. The--well, I think if biopsies are performed 20 in a clinic or in a radiology suite that those 21 people need to be instructed that as soon as 22 the tissue is available, it should go into a 23 container of formalin and sent immediately to 24 the laboratory. Tissues coming from the 25 operating rooms, the operating room personnel</p>
<p>1 tissue on ER/PR testing. What's your 2 understanding of the current view on that?</p> <p>3 DR. DABBS:</p> <p>4 A. Refrigeration of specimens, I think that-- 5 well, first of all there really isn't--there 6 really to my knowledge aren't any studies that 7 look at refrigerated tissue versus non or 8 those that are immediately put into fixative 9 regarding ER/PR or other testing. I think 10 what I described yesterday from the consensus 11 view of the committee was to get tissue as 12 soon as possible in all instances under one 13 hour into fixative, and if that means would 14 the specimen be better off in the refrigerator 15 for that period of time, one hour before 16 formalin, I don't know that anyone has really 17 looked at that specifically. So that remains 18 to be an unknown. It probably would not have 19 an adverse effect.</p> <p>20 COFFEY, Q.C.:</p> <p>21 Q. How would, Doctor, the cooling of formalin 22 itself, like, for example, the fixative 23 process and the chilling of formalin --</p> <p>24 DR. DABBS:</p> <p>25 A. Uh-hm.</p>	<p>1 need to be instructed to send the tissue fresh 2 immediately to the interoperative consult area 3 so that the tissue can be--the margins 4 typically are inked in six different colours 5 for purposes of orientation for the final 6 report. The tissue is sliced extremely thin, 7 as thin as possible, and then we typically 8 report on the margins, how close they are, and 9 things like that. We then get that into 10 fixative immediately and also at the same time 11 procure fresh tissue for tumour bank for 12 potential research. That's what we do at our 13 institution. So these cases, everyone is 14 aware of the importance of getting to the 15 specimens as soon as possible, and I think one 16 hour is actually fairly liberal. In an 17 institution where communication is optimal, it 18 should be within minutes and not, you know, as 19 long as an hour.</p> <p>20 THE COMMISSIONER:</p> <p>21 Q. Dr. Dabbs, actually that was something I had 22 noted from your slide presentation yesterday, 23 one of the recommendations was that breast 24 resection specimens must be sectioned fresh as 25 soon as possible, fresh meaning not having</p>

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<p>1 gone in--before they go into formalin?</p> <p>2 DR. DABBS:</p> <p>3 A. Correct.</p> <p>4 THE COMMISSIONER:</p> <p>5 Q. So in your institution, is there a space near</p> <p>6 the operating room in which this is done</p> <p>7 before it gets transported to the lab or does</p> <p>8 it go directly from the operating room to a</p> <p>9 lab section where that's done?</p> <p>10 DR. DABBS:</p> <p>11 A. Yes, we have--like, many hospitals have an</p> <p>12 area. It might not necessarily be next to the</p> <p>13 ORs, but we do have a room next to the ORs</p> <p>14 which is a place where we do interoperative</p> <p>15 consultations on frozen sections.</p> <p>16 THE COMMISSIONER:</p> <p>17 Q. Uh-hm.</p> <p>18 DR. DABBS:</p> <p>19 A. So it's a small laboratory area where we</p> <p>20 receive these, and we have a bench there where</p> <p>21 we can place the specimen, ink it, and then</p> <p>22 section it thin like that. Tumour procurement</p> <p>23 takes it's--tumour procurement takes its bit</p> <p>24 of tissue if there's adequate tissue and then</p> <p>25 this goes into fixative, and it's then</p>	<p>1 without sectioning and having the entire</p> <p>2 tissue exposed to the formalin, that fixation</p> <p>3 will not begin--will not be optimal because</p> <p>4 penetration of the tissue from the outside is</p> <p>5 slow, it's about one millimetre per hour.</p> <p>6 THE COMMISSIONER:</p> <p>7 Q. Uh-hm.</p> <p>8 DR. DABBS:</p> <p>9 A. So maximum in a portion of unfixed tissue, if</p> <p>10 you let it even sit overnight, it'll penetrate</p> <p>11 maybe four or five millimetres maximum. So if</p> <p>12 you section that tissue the next morning, the</p> <p>13 entire aspect of it will be raw. It will be -</p> <p>14 it will give very unsatisfying histologic</p> <p>15 stains and that's not to mention the fact that</p> <p>16 if you're ever going to do any complex</p> <p>17 testing, it would be futile. The tissue would</p> <p>18 be, in effect, liquifacted and unusable for</p> <p>19 that. Now if you're asking if you take that</p> <p>20 specimen, put it in a bucket of formalin</p> <p>21 without sectioning it and then section it</p> <p>22 within one hour, that would probably be okay</p> <p>23 as well.</p> <p>24 THE COMMISSIONER:</p> <p>25 Q. Right.</p>
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<p>1 processed and the time in formalin is</p> <p>2 recorded. So this is done at our institution</p> <p>3 in a room. It's a modest--very modest size</p> <p>4 adjacent to the ORs. We actually--our</p> <p>5 laboratory, the main laboratory, is one floor</p> <p>6 up and probably maybe a tenth or two tenths of</p> <p>7 a mile away. So it's a slight hike down to</p> <p>8 that room where we get called every time for</p> <p>9 interoperative consultation, and I think many</p> <p>10 institutions are similar to that. Some</p> <p>11 laboratories have the luxury of actually</p> <p>12 having the entire laboratory on the same floor</p> <p>13 as the operating room and that's an ideal</p> <p>14 situation, but it's by no means the norm.</p> <p>15 THE COMMISSIONER:</p> <p>16 Q. And would it be the norm--I mean, obviously</p> <p>17 this is the recommendation of the group here</p> <p>18 about cutting fresh. Are there studies which</p> <p>19 deal with comparison between having a cutting</p> <p>20 of fresh as opposed to cutting after the</p> <p>21 breast tissue would have been in formalin for</p> <p>22 a period of time and transported to a lab?</p> <p>23 DR. DABBS:</p> <p>24 A. Well, we do know from specimens in general</p> <p>25 that if material is placed into formalin</p>	<p>1 DR. DABBS:</p> <p>2 A. But the key thing is exposure of the tumour</p> <p>3 tissue as soon as possible in formalin, and in</p> <p>4 essence, it's also conceivable if you're</p> <p>5 dealing with a remote location, to have an</p> <p>6 assistant cut into that, take a thin piece of</p> <p>7 tumour, several thin pieces of tumour, put</p> <p>8 them in a tissue cassette and put them in the</p> <p>9 same bucket with the formalin. That way</p> <p>10 you're getting the tumour fixed while it's on</p> <p>11 its way to the lab. That's doable as well.</p> <p>12 One can always deal with the inking after the</p> <p>13 fact. So that's possible.</p> <p>14 THE COMMISSIONER:</p> <p>15 Q. So--okay, I just want to make sure that I</p> <p>16 understand. So for those--because you raised</p> <p>17 two different things. One is really if you're</p> <p>18 in a hospital where there is a lab relatively</p> <p>19 close by, I understand you to say that if you</p> <p>20 can't cut it fresh, the optimum thing would be</p> <p>21 to put it in formalin, get it to the lab, and</p> <p>22 still have it sliced.</p> <p>23 DR. DABBS:</p> <p>24 A. Yes.</p> <p>25 THE COMMISSIONER:</p>

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<p>1 Q. Within about an hour?</p> <p>2 DR. DABBS:</p> <p>3 A. Yes.</p> <p>4 THE COMMISSIONER:</p> <p>5 Q. If you are--if you happen, as we have in this</p> <p>6 province, to be in a remote location where, in</p> <p>7 fact, the lab may not be in the same</p> <p>8 institution where the tissue sample is taken,</p> <p>9 then that presents other kinds of problems,</p> <p>10 and one of the potential ways of dealing with</p> <p>11 that would be to have placed in the same</p> <p>12 bucket a slice which had been taken, as I</p> <p>13 understand?</p> <p>14 DR. DABBS:</p> <p>15 A. Yes, of the tumour.</p> <p>16 THE COMMISSIONER:</p> <p>17 Q. And then transported, so that it is, in fact,</p> <p>18 in the formalin doing its thing in terms of</p> <p>19 fixation while it's being transported to the</p> <p>20 lab, which may be some distance away?</p> <p>21 DR. DABBS:</p> <p>22 A. Correct.</p> <p>23 THE COMMISSIONER:</p> <p>24 Q. Are there other ways of dealing with the</p> <p>25 question of having to transport because</p>	<p>1 marked cassettes. They could simply cut the</p> <p>2 tissue with a broad knife into one centimetre</p> <p>3 or less sections, put it in formalin, and have</p> <p>4 it transported, and if it takes, you know, 48</p> <p>5 hours to get to the destination, then the</p> <p>6 laboratory director just needs to be able to</p> <p>7 validate that their assay they're using, the</p> <p>8 ER/PR or HER2, or whatever, works under those</p> <p>9 conditions of fixation beyond 48 hours. Now,</p> <p>10 for example, if you recall from the</p> <p>11 recommendations, it said up to 72 hours.</p> <p>12 Well, for our laboratory at Magee, what I did</p> <p>13 is I validated it for 96 hours to make sure</p> <p>14 that if there's any issues with</p> <p>15 transportation, especially in the unlikely</p> <p>16 event that something got to the laboratory</p> <p>17 late on a Friday, and it happened to be a long</p> <p>18 three day weekend, to take into account for</p> <p>19 that. One of the things that I did not</p> <p>20 mention, but you will, is that overfixation</p> <p>21 for formalin is almost never an issue. It can</p> <p>22 be--the assay can be altered with antigen</p> <p>23 retrieval, and that's what antigen retrieval</p> <p>24 does, it levels the playing field for</p> <p>25 specimens that have been fixed for however</p>
<p>1 sometimes you might be transporting across</p> <p>2 town, but there's at least--there are at least</p> <p>3 two institutions which from the evidence I've</p> <p>4 heard within this province where the</p> <p>5 transportation may take some time. In one</p> <p>6 case, perhaps 24 to 48 hours.</p> <p>7 DR. DABBS:</p> <p>8 A. Uh-hm.</p> <p>9 THE COMMISSIONER:</p> <p>10 Q. So would that same method be a way of dealing</p> <p>11 with it or are there other ways of dealing</p> <p>12 with it?</p> <p>13 DR. DABBS:</p> <p>14 A. I think the transportation issues can also be</p> <p>15 dealt with on an individualized basis, and by</p> <p>16 that I mean at these hospitals where the</p> <p>17 surgery is being performed, there's probably</p> <p>18 at least someone from the laboratory who I</p> <p>19 think could be trained to section the tissue,</p> <p>20 cut it with a knife into one centimetre or</p> <p>21 less thick sections, put it in a bucket of</p> <p>22 significant size with formalin, and then the</p> <p>23 transportation could occur. They wouldn't</p> <p>24 have to actually cut into any tumour and</p> <p>25 specifically put it into, you know, specially</p>	<p>1 long. It's underfixation that you cannot</p> <p>2 repair. So the key thing is to get the</p> <p>3 specimen into formalin as soon as possible and</p> <p>4 once that's done, then just, you know, adjust</p> <p>5 your assay if you have to adjust your antigen</p> <p>6 retrieval a little bit and your optimization</p> <p>7 process then for specimens like that, and</p> <p>8 that's why we keep track of how long specimens</p> <p>9 are in formalin, so that if you--you know that</p> <p>10 you're getting specimens from hospital "B" and</p> <p>11 they typically don't get to the lab for 48</p> <p>12 hours, and then it takes another 24 hours to</p> <p>13 process, then you look at those assays and</p> <p>14 compare them to your standard operating</p> <p>15 procedure, and if your results look fine, then</p> <p>16 you don't have to do anything, but if signals</p> <p>17 are appearing weak with your controls from</p> <p>18 that tissue, then you can up your antigen</p> <p>19 retrieval and that way whenever you receive</p> <p>20 specimens from hospitals out in a remote area,</p> <p>21 you know that once you've received them that</p> <p>22 your machine, you're going to program it on a</p> <p>23 different protocol to take into account the</p> <p>24 fact that it was fixed longer.</p> <p>25 COFFEY, Q.C.:</p>



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<p>1 Q. So you have to adjust how the particular 2 tissue sample is handled or processed overall 3 to the ER/PR process, bearing in mind how it's 4 being handled before you received it?</p> <p>5 DR. DABBS:</p> <p>6 A. Correct, exactly, and like I say, the 7 wonderful thing about formalin fixation is 8 it's very forgiving. Overfixing will never 9 destroy a specimen, but underfixing will 10 destroy it. So that's the importance of 11 getting it in formalin up front as soon as 12 possible. As I mentioned, 96 hours, I see no 13 change whatsoever in our ER/PR or HER2 at our 14 institution, and so on our path reports, it 15 says that our fixation time is between 8 and 16 96 hours.</p> <p>17 COFFEY, Q.C.:</p> <p>18 Q. Now, Doctor, to make sure I understand it, you 19 pointed out making cuts in the tissue at one 20 centimetre distances or less if possible, I 21 take it that that means, in effect, that if 22 that's done all the way through the tissue, 23 and it's one centimetre, say, the cuts are at 24 that distance, that spacing, that any piece of 25 tissue within the specimen is within a half a</p>	<p>1 to be exposed to formalin?</p> <p>2 DR. DABBS:</p> <p>3 A. Correct.</p> <p>4 COFFEY, Q.C.:</p> <p>5 Q. In order for the fixation process to do what 6 it's supposed to?</p> <p>7 DR. DABBS:</p> <p>8 A. Uh-hm.</p> <p>9 COFFEY, Q.C.:</p> <p>10 Q. And that, I take it, is why it's important to 11 have the tissue slices as narrow as possible?</p> <p>12 DR. DABBS:</p> <p>13 A. Yes, and I think that one centimetre is 14 actually quite generous. I think - I'm 15 usually pretty successful in getting it at 16 half centimetre or less. It takes a thin 17 knife, a very sharp instrument, to do that for 18 larger specimens, but it is entirely doable.</p> <p>19 COFFEY, Q.C.:</p> <p>20 Q. And that, I take it--so there's particular 21 types of knives that one would use to do it.</p> <p>22 DR. DABBS:</p> <p>23 A. Uh-hm.</p> <p>24 COFFEY, Q.C.:</p> <p>25 Q. And I take it, it requires experience in</p>
<p>1 centimetre of fluid to start - of formalin to 2 start?</p> <p>3 DR. DABBS:</p> <p>4 A. Yes.</p> <p>5 COFFEY, Q.C.:</p> <p>6 Q. And your penetration rate is one millimetre 7 per hour?</p> <p>8 DR. DABBS:</p> <p>9 A. Yes.</p> <p>10 COFFEY, Q.C.:</p> <p>11 Q. So within five hours at least there's some 12 formalin in every part of the tissue should 13 have been in contact with formalin?</p> <p>14 DR. DABBS:</p> <p>15 A. Yes.</p> <p>16 COFFEY, Q.C.:</p> <p>17 Q. That, I take it, is the way it works in terms 18 of the actual mechanics of it?</p> <p>19 DR. DABBS:</p> <p>20 A. Yes.</p> <p>21 COFFEY, Q.C.:</p> <p>22 Q. And, though, just as you pointed out 23 yesterday, the fact that formalin has arrived 24 on a particular piece of tissue doesn't 25 necessarily end the matter, it has to continue</p>	<p>1 manual dexterity?</p> <p>2 DR. DABBS:</p> <p>3 A. Yes, it does.</p> <p>4 COFFEY, Q.C.:</p> <p>5 Q. Doctor, I haven't raised this with anyone 6 else, and I haven't raised it with you as of 7 yet, but I'll ask you, is there to your 8 knowledge any devise or thought given to 9 actually creating a device, a mechanical 10 device, that would compensate for any lack of 11 ability on the part of the person who--lack of 12 ability to slice very thinly by the person who 13 is actually doing the processing of the 14 tissue?</p> <p>15 DR. DABBS:</p> <p>16 A. What I can tell you is that because the Sakura 17 tissue processor requires extremely thin 18 slices, and we're talking two millimetres, 19 they did develop some tools for that. It's 20 specifically designed for that processor. 21 It's very labour intensive, but there you're 22 talking about cutting sections for a cassette. 23 Actual devices for cutting gross specimens, 24 the only kind of device that I'm aware of is 25 one that is used by neuropathologists for</p>

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<p>1 slicing autopsy brains. Basically, if you can 2 picture a plexiglass board that has two raised 3 rails of approximately, let's say, ten 4 centimetres apart, okay, once you section the 5 brain in half and you put one half face down, 6 and you slide your knife using those rails as 7 a guide, you get something like five 8 millimetre sections, okay, and then you lay 9 them all out. That's how the 10 neuropathologists do their examination for 11 autopsies of the brain. Nothing like that 12 exists for the breast. Some people have 13 devised other whole breast section methods 14 which involves slicing on an electric device, 15 sort of analogous to what you see in a deli, 16 okay, but there's nothing that's really been 17 recommended or is in general use or even 18 marketed for that purpose for the breast.</p> <p>19 COFFEY, Q.C.: 20 Q. Doctor, the Commissioner has heard references 21 to the idea of reprocessing of tissue, I mean, 22 after it's been--after it has arrived in a 23 block, paraffin block, and at times, at least 24 certainly in one of the hospitals involved in 25 this matter there was a certain amount of</p>	<p>1 there's something wrong with the alcohols, 2 let's suppose that the alcohols are not 3 frequently changed, alcohols can accumulate 4 water just by sitting, alcohols if they're not 5 changed can form esters within the container, 6 so you're not getting a good dehydration and 7 if you don't remove all the water from the 8 tissue, it will not dehydrate, and so it will 9 be relatively wet and soft and that's another 10 reason why the histotechnologist would not be 11 able to make a good section from that. So it 12 could be fixation, it could be inappropriate 13 dehydration. Another would be if the section 14 is cut too thick when it's put into a 15 cassette, what happens there is when the lid 16 goes on the cassette, the tissue gets 17 compressed because it's too thick and it will 18 not infiltrate with paraffin well at the last 19 step, and so that will appear, to the 20 histotechnologist, to be a soft area that they 21 can't cut. It sort of would be like trying to 22 cut, you know, lard. It just doesn't cut. It 23 just sort of spreads. So those are the three, 24 I think, most common reasons why tissue would 25 need to be reprocessed.</p>
<p>1 reprocessing of tissue that occurred. Are you 2 familiar with the idea of reprocessing of 3 tissue?</p> <p>4 DR. DABBS: 5 A. Reprocessing of tissue is a phenomenon that is 6 in general common knowledge, yes.</p> <p>7 COFFEY, Q.C.: 8 Q. And in what circumstances is it used and what 9 effect, if any, could it have on ER and PR 10 results?</p> <p>11 DR. DABBS: 12 A. I think the reason why tissue is reprocessed 13 is because whenever a paraffin block gets to 14 the histotechnologist to slice in their 15 microtome, they find that they cannot cut it 16 and get a good section. Usually what that 17 means is the centre of the specimen falls out 18 and you end up if they cut that, they get a 19 big hole in the centre of the specimen, and 20 there could be several reasons for that. If 21 the tissue is not properly fixed, then tissue 22 will be soft as opposed to being hardened by 23 the fixative. That can be one potential 24 cause. Another could be insufficient 25 dehydration through the tissue processor. If</p>	<p>1 Now the question is does reprocessing per 2 se affect immunohistochemistry? And my answer 3 to that would be that there are no studies 4 that I'm aware of that have looked at that per 5 se. However, what I can say is if the tissue 6 is not properly fixed upfront, it doesn't 7 matter what you do to it, it's not going to 8 harm it any further, and the same goes if the 9 tissue is properly fixed, no matter what you 10 do to it in reprocessing, when you look at 11 what the actual steps are in reprocessing, 12 it's not going to affect the tissue as long as 13 it's been properly fixed. But if it's not 14 been properly fixed, you're still going to get 15 a poor result for a complex test like ER/PR 16 regardless of tissue processing, reprocessing.</p> <p>17 COFFEY, Q.C.: 18 Q. So that, from your perspective, the 19 reprocessing process itself won't remedy any 20 damage, I'll use that word, in the sense of 21 due to fixation problems that has already 22 occurred?</p> <p>23 DR. DABBS: 24 A. Correct.</p> <p>25 COFFEY, Q.C.:</p>

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1 Q. But also, if there--it won't cause any damage  
 2 to fixation that has properly occurred?  
 3 DR. DABBS:  
 4 A. Correct, because the steps that occur during  
 5 tissue reprocessing really have already been  
 6 done and to do them again, in the mode that's  
 7 been recommended, no extreme temperatures,  
 8 etcetera, will not harm the tissue and I think  
 9 it's also important for the laboratory to  
 10 monitor how often tissues are reprocessed  
 11 because I think that's a quality measure. If  
 12 you're having a lot of tissues reprocessed, it  
 13 suggests that something is going wrong that  
 14 could be anywhere from the person who's  
 15 cutting the initial sections to the tissue  
 16 processors, and you know, people who are  
 17 involved with that. So that's distinctly a  
 18 quality measure is to find out how frequent  
 19 are tissues being reprocessed.  
 20 COFFEY, Q.C.:  
 21 Q. Doctor, and I take it, if there is any  
 22 significant amount of reprocessing going on or  
 23 being required to go on in the laboratory,  
 24 from your perspective, there should be  
 25 inquiries made about why that would be so?

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1 DR. DABBS:  
 2 A. Yes, and by keeping track of this, you're  
 3 basically looking at the people involved who  
 4 are involved with processing, grossing,  
 5 cutting, processing of tissue, and this is  
 6 really the only way to get a grip or a  
 7 complete handle on quality, so that you can go  
 8 back and see, okay, what areas in the process  
 9 need to be altered so that we can minimize or  
 10 decrease the tissues that are being  
 11 reprocessed, because tissue should not have to  
 12 be reprocessed.  
 13 COFFEY, Q.C.:  
 14 Q. Doctor, just on the point of dealing with the  
 15 idea of tissue taken in hospitals that are  
 16 somewhat remote from the site where they're  
 17 going to be processed into blocks. Doctor,  
 18 you've referred to someone could be trained on  
 19 site, wherever the surgery is occurring, to  
 20 properly section the specimen. Doctor, you've  
 21 also referred to, though in your own  
 22 institution, that core biopsy are utilized  
 23 generally or at least initially for ER/PR  
 24 testing?  
 25 DR. DABBS:

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1 A. Yes.  
 2 COFFEY, Q.C.:  
 3 Q. Would you have any thoughts on, at least in  
 4 these--for example, and I'll refer to it as  
 5 relatively remote institution, that's an hour  
 6 by vehicle away from the centre where the  
 7 blocks are going to be processed, or the  
 8 tissue is going to be processed into blocks,  
 9 or for that matter, 24 hours away, okay, in  
 10 some instances in this province. Would there  
 11 be any advantage to utilizing, at least  
 12 initially, core biopsy process, because I take  
 13 it the specimen is so much smaller than a  
 14 mastectomy specimen?  
 15 DR. DABBS:  
 16 A. Yes, and I think that core biopsies, I think  
 17 the vast majority of institutions in the  
 18 States use core biopsies as the initial  
 19 testing mode for hormone receptors and HER2  
 20 analysis. I think they do that for several  
 21 reasons. Historically, they know that they  
 22 got better results from core biopsies because  
 23 they generally were better fixed specimens,  
 24 but also, I think the demands of patients and  
 25 oncologists who want to have results, you

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1 know, soon, so that in some instances actually  
 2 patients are treated before definitive  
 3 surgery. So it's important to get a good  
 4 result and get it in a timely fashion, and so  
 5 there's a great deal of timeliness as well  
 6 about patients who are anxious and doctors who  
 7 want to begin treatment, either with hormonal  
 8 manipulation or even chemotherapy. So that's  
 9 sort of a mini history, if you will, of the  
 10 reasons why core biopsies, and I would say  
 11 that if you're dealing with patients in remote  
 12 areas, probably the best way would be to do  
 13 the hormone receptors and HER2 on a core  
 14 biopsy. That requires a small container that  
 15 tissue can be put right into formalin and  
 16 shipped here, and if it takes longer, then it  
 17 shouldn't be an issue.  
 18 COFFEY, Q.C.:  
 19 Q. Doctor, slides, the ER and PR slides, okay, if  
 20 they're--once they're prepared and examined by  
 21 a pathologist, does long term storage have any  
 22 effect on the slides, to your knowledge, in  
 23 particular with IHC?  
 24 DR. DABBS:  
 25 A. Sure. Long term storage should not have any

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1 effect on immunohistochemistry result per se.  
 2 Other things can happen to slides. They can  
 3 become a little bit dehydrated. Bubbles can  
 4 appear under the cover slip, but that's  
 5 nothing. That can be fixed very easily just  
 6 by recover slipping. But the test result per  
 7 se for immunohistochemistry should not be  
 8 altered over time.  
 9 COFFEY, Q.C.:  
 10 Q. How about long term storage of blocks before a  
 11 particular ER or PR test is done?  
 12 DR. DABBS:  
 13 A. Yes, in general, if the specimen is well fixed  
 14 and held and stored in an area where the  
 15 paraffin is not going to be melt down, in an  
 16 air conditioned facility, I think that one can  
 17 expect that immunoreactivity will be  
 18 maintained for quite a long time. I mean,  
 19 immunohistochemistry has been performed on  
 20 archive specimens that have been hundreds of  
 21 years old and you know, it's quite doable.  
 22 Storage per se will not result in destruction  
 23 of immunostaining.  
 24 COFFEY, Q.C.:  
 25 Q. Doctor, you referred to metrics. I take it

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1 they're used in your own laboratory. You use  
 2 them?  
 3 DR. DABBS:  
 4 A. Yes.  
 5 COFFEY, Q.C.:  
 6 Q. From your perspective, what role should they  
 7 play and how important are they? And could  
 8 you explain to the Commissioner really what  
 9 metrics you mean by metrics?  
 10 DR. DABBS:  
 11 A. Sure. The metrics that we monitor, we have a  
 12 person who is dedicated in the laboratory to  
 13 quality assurance and so she will keep track  
 14 of all of our pathology reports that have  
 15 predictive and prognostic markers. I've  
 16 especially given her the charge of keeping  
 17 track of ER/PR and HER2 results, as well as  
 18 fluorescence in situ hybridization test for  
 19 HER2. So what she does is she will abstract  
 20 this information from pathology reports from  
 21 our computer system and send me quality  
 22 reports, and the quarterly reports basically  
 23 are spreadsheets, Excel sheets, that will give  
 24 me information on, for example, for hormone  
 25 receptor, the overall number of cases that are

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1 ER positive, the percent of cases, of those  
 2 cases that are ER positive and PR positive,  
 3 the percent that are ER positive and PR  
 4 negative, the percent that are ER negative and  
 5 PR positive and the percent that are ER  
 6 negative and PR negative. She will give me  
 7 information on the percent of cases that are  
 8 HER2 three plus, the percent of cases that are  
 9 HER2 two plus and the percent of cases of  
 10 those that whenever the FISH is performed, the  
 11 percent of those that are actually amplified,  
 12 the percent of cases that are HER2 one plus  
 13 and percent that are zero. So that what that  
 14 does for me is it tells me, it gives me a  
 15 view, if you will, at 35,000 feet of how are  
 16 we doing with our percentages in each of these  
 17 categories, and as I watch them over time,  
 18 provided that I haven't changed anything in  
 19 the system or tissue processor or  
 20 immunohistochemistry, they should be fairly  
 21 steady. There should be no wild fluctuations,  
 22 and that is, in fact, the case.  
 23 I can tell you that there was once one--  
 24 there was some information in the literature  
 25 suggesting that patients who are ER negative

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1 PR positive, that the reason why that category  
 2 exists is because those specimens were not  
 3 properly fixed and were false negatives, and  
 4 so what I did, I took advantage of the fact  
 5 that we went to this controlled timed fixation  
 6 at our institution January 1 of 2007. So what  
 7 I did, at that point, I decided to monitor our  
 8 results over the next six months and compare  
 9 it to the prior two years specifically for  
 10 that category, ER negative PR positive group.  
 11 The ER negative PR positive group, prior to  
 12 controlled fixation, for 24 months, was 5.7  
 13 and 5.6 percent, and for the first six months  
 14 of controlled fixation, according to the  
 15 recommended guidelines, it was 5.7 percent,  
 16 which clearly demonstrated to me that it was  
 17 not an artifact of fixation, and we presented  
 18 that information at our national meeting in  
 19 December last March.  
 20 However, it--and so that was one example  
 21 of how I could look at the metrics and say  
 22 "I've changed fixation. What effect is this  
 23 going to have?" and I took advantage of the  
 24 fact that looking at this and finally disputed  
 25 the argument or--well, the argument that it's

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<p>1 poor fixation results in that ER negative PR 2 positive group. It does not. It's 3 independent of fixation, and that percent in 4 that category was unchanged for that entire 5 30-month period.</p> <p>6 More recently, we changed our antibody 7 clones to the rabbit monoclonals, the SP1 and 8 the 1E2. They're both rabbit monoclonals. 9 And what I noticed, and I just got these 10 metrics about two weeks ago, in comparing the 11 ER negative PR positive, which as I mentioned 12 was about 5.7 percent, that has gone to one 13 percent with the new batch of rabbit 14 monoclonals. So what that says is that that 15 is strictly antibody dependent, that that 16 particular clone of PR, the 1E2, is different 17 and is obviously seeing a different epitope 18 PR, and as a result, the percent of ER 19 negative PR positive cases is now one percent 20 versus it used to be 5.7 percent.</p> <p>21 COFFEY, Q.C.:</p> <p>22 Q. Using the different mono -</p> <p>23 DR. DABBS:</p> <p>24 A. Using the different clone, correct. So it is 25 clone dependent and whenever I looked at those</p>	<p>1 A. It's not complicated at all. We have a 2 person, as I mentioned, who's dedicated to 3 quality assurance and quality assurance 4 projects at our institution, and the number of 5 breast cases that we handle are a fair number, 6 but it's fairly simple to go into the lab 7 information system, abstract that information 8 and just tally it up on an Excel sheet. So 9 it's all electronic. There's really no 10 pushing of paper.</p> <p>11 THE COMMISSIONER:</p> <p>12 Q. And the comparison that you're doing are 13 internal comparisons?</p> <p>14 DR. DABBS:</p> <p>15 A. That's correct.</p> <p>16 THE COMMISSIONER:</p> <p>17 Q. You're comparing your results to results that 18 you would have gotten in prior period of time, 19 so presumably factors such as population base 20 and all that kind of stuff don't enter into 21 it. It's strictly what you are achieving 22 internally.</p> <p>23 DR. DABBS:</p> <p>24 A. It's what I'm achieving internally, but also 25 it gives me the ability to look at the</p>
<p>1 metrics, I also compared it to the PR 636 2 clone and our original clone that we were 3 using. So I have three PR antibodies there 4 and the results, while varying, are--you know, 5 they're still robust results, but the 6 expectations now in using this as a metric are 7 different than what they were before. So 8 that's the importance of metrics. It tells 9 you where you are so that if something 10 drastically goes wrong with your system that 11 the medical director, who is a busy person 12 doing lots of things, or the lab 13 administrator, again a busy person doing lots 14 of things, if there all of a sudden turns out 15 to be a wild fluctuation, you can catch it 16 quick. Years aren't going to go by, but a 17 quarter will go by. But at least you'll say, 18 it's time to put on the brakes. We got to 19 figure out why this number has changed so 20 drastically. That's what I mean by metrics.</p> <p>21 COFFEY, Q.C.:</p> <p>22 Q. Doctor, how--in terms of, for example, ER/PR 23 and HER2/neu, how complicated, in fact, is it 24 to actually keep the metric?</p> <p>25 DR. DABBS:</p>	<p>1 literature and see, okay, what are the report 2 of ER negative PR positive rates? And if you 3 look at them, you know, they vary between two 4 and eight percent. So, for example, if you're 5 getting 10 percent or 12 percent, there's 6 something wrong. That suggests to me that 7 there may be an ER fixation issue or I would 8 want to know what PR clone are you using.</p> <p>9 THE COMMISSIONER:</p> <p>10 Q. So let me make sure I understand this. What 11 you're saying is that in doing what you call 12 your metrics, which once again is a sort of 13 look at things from somewhat of a distance, 14 you are comparing internally. You're looking 15 at what was being used at the time as an 16 explanation for any differences, but in 17 addition, you're looking to how you stack up 18 against the available literature and a 19 variation either from what the available 20 literature would say to you is appropriate or 21 from past experience using the same clone 22 would cause you to say "do we have a problem?" 23 Let's look at it."</p> <p>24 DR. DABBS:</p> <p>25 A. Exactly. It gives you--it allows you to put</p>

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1 your finger on the pulse of the results. You  
 2 know, an example I might construct would be if  
 3 you had a laboratory that was a two-day drive  
 4 from here, or a hospital a two-day drive from  
 5 here, and it contributed say 30 percent of  
 6 your breast cancer specimens, if fixation was  
 7 not optimal at that particular institution,  
 8 it's going to affect your metrics. So if you  
 9 change anything, if you change the fixation,  
 10 the front, if you change the primary antibody,  
 11 if you change the detection system, if you  
 12 change the paraffin, you need to reoptimize  
 13 and make sure that the results that you're  
 14 getting are the same as before and the metrics  
 15 is just another global way of looking at that.  
 16 It's an internal comparison and it also gives  
 17 you a connection to the outside world, what  
 18 has been published. Should we be getting  
 19 between 70 and 80 percent ER positive cases  
 20 overall? And our metrics show 52 percent,  
 21 there's something wrong inside. We're not  
 22 doing well.

23 COFFEY, Q.C.:

24 Q. Another topic I wanted to ask you about is the  
 25 purposes for which, in your experience, ER and

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1 PR tests are ordered by pathologists. I  
 2 appreciate that they're certainly ordered  
 3 routinely for primary breast cancer.

4 DR. DABBS:

5 A. Yes.

6 COFFEY, Q.C.:

7 Q. Are they utilized for any other purpose, in  
 8 your experience?

9 DR. DABBS:

10 A. There are two other instances where one may  
 11 order ER and/or PR. One would be specific  
 12 requests by oncologists, and the group that I  
 13 can think of at our institution would be the  
 14 gynecologic oncologists, occasionally they  
 15 will ask us for hormone receptors for  
 16 endometrial cancers, rarely for certain kinds  
 17 of ovarian cancers. That gives them  
 18 documented evidence if they, for example, want  
 19 to add an anti-estrogen therapy to patients  
 20 who are already getting other therapies for  
 21 disease. So that's one instance.

22 The other instance would be if it were in  
 23 the process of working up tumours of unknown  
 24 origin. Now let me explain that just a bit  
 25 further. The presence of estrogen receptor

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1 can be useful in the work up of tumours of  
 2 unknown primary site obviously in women.  
 3 We're always looking for treatable diseases.  
 4 So in our work up of tumours of unknown  
 5 primaries, which generally are fairly  
 6 extensive and have multiple antibody panels,  
 7 the presence of estrogen receptor can point to  
 8 either a GYN or a breast primary tumour. Now  
 9 by itself, an estrogen receptor positive  
 10 tumour does not necessarily mean a breast  
 11 origin or a GYN. You have to take into  
 12 account the entire panel before you arrive at  
 13 that conclusion. But an ER positive can be a  
 14 powerful piece of that puzzle, doing that  
 15 detective work and trying to figure out what  
 16 the source of the primary tumour is. So that  
 17 would be the second instance in using that.

18 COFFEY, Q.C.:

19 Q. In that instance, the second instance, if one  
 20 had reason to believe that for an extended  
 21 period of time the ER results were producing  
 22 at least a number of false negatives  
 23 utilizing, in the second scenario, and that  
 24 came to your attention, what, if anything,  
 25 would that cause you to do?

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1 DR. DABBS:

2 A. Well, in the situation of the work up of  
 3 tumours of unknown primary, it might cause  
 4 some concern about the impact that a positive  
 5 ER would have had in that particular case, and  
 6 I think you would have to look at it on a  
 7 case-by-case basis, because as I mentioned,  
 8 there are a lot of other antibodies that are  
 9 used in that work up and the case may be  
 10 solved, even without an ER, okay. So -

11 COFFEY, Q.C.:

12 Q. An accurate ER?

13 DR. DABBS:

14 A. An accurate ER, correct. So could it have had  
 15 an impact, yes, but I think you'd probably  
 16 have to look at that on a case-by-case basis,  
 17 because as I say, the ER result is just one  
 18 part of that work up in that detective work.

19 COFFEY, Q.C.:

20 Q. And for example, if you were consulted and  
 21 asked--you know, or told, look, we have--we've  
 22 looked at and reexamined all of the primary ER  
 23 negative tests, primary breast, I'm sorry,  
 24 primary breast ER tests and negative tests  
 25 originally, all primary breast ER negatives,

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1 we've gone through all them and we've done our  
 2 examination, reexamination, that's done. Then  
 3 you were told that we haven't looked at all  
 4 the ER negatives for non-primary, and this  
 5 covers seven or eight years, and you were  
 6 asked, well, do you have any thoughts on what,  
 7 if anything, we should do, we the institution  
 8 should do? What would your view be?  
 9 DR. DABBS:  
 10 A. In that scenario, I would recommend that the  
 11 tests be repeated with a properly functioning  
 12 assay, because the goal there, as I mentioned,  
 13 specifically with unknown primary, is to be  
 14 able to identify those tumours that are  
 15 treatable and one of them that is highly  
 16 treatable would be a tumour that's ER  
 17 positive, because there's a therapy for that.  
 18 There's a medical therapy for that.  
 19 COFFEY, Q.C.:  
 20 Q. Doctor, the endometrial cancers that you  
 21 referred to.  
 22 DR. DABBS:  
 23 A. Yes.  
 24 COFFEY, Q.C.:  
 25 Q. And same scenario and if it was used for

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1 endometrial cancers, would your response be  
 2 the same, that it should be repeated?  
 3 DR. DABBS:  
 4 A. Yes.  
 5 COFFEY, Q.C.:  
 6 Q. So from your perspective, if there is cause to  
 7 believe that the ER test was, to use, I think,  
 8 Dr. Ejeckam's words, unreliable, erratic and  
 9 unhelpful, your view would be that all the ER  
 10 negatives should be redone?  
 11 DR. DABBS:  
 12 A. Yes.  
 13 COFFEY, Q.C.:  
 14 Q. Doctor, and I say all, not limited to primary  
 15 breast, but include all?  
 16 DR. DABBS:  
 17 A. Correct.  
 18 COFFEY, Q.C.:  
 19 Q. Doctor, the subject of false positives has  
 20 come up here at times. Could you tell us,  
 21 please, about what you know about false  
 22 positives in ER/PR testing?  
 23 DR. DABBS:  
 24 A. In false positives?  
 25 COFFEY, Q.C.:

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1 Q. Is there such a thing, first of all, as false  
 2 positives, and if so, how common are they and  
 3 how are they handled?  
 4 DR. DABBS:  
 5 A. I personally have not seen a false positive  
 6 hormone receptor result, other than something  
 7 that was fixed primarily in alcohol. So that  
 8 brings to mind that if a tissue is improperly  
 9 fixed in formalin, as I mentioned before, the  
 10 next three solutions on the tissue processor  
 11 are alcohol. So if something is getting just  
 12 a very minimal exposure to formalin, it's  
 13 theoretically possible that one could obtain a  
 14 false positive result, based on alcohol  
 15 fixation. The only other incident that I can  
 16 think of would be with over antigen retrieval  
 17 giving a simulated nuclear expression of  
 18 something which happens to be biotin. If  
 19 you're using a certain--the ABC method, as the  
 20 method for immunohistochemistry in that  
 21 situation, but overall, that should be  
 22 exceedingly rare.  
 23 COFFEY, Q.C.:  
 24 Q. And Doctor, the mechanism in relation to the  
 25 alcohol fixation, how does that actually--your

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1 understanding of how that works, if indeed  
 2 that was to happen as the tissue which was not  
 3 properly fixed to start with in formalin goes  
 4 through the tissue processor -  
 5 DR. DABBS:  
 6 A. Yes.  
 7 COFFEY, Q.C.:  
 8 Q. - you know, how would that actually work then,  
 9 the mechanism?  
 10 DR. DABBS:  
 11 A. Well, we do know that for certain antibodies,  
 12 alcohol is not a bad fixative and the reason  
 13 for that is because it doesn't generate all  
 14 the chemical reactions that formalin does. So  
 15 in some respects, some people use alcohol  
 16 fixation routinely for a wide variety of  
 17 antibodies, because the sensitivity is  
 18 greater, and they get to use less antibody and  
 19 don't even require antigen retrieval.  
 20 However, as I mentioned before, the database  
 21 that is built on hormone receptors, the whole  
 22 data base and the outcomes associated with  
 23 that have been on formalin fixed tissue, not  
 24 alcohol fixed. So if you begin using alcohol  
 25 fixative, and you say, well, I have, you know-

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<p>1 -I'm getting positive results at a lower 2 sensitivity, people don't know what that means 3 with regards to what the outcome is. So there 4 are--in immunohistochemistry, there are other 5 items that can enhance your sensitivity for 6 detection. Does that mean that we jump to use 7 them all the time? No, not necessarily. For 8 hormone receptor testing and HER2, we have a 9 prescription for using this based on outcomes 10 and to use something outside of that, then 11 basically, your results are not within the 12 parameters that have been previously performed 13 and associated with outcomes. So that's the 14 best way I can describe it.</p> <p>15 COFFEY, Q.C.: 16 Q. Doctor, in your--from your perspective, if-- 17 well, I'll just ask, phrase the question in 18 this way. What sort of circumstances, in your 19 view, would warrant a laboratory, clinical 20 laboratory, looking beyond the necessity of 21 repeating a single test and requiring a wider 22 review? What sort of circumstances, just kind 23 of in general?</p> <p>24 DR. DABBS: 25 A. Well, I think -</p>	<p>1 So, you know, an unexpected marked 2 significant change in a result is always a red 3 flag, be it immunohistochemistry or a serum 4 sodium or serum potassium or whatever. That's 5 an issue that needs to be looked at by a team 6 in the laboratory.</p> <p>7 COFFEY, Q.C.: 8 Q. A quality assurance program in relation to an 9 IHC laboratory, what would you expect to find 10 or to be included in such a program, quality 11 assurance, the approach to it?</p> <p>12 DR. DABBS: 13 A. Quality assurance. Well, I think that first 14 and foremost, one needs to have metrics in 15 place so that you know where you are and you 16 know how things are operating. You need to 17 have all the items that I mentioned before and 18 basically went through the consensus 19 recommendation. Everything from proper 20 grossing and fixation of tissue, proper thin 21 slicing, and all the items associated with 22 that, positive and negative, internal and 23 external controls on the slide, the external 24 controls on the slides, all those items that I 25 showed from the, you know, recent consensus,</p>
<p>Page 62</p> <p>1 COFFEY, Q.C.: 2 Q. And I take it, repeating a single test is not 3 unknown at all. It's not common and you 4 pointed to a percentage, I think it was less 5 than two percent, yesterday.</p> <p>6 DR. DABBS: 7 A. Right.</p> <p>8 COFFEY, Q.C.: 9 Q. But, and I take it if it gets beyond two 10 percent, your metrics are showing you that, 11 you make inquiries but what else?</p> <p>12 DR. DABBS: 13 A. Sure. Well, I think if for some reason, the 14 clinician oncologists request a case to be 15 repeated because it's negative, because the 16 patient doesn't have many other options in 17 terms of therapy, and if it turns out to be 18 strikingly positive, that is a red flag that 19 something definitely was not correct with that 20 initial test result, and that should initiate, 21 I think, a full scale look at when that case 22 was done, under what conditions and you could 23 probably track it down to who actually 24 performed the test that day on a given 25 instrument.</p>	<p>Page 64</p> <p>1 those, to me, are best practices for 2 immunohistochemistry and, you know, the 3 metrics part of it and the use of FDA approved 4 kits, all of that is, in my opinion, the 5 optimal and the ultimate in terms of quality 6 assurance for these complex tests that affect 7 patient care.</p> <p>8 COFFEY, Q.C.: 9 Q. Doctor, you have referred to FDA approved 10 kits. Are there such things for ER and PR?</p> <p>11 DR. DABBS: 12 A. Yes, there are.</p> <p>13 COFFEY, Q.C.: 14 Q. Okay, and in the context of, for example, the 15 Ventana automated machine -</p> <p>16 DR. DABBS: 17 A. Yes.</p> <p>18 COFFEY, Q.C.: 19 Q. - how does a kit figure into it? Perhaps you 20 could just comment.</p> <p>21 DR. DABBS: 22 A. Sure. Well, as with any FDA approved kit, it 23 comes with instructions and reagents and it's 24 a prescription. It's a cookbook, if you will. 25 It says this is the way you do this test. If</p>



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<p>1 the test says that you incubate the primary 2 antibody for 32 minutes, then you have to 3 incubate it for 32 minutes. If it gives you a 4 window, it says you can incubate it between, 5 you know, 28 and 34 minutes, that's fine. But 6 if you go lower or beyond that, it's not an 7 FDA approved kit. So that's what the FDA kit 8 means. You have to use, under these 9 parameters that the company has tried and 10 tested and brought it to us and have shown us 11 comparable results with other outcomes, that's 12 the reason for the FDA approved kit. So it 13 has to be used to prescription. You can't 14 just take the antibody out and use your own, 15 you know, home brew, so to speak. So that's 16 what -</p> <p>17 THE COMMISSIONER: 18 Q. When you say FDA approved kits, I think in 19 terms of things like, you know, approval of 20 drugs, for example.</p> <p>21 DR. DABBS: 22 A. Yes.</p> <p>23 THE COMMISSIONER: 24 Q. Which means that somebody is looking at a 25 particular drug and after X number of months</p>	<p>1 COFFEY, Q.C.: 2 Q. Doctor, is there, within the pathology 3 community, is there any disagreement about the 4 need for FDA approval of the kits that are 5 utilized?</p> <p>6 DR. DABBS: 7 A. Well, I think that you will get differing 8 opinions upon the necessity. There are good 9 laboratories that will say that they do a fine 10 job of using analyte specific reagents. These 11 are not FDA approved kits. The burden is on 12 that medical laboratory director to prove that 13 their results are, you know, comparable. So 14 that's a burden that is upon the medical 15 director. There are differences of opinion, I 16 think, in this consensus committee that was 17 held in Santa Barbara. There were people who 18 were balking at that. The cost is certainly a 19 consideration and these kits are more 20 expensive than building your own assay in 21 house. But again, my point that I brought to 22 the group was we're here for standardization 23 and we're talking about all these issues 24 related to pre-analytic variables. Why would 25 you not want to standardize the test platform?</p>
<p>1 or years, in some cases, examining within a 2 laboratory, it says "okay, you can now use 3 that." Would the same thing be happening to 4 the Ventanas of the world who wanted to do 5 this, they would have to present to some 6 approval authority, their machine, the 7 guidelines that they have arrived at and the 8 authority would then, in turn, presumably, 9 independently, examine those claims?</p> <p>10 DR. DABBS: 11 A. That is correct, and an example would be, you 12 know, for HER2 testing, when that first came 13 out, DAKO had the Hercept test and that was 14 the only approved test for that. Over time, 15 another--Ventana came out with another 16 antibody or actually took the CB11 antibody to 17 FDA approval, and more recently, they have 18 another HER2 clone, the 4B5, and in like 19 fashion, the ER and PR for the SP1 and 1E2, I 20 think have cleared, and DAKO has its set, and 21 so each company, there are several companies 22 out there that have approved kits that are 23 available.</p> <p>24 THE COMMISSIONER: 25 Q. Okay.</p>	<p>1 COFFEY, Q.C.: 2 Q. The analytic part of it?</p> <p>3 DR. DABBS: 4 A. The analytic part of it, and so subsequently, 5 most of the people there agree that that 6 should have been included. Are there some 7 people who have different opinions? Yes, 8 there always will be.</p> <p>9 COFFEY, Q.C.: 10 Q. Ask you, Registrar, please, Exhibit P-2728? 11 Doctor, this is a letter dated--memo or letter 12 dated July 22nd, 2008. It's addressed to Dr. 13 Nash Denic, clinical chief at Eastern Health. 14 It's from Dr. Nik Makretsov. See him there. 15 Have you had a chance to have a look at this 16 document, Doctor?</p> <p>17 DR. DABBS: 18 A. Yes, I have.</p> <p>19 COFFEY, Q.C.: 20 Q. And Doctor, can you give us your thoughts on 21 this, please? It's styled or introduced as, 22 "following the discussion with you, I'd like 23 to propose the draft describing the plan of 24 action regarding the breast pathology practice 25 at Eastern Health."</p>

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1 DR. DABBS:  
 2 A. Yes. You know, as an overall statement, I  
 3 felt that the content of this letter was  
 4 really well put together and on target and I  
 5 think really reflects a lot of best practices  
 6 that are currently--that we currently have at  
 7 our institution. He suggests using--to  
 8 endorse the Royal College of Pathologists and  
 9 UK Guidelines for reporting of breast disease,  
 10 and these are sort of along the guidelines of  
 11 the CAP synoptic reporting guidelines, which  
 12 is what we use, and to operate and update,  
 13 enrich current standard operating procedures  
 14 regarding breast specimens based on those  
 15 documents. Because what the synoptics do,  
 16 basically, synoptics, barring anything else, if  
 17 you look at that, it's sort of a starting  
 18 point, because it tells you what you need to  
 19 do upfront in order for the person who's doing  
 20 the grossing and the person who's doing the  
 21 microscopy and the person who's doing any  
 22 additional complex testing. So synoptic  
 23 reportings are standard operating procedure  
 24 and a necessity for accreditation by the CAP  
 25 and hospital laboratories in the States.

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1 And to implement weekly mandatory  
 2 interdepartmental breast slides review by a  
 3 panel of at least two pathologists, this is an  
 4 excellent practice. I can tell you that, at  
 5 our institution, we have several things.  
 6 Every day at 1:30, we gather around a multi-  
 7 headed microscope, and there's also a wall-  
 8 mounted television screen, where we discuss  
 9 cases that are of interest or difficult,  
 10 difficulty, or just have educational aspects  
 11 to it, because residents, fellows, and  
 12 attending pathologists are there. But the  
 13 other aspect that we do is for all new cancer  
 14 cases, first diagnosis, a second pathologist  
 15 reviews that and that's documented, and then  
 16 the other thing that we do for all negative  
 17 breast core biopsies is a second pathologist  
 18 also reviews that. So that the goal there is  
 19 to minimize any false negative reports on  
 20 breast biopsies. So this is--number two is an  
 21 excellent method of assuring quality. Number  
 22 3, "To reinstate breast pathology, radiology  
 23 weekly grand rounds." Again, that's an  
 24 excellent collegial item that, by the way, all  
 25 these items that have been mentioned here are

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1 also seen in white paper by the Susan Komen  
 2 Foundation that was published in the Breast  
 3 Journal about a year and a half ago indicating  
 4 that all these items here are sort of  
 5 desirable aspects of an interdisciplinary  
 6 breast team.  
 7 No. 4, "Organization steps towards the  
 8 creation of a multidisciplinary breast unit  
 9 engaging surgery, pathology, radiology." Yes,  
 10 weekly management meetings. And we currently  
 11 have that at our institution, as well. Again,  
 12 this fosters interdisciplinary collegiality,  
 13 exchange of information and whatnot. And you  
 14 know, one of the nice things about this is  
 15 that you get challenged by your colleagues.  
 16 For example, if you're presenting a lobular  
 17 cancer and you're telling the group in that  
 18 room that it's ER negative, someone is going  
 19 to let you know right then and there that  
 20 that's not right, what else could this be,  
 21 have you looked at it and so forth. So is a  
 22 very open style meeting in our institution  
 23 that enriches everyone.  
 24 No. 5, "Dedicate two pathologist  
 25 assistants to breast pathology as a primary

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1 duty." That sounds like an excellent sort of  
 2 centre of excellence approach, if you will,  
 3 two people who will handle these specimens the  
 4 best possible way. I would just caution and  
 5 encourage that if those two pathologist  
 6 assistants are away on vacation, that there  
 7 are other people as competent to step up to  
 8 the plate and do the same thing.  
 9 So, "to implement specimen audit in  
 10 breast pathology in order to monitor any  
 11 deficiencies in the specimen accession, gross  
 12 examination." Yes, that's excellent. We have  
 13 that, as well. Since we have pathologist  
 14 assistants and residents rotating through our  
 15 institution, our pathologist assistants are  
 16 really the stable element there. And I treat  
 17 them and actually established, I think, four  
 18 years ago now, a method of examining them in  
 19 terms of the quality of the work that they do.  
 20 And so basically what we did was generate  
 21 lists of all the things that they do and we  
 22 look at the--at these lists quarterly and  
 23 determine how people are doing in their  
 24 position. Are there people who are, for  
 25 example, cutting sections too thick, are there

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1 people who are--whose tissues they're  
 2 submitting need to be reprocessed and just  
 3 issues like that, so that we get feedback to  
 4 people and are able to improve the system from  
 5 within and how this is going on a quarterly  
 6 basis.  
 7 And then finally, he's suggesting tissue  
 8 microarrays for ER/PR and HER2 testing, which  
 9 is an excellent valid way of monitoring  
 10 quality assurance by putting these TMAs on  
 11 individual patient's slides. It doesn't get  
 12 any better than that. So it sounds like a  
 13 very ambitious and a plan that's devoted to  
 14 high quality.  
 15 COFFEY, Q.C.:  
 16 Q. They're the questions I have, Doctor. Thank  
 17 you, Commissioner.  
 18 THE COMMISSIONER:  
 19 Q. That's it. Do you have questions of this  
 20 witness?  
 21 MR. PRITCHARD:  
 22 Q. I don't have any questions, Commissioner.  
 23 Thank you for your evidence, Dr. Dabbs.  
 24 THE COMMISSIONER:  
 25 Q. Mr. Simmons, would you like us to take the

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1 morning break before you begin? I'm assuming  
 2 you want to ask questions.  
 3 MR. SIMMONS:  
 4 Q. I will have a few questions.  
 5 THE COMMISSIONER:  
 6 Q. Was that an unsafe assumption?  
 7 MR. SIMMONS:  
 8 Q. That's a safe assumption. And a break would  
 9 be helpful, thank you.  
 10 THE COMMISSIONER:  
 11 Q. All right, then, why don't we take the morning  
 12 break and then we'll proceed with your  
 13 questions.  
 14 (RECESS)  
 15 THE COMMISSIONER:  
 16 Q. Please be seated. Mr. Simmons.  
 17 DR. DAVID DABBS, EXAMINATION BY MR. DANIEL SIMMONS  
 18 MR. SIMMONS:  
 19 Q. Thank you, Commissioner. Dr. Dabbs, I'm Dan  
 20 Simmons, I'm the lawyer here for Eastern  
 21 Health, which is the regional health authority  
 22 that's responsible for the  
 23 immunohistochemistry laboratory.  
 24 DR. DABBS:  
 25 A. Um-hm.

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1 MR. SIMMONS:  
 2 Q. I was very interested in your presentation, as  
 3 I'm sure many people back at the lab and  
 4 others were. And I want to start just by  
 5 asking you some questions about the ad hoc  
 6 working group that you referred to when you  
 7 began your presentation because I understand  
 8 it was from this ad hoc working group that met  
 9 that these recommendations, consensus  
 10 recommendations have been generated. Can you  
 11 tell me a little more about how the working  
 12 group was composed and how it came to be that  
 13 this group of people have been addressing this  
 14 question of developing standardized  
 15 procedures?  
 16 DR. DABBS:  
 17 A. Sure. I think based on e-mail list serve type  
 18 of communications that it began probably about  
 19 three years ago that we decided that it would  
 20 be a good idea to get together to formulate  
 21 ideas based on evidence and to exchange this  
 22 information and to meet at one place where we  
 23 could do this in a more efficient manner and  
 24 be able to have cross talk. And basically the  
 25 people who subsequently got together were

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1 supported at, let's see, I think the first  
 2 place that we met was in Santa Barbara and  
 3 then the second place we meet was in Marathon,  
 4 Florida. The first meeting, I think, was in  
 5 2006. This was sponsored by DAKO, and we had  
 6 our first committee meeting there. The  
 7 composition of the group was, as I mentioned,  
 8 they were people in academia, reference  
 9 laboratories, scientists. I probably wouldn't  
 10 do justice to all the names of the people  
 11 there, but basically all the people who have a  
 12 high profile in immunohistochemistry in terms  
 13 of publishing were invited.  
 14 MR. SIMMONS:  
 15 Q. Um-hm.  
 16 DR. DABBS:  
 17 A. Some of those people did not make it, some of  
 18 those people who did not make it sent  
 19 representatives from their laboratory who were  
 20 there, so it was a pretty good cross section  
 21 of people in academia, reference laboratories  
 22 and people associated with government who were  
 23 there. The first meeting that actually  
 24 generated a paper, the paper that was  
 25 published last year on immunohistochemistry

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1 was actually, that took place in Marathon,  
 2 Florida just prior to a course that is offered  
 3 down there. It was offered at the end of  
 4 January that year and it was offered by Dr.  
 5 Yazidgee; he was the host for that conference.  
 6 That conference was then repeated in Santa  
 7 Barbara January of this year and we met right  
 8 before that conference again. So that seems  
 9 to--we've done that twice now. That seems to  
 10 be a pattern. I don't know if we're scheduled  
 11 to meet again. The next meeting is supposed  
 12 to be in January for Dr. Yazidgee's course,  
 13 actually, which I will be speaking at. So  
 14 whether this group meets again, I'm uncertain  
 15 at this point.

16 MR. SIMMONS:  
 17 Q. Okay. Would it be fair to say that the ad hoc  
 18 committee, then, represented a fair cross  
 19 section of the leaders in the field in  
 20 immunohistochemistry?

21 DR. DABBS:  
 22 A. Very much so, yes.

23 MR. SIMMONS:  
 24 Q. In the United States?

25 DR. DABBS:

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1 A. Yes.

2 MR. SIMMONS:  
 3 Q. Any representation from outside of the United  
 4 States?

5 DR. DABBS:  
 6 A. I hope I don't get this wrong. I don't know  
 7 if there was anyone there from Canada or not.  
 8 Like I say, I don't remember the names of all  
 9 the people who were there, but I'm not  
 10 certain. There were--well, at the meeting in  
 11 Santa Barbara there were some people from  
 12 Europe. There was Moensvyberg, who is the  
 13 person who is the basically the director of  
 14 Nordic QC out of Copenhagen. And I believe  
 15 there was at least one person, perhaps two  
 16 from UK NEQAS. I think Dr. Miller might have  
 17 been one of the people, but I don't want to  
 18 guess on their names. It was at least one  
 19 person, perhaps two from UK NEQAS and other  
 20 people from the States.

21 MR. SIMMONS:  
 22 Q. Now you mentioned it was three years ago that  
 23 this initiative began through, I gather you  
 24 referred to list serve?

25 DR. DABBS:

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1 A. Yes.

2 MR. SIMMONS:  
 3 Q. So I presume there is e-mail or other  
 4 conversations among people?

5 DR. DABBS:  
 6 A. Yes.

7 MR. SIMMONS:  
 8 Q. That lead to the formation of this ad hoc  
 9 working group?

10 DR. DABBS:  
 11 A. Yes.

12 MR. SIMMONS:  
 13 Q. Why was it initiated, what were the background  
 14 reasons for wanting to bring this group  
 15 together to do this work?

16 DR. DABBS:  
 17 A. Well, I think that there was some inherent  
 18 frustration on the part of these pathologists  
 19 that given the way that things went with HER2  
 20 testing that now pathologists were trying to  
 21 get a better handle on hormone receptor  
 22 testing, which is also as important a  
 23 prognostic and predictive test as HER2. And  
 24 so the pathologists wanted to take the  
 25 initiative, seeing what had happened with HER2

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1 testing and trying to optimize it and  
 2 standardize it for pathologists across the  
 3 country.

4 MR. SIMMONS:  
 5 Q. What was it that had happened with HER 2  
 6 testing?

7 DR. DABBS:  
 8 A. Well, the history of the HER2 testing was such  
 9 that there was a fair amount of  
 10 interlaboratory variation regarding results.  
 11 This lead to dissatisfaction on the part of  
 12 clinicians, our clinician colleagues,  
 13 oncologists who treat breast cancer patients.  
 14 And as a result of that there was a joint  
 15 meeting, a gathering of pathologists from the  
 16 College of American Pathologists and ASCO, the  
 17 American Society of Clinical Oncologists to  
 18 get together to try to come up with some  
 19 scheme, proper scheme that would reflect more  
 20 accuracy in HER2 testing. And as a result of  
 21 that meeting guidelines came out for HER 2  
 22 testing and one of those guidelines was for  
 23 the very first time that there was a statement  
 24 regarding the mandatory minimum fixation time  
 25 in formalin for HER2 and so on and all those

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<p>1 guidelines came from this joint organization.  2 So that's basically a synopsis of the HER2  3 story.  4 MR. SIMMONS:  5 Q. Those guidelines, I believe they came out, was  6 it as late as 2007 that those were actually  7 released?  8 DR. DABBS:  9 A. That sounds about right, yes, about two years  10 ago.  11 MR. SIMMONS:  12 Q. Yes, okay. So because of this experience with  13 HER2, I gather then that there was a  14 recognition on the part of these leading  15 pathologists who you were in communication  16 with that the issue of ER/PR testing needed to  17 be looked at similarly?  18 DR. DABBS:  19 A. Yes.  20 MR. SIMMONS:  21 Q. Is that a fair statement?  22 DR. DABBS:  23 A. Correct.  24 MR. SIMMONS:  25 Q. Okay. And what were the types of concerns</p>	<p>1 regulating body?  2 DR. DABBS:  3 A. No, there was not. Although there were people  4 from such bodies there, there was a person who  5 represented the Association of Directors of  6 Anatomic and Surgical Pathology, also known as  7 ADASP, A-D-A-S-P, there was a person there who  8 represented CLIS, Clinical Laboratories  9 Standards Institute, CLSI, I'm sorry and  10 other--but no other formal, it wasn't done  11 under the aegis of any particular organizing  12 membership or body.  13 MR. SIMMONS:  14 Q. So I'm curious then about what the effect and  15 impact is of releasing a consensus statement  16 like this with recommendations for  17 standardization of parts of the process of ER  18 and PR testing. Without an organization  19 standing behind it, some licensing or  20 professional organization, how do these  21 recommendations then find their way into use  22 in clinical practice in different  23 laboratories?  24 DR. DABBS:  25 A. Yes, the, one of the people on this committee,</p>
<p>1 that people had about ER/PR testing that made  2 these leaders want to take on this effort?  3 DR. DABBS:  4 A. Well this wasn't necessarily a completely new  5 issue. But if you look at the literature and  6 what had been done worldwide, there were  7 issues with fixation, there were papers  8 written about different methodologies,  9 different reporting schemes and there was  10 generally an unevenness in all of these  11 parameters in the States.  12 MR. SIMMONS:  13 Q. Um-hm.  14 DR. DABBS:  15 A. And so this attempt was to get together, to  16 come to some consensus based on the evidence  17 that was out there to try to make it more  18 uniform so that laboratories would be able to  19 adopt a more uniform method of reporting.  20 MR. SIMMONS:  21 Q. Okay. And you mentioned that the first  22 meeting was sponsored by DAKO. Was the work  23 of the ad hoc committee carried out under the  24 authority or in connection with any kind of  25 professional organization or governing body or</p>	<p>1 the person associated with CLSI, indicated  2 that this was information from the proceedings  3 of this would be given to the CLSI. And also  4 there were people there who were associated  5 with committee memberships on the CAP. So at  6 least in part while it wasn't, not formally  7 set up, this information does get back to  8 these governing bodies. And I can tell you  9 that since the first paper that came out in  10 the AIM Journal that some of those items have  11 already showed up on CAP checklists regarding  12 fixation and documentation and things of that  13 nature. So while it's not done under the  14 aegis of a formal body, the informal nature of  15 it is an attestation that there's a need and  16 the information does disseminate sort of  17 upstream, if you will, to governing bodies who  18 take notice of the importance of this. So  19 it's, that's generally the way that process  20 worked.  21 MR. SIMMONS:  22 Q. Right. Now, your first meeting was in 2006?  23 DR. DABBS:  24 A. Yes.  25 MR. SIMMONS:</p>

<p style="text-align: right;">Page 85</p> <p>1 Q. By that time, at least here in Newfoundland 2 and Labrador and likely in other parts of 3 Canada the fact that there was a large scale 4 ER/PR testing retesting being done here was 5 known, it was public information. Was that 6 known to you or other participants at the time 7 that you embarked on this work in 2006?</p> <p>8 DR. DABBS:</p> <p>9 A. In 2006 it was unknown to me. I am uncertain 10 if it was known to anyone else. It was not 11 brought up during the proceedings of that 12 committee. I would have remembered that.</p> <p>13 MR. SIMMONS:</p> <p>14 Q. Okay. And there are consensus 15 recommendations, there's been two papers, one 16 after the 2006 meeting and one now to be 17 published out of the 2007 meeting. You say 18 you're uncertain whether the consensus group 19 will come back together again. Can you give 20 me your view as to how far along this ad hoc 21 working group has moved the issue of 22 addressing the things on which consensus needs 23 to be found and which standardization needs to 24 be looked at in immunohistochemical testing 25 for ER/PR?</p>	<p style="text-align: right;">Page 87</p> <p>1 DR. DABBS:</p> <p>2 A. Um-hm. Well, I think that every item that 3 came up in the recommendations, that 4 ultimately came up, were discussed very 5 thoroughly.</p> <p>6 MR. SIMMONS:</p> <p>7 Q. Um-hm.</p> <p>8 DR. DABBS:</p> <p>9 A. Everything from fixation to the antibodies 10 that were discussed to the reporting method. 11 Perhaps one of the more contentious was the 12 issue of FDA approved kits. But again, I 13 think that once the discussions were over, 14 people had no problem including that in their 15 recommendation. There was a varying degree of 16 experience on the part of everyone there, 17 everyone had different experiences. I'm sure 18 that people from UK NEQAS and Nordic QC had 19 different experiences from many of the 20 Americans sitting around the table, and we all 21 shared evidence, the best that we knew it. 22 And so there was no single item that stood out 23 and people pretty much came to an agreement 24 that this is what needed to be done and 25 basically everyone is on board with those</p>
<p style="text-align: right;">Page 86</p> <p>1 DR. DABBS:</p> <p>2 A. Well, I think that the publication will 3 certainly have impact and I think, as well, 4 the governing bodies of which some of the 5 members are associated with, CAP, CLSI, that 6 information has gone back to those governing 7 bodies. So I think we're still in the early 8 phase of seeing what the potential fallout of 9 that will be. But I feel fairly confident in 10 that when these recommendations do come out 11 and are actually published, that these will be 12 taken up by the accrediting agencies for 13 laboratories in the US, specifically the CAP. 14 I have little doubt that that will occur.</p> <p>15 MR. SIMMONS:</p> <p>16 Q. Were there areas where there was--well, 17 obviously consensus was reached for all the 18 recommendations. But I gather from what 19 you've said before that there may have been 20 some degree of debate on some of these issues 21 as to what the consensus would be. What were 22 the more significant areas in which that 23 debate had to take place in which there were 24 differing views or opinions about what should 25 be recommended?</p>	<p style="text-align: right;">Page 88</p> <p>1 consensus recommendations.</p> <p>2 MR. SIMMONS:</p> <p>3 Q. Okay. I gather from your evidence as a whole 4 that since you've reviewed a number of papers 5 that have come through at different times that 6 have seemed to advance the knowledge and 7 understanding of ER/PR by immunohistochemistry 8 that the basic science of it has been better 9 understood as time has gone on, is that a fair 10 statement to make?</p> <p>11 DR. DABBS:</p> <p>12 A. Yes.</p> <p>13 MR. SIMMONS:</p> <p>14 Q. And that there's been development and change 15 in the testing methods and the available 16 antibodies, reagents, detection kits and 17 hardware over time, as well?</p> <p>18 DR. DABBS:</p> <p>19 A. Yes.</p> <p>20 MR. SIMMONS:</p> <p>21 Q. Yes, okay. Would it have been possible before 22 the last couple of years to generate the kind 23 of consensus on recommendations like this that 24 you were able to do, if you had tackled that 25 five years earlier, would there have been more</p>

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1 uncertainty about what the recommendations  
 2 should be at that time?  
 3 DR. DABBS:  
 4 A. I think that based on the literature that was  
 5 in existence five years ago that probably very  
 6 similar information would have come out of  
 7 this.  
 8 MR. SIMMONS:  
 9 Q. Um-hm.  
 10 DR. DABBS:  
 11 A. The only difference would have been that the  
 12 SP1 antibody wasn't around at that time.  
 13 MR. SIMMONS:  
 14 Q. So can you offer any observation as to why it  
 15 wasn't until '06, '07 that this effort was  
 16 undertaken rather than, say, five years  
 17 earlier, in 2001 or 2002?  
 18 DR. DABBS:  
 19 A. Yeah. No, I really can't speculate on that.  
 20 MR. SIMMONS:  
 21 Q. Okay. Thank you. The recommendations that  
 22 the committee has made, this may be obvious,  
 23 but I'll ask you anyway, do they represent the  
 24 direction that IHC for ER/PR testing should be  
 25 going in or, in your view, do they represent

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1 the existing state of testing as carried out  
 2 in labs through the United States? In other  
 3 words, once labs look at these recommendations  
 4 are many labs going to have things to do to  
 5 bring themselves into compliance with them?  
 6 DR. DABBS:  
 7 A. I think that this document was put together to  
 8 show direction. I think that there are  
 9 laboratories that have probably always  
 10 practised a good practice similar to these  
 11 recommendations.  
 12 MR. SIMMONS:  
 13 Q. Um-hm.  
 14 DR. DABBS:  
 15 A. I think that it's meant to be a direction and  
 16 that, yes, there will be laboratories that  
 17 will need to pay attention to certain of these  
 18 recommendations, perhaps some more than  
 19 others.  
 20 MR. SIMMONS:  
 21 Q. Um-hm, okay. In your experience, when new  
 22 information comes out in the literature about  
 23 practices that are appropriate to be followed  
 24 or that should be considered in something like  
 25 IHC testing, how long does it take for those

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1 things to find their way into actual clinical  
 2 practice in the laboratories, is there a lag  
 3 time between the doing of the science and the  
 4 research and then the implementation on a  
 5 large scale?

1 DR. DABBS:  
 2 A. I think that generally there is a lag time.  
 3 It's difficult because there are so many  
 4 publications that are available to sort of  
 5 wade through these and try to discern what  
 6 impact they have. I think that papers such as  
 7 the consensus recommendation with the list of  
 8 people who were involved in putting that  
 9 together, probably have more of an immediate  
 10 impact just because of the nature of the group  
 11 that gets together and puts together  
 12 recommendations as opposed to a scientific  
 13 paper, for example, with new information. So  
 14 --  
 15 MR. SIMMONS:  
 16 Q. So would an advantage of the work of the  
 17 consensus group be that the leaders in the  
 18 field will put their heads together, consider  
 19 the accumulated body of research that's been  
 20 carried out, and distil that down into a set

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1 of recommendations that are more easily  
 2 adapted by either clinicians into their  
 3 regular practises?  
 4 DR. DABBS:  
 5 A. Yes, that's fair to say.  
 6 MR. SIMMONS:  
 7 Q. So the consensus statement makes it easier for  
 8 someone else to come to these conclusions and  
 9 to know what are the best practises to follow?  
 10 DR. DABBS:  
 11 A. It would.  
 12 MR. SIMMONS:  
 13 Q. Yeah. You were asked some questions by Mr.  
 14 Coffey about laboratory accreditation in the  
 15 United States, which is of interest to us  
 16 because you may be aware there is no  
 17 accreditation in this province for  
 18 laboratories, and has not been aside from the  
 19 general accreditation available for  
 20 institutions. The Clinical Laboratory  
 21 Improvement Act of 1988 --  
 22 DR. DABBS:  
 23 A. Yes.  
 24 MR. SIMMONS:  
 25 Q. Did that have anything to do with encouraging

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1 or mandating laboratory accreditation in the  
 2 United States?  
 3 DR. DABBS:  
 4 A. Well, it was--that was just one part of an  
 5 ongoing act that came up with various  
 6 improvements over time.  
 7 MR. SIMMONS:  
 8 Q. Uh-hm.  
 9 DR. DABBS:  
 10 A. One of the key items of CLIA 88 actually had  
 11 to do with cytopathology and PAP testing, but  
 12 each--whenever revisions or new information  
 13 would come out regarding that Act, they were  
 14 usually related to the laboratory. The  
 15 inspection process has been in the States  
 16 basically a function of the federal  
 17 government.  
 18 MR. SIMMONS:  
 19 Q. Uh-hm.  
 20 DR. DABBS:  
 21 A. And they use agencies such as CMS, JCHO, and  
 22 the CAP as bona fide accrediting agencies. So  
 23 they operate at the pleasure of the federal  
 24 government.  
 25 MR. SIMMONS:

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1 Q. So all laboratories have to be subject to  
 2 accreditation by one of those agencies?  
 3 DR. DABBS:  
 4 A. Yes, they do.  
 5 MR. SIMMONS:  
 6 Q. And how long has that been the case, do you  
 7 know?  
 8 DR. DABBS:  
 9 A. I don't remember exactly how long that's been,  
 10 but it has been for quite a long time. I  
 11 don't have the answer to that.  
 12 MR. SIMMONS:  
 13 Q. Would you say at least for the last ten years,  
 14 if not longer?  
 15 DR. DABBS:  
 16 A. Oh, certainly, yes, yes.  
 17 MR. SIMMONS:  
 18 Q. I presume you're familiar with some of the  
 19 work done in the United Kingdom done by Dr.  
 20 Rhodes in which he looked at inter-laboratory  
 21 variability of ER and PR testing results?  
 22 DR. DABBS:  
 23 A. Yes.  
 24 MR. SIMMONS:  
 25 Q. Has any similar work been done in the United

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1 States, any similar research?  
 2 DR. DABBS:  
 3 A. There have been similar studies performed on  
 4 immunohistochemistry, in general, regarding,  
 5 for example, epitope retrieval or antigen  
 6 retrieval, and I think that was sort of a star  
 7 point of Dr. Rhodes paper regarding hormone  
 8 receptor, but ever since the introduction of  
 9 that, there have been ongoing studies trying  
 10 to compare methods in heating methods and  
 11 different solutions for antigen retrieval.  
 12 That all originated out of actually from Dr.  
 13 Shon R. Chi who spent a great deal of time  
 14 with Dr. Clive Taylor at the University of  
 15 Southern California, and there's a lot of  
 16 papers on antigen retrieval. It really opened  
 17 up the field of immunohistochemistry because  
 18 prior to that there were many antibodies that  
 19 were desirable to use on formalin fixed  
 20 paraffin embedded tissue that just did not  
 21 work until antigen retrieval. So it opened up  
 22 a whole new world and it also, as I mentioned  
 23 before, it levelled the playing field for  
 24 formalin, for fixation issues that you can  
 25 have tissues fixed for any length of time, you



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<p>1 could use antigen retrieval to bring it to a</p> <p>2 proper reaction product that can be used in</p> <p>3 the clinical sense, but in terms of other</p> <p>4 antigen retrieval methods in estrogen</p> <p>5 receptor, hormone receptor testing, there's</p> <p>6 not much.</p> <p>7 MR. SIMMONS:</p> <p>8 Q. And I--and I may have this wrong, but I</p> <p>9 understand that some of the work done by</p> <p>10 Rhodes and those with him in the UK, actually</p> <p>11 involved looking at the end result of hormone</p> <p>12 receptor testing and comparing it across</p> <p>13 laboratories where each laboratory was given</p> <p>14 the same tissue and asked to take it, prepare</p> <p>15 a slide, assess it, and report the result.</p> <p>16 Have I got that?</p> <p>17 DR. DABBS:</p> <p>18 A. That's correct.</p> <p>19 MR. SIMMONS:</p> <p>20 Q. Yes, and one of the outcomes of that was there</p> <p>21 was a significant variation found among</p> <p>22 laboratories for the results that they</p> <p>23 reported back on these testing at the time</p> <p>24 they did their study?</p> <p>25 DR. DABBS:</p>	<p>1 MR. SIMMONS:</p> <p>2 Q. As far as patient care, whether it initiated a</p> <p>3 concern that any patients had not had the</p> <p>4 correct results they needed for their clinical</p> <p>5 care as a result of this finding that there</p> <p>6 was considerable variation in some cases</p> <p>7 between laboratories and the results?</p> <p>8 DR. DABBS:</p> <p>9 A. Well, I think one of the directions that paper</p> <p>10 would have had an impact would have been on</p> <p>11 attempting to standardize the test kits and</p> <p>12 the testing method, and that's where I think</p> <p>13 companies ultimately saw that utilizing</p> <p>14 analytes specific reagents in home brew tests</p> <p>15 was a variation that was undesirable, and</p> <p>16 hence there was a push, at least in the</p> <p>17 States, to FDA approved testing kits where</p> <p>18 antigen retrieval was prescribed and the</p> <p>19 antibody detection methods were all</p> <p>20 prescribed.</p> <p>21 MR. SIMMONS:</p> <p>22 Q. So the research produced information that was</p> <p>23 useful to improve the quality of testing from</p> <p>24 that point forward?</p> <p>25 DR. DABBS:</p>
<p>1 A. Yes, it was variation that was in the end</p> <p>2 thought to be due largely to antigen</p> <p>3 retrieval.</p> <p>4 MR. SIMMONS:</p> <p>5 Q. Uh-hm, okay, and--but I gather from what</p> <p>6 you've said, that there has not been a similar</p> <p>7 study done in the United States to assess</p> <p>8 whether at any point different laboratories in</p> <p>9 the United States were similarly reporting</p> <p>10 different results?</p> <p>11 DR. DABBS:</p> <p>12 A. Correct.</p> <p>13 MR. SIMMONS:</p> <p>14 Q. Okay. Just in relation to the work done in</p> <p>15 the UK, as a result of the studies which</p> <p>16 showed variability among laboratories, do you</p> <p>17 know if there were any clinical consequences</p> <p>18 from that, and by that I don't mean changes in</p> <p>19 practises going forward in the future, but do</p> <p>20 you know if that initiated any concern about</p> <p>21 the validity of test results that had been</p> <p>22 already performed at any of those</p> <p>23 laboratories?</p> <p>24 DR. DABBS:</p> <p>25 A. Well, as far as antigen retrieval goes?</p>	<p>1 A. Yes.</p> <p>2 MR. SIMMONS:</p> <p>3 Q. And that was the use which was made, to your</p> <p>4 knowledge, of that research, was it?</p> <p>5 DR. DABBS:</p> <p>6 A. Yes.</p> <p>7 MR. SIMMONS:</p> <p>8 Q. Okay. You've referred to your text which</p> <p>9 we've heard of before in this Commission. I</p> <p>10 think it's a reference valued by the</p> <p>11 technologists here now, and you mentioned it's</p> <p>12 in the second edition. The first edition came</p> <p>13 out in 2002, I believe, did it?</p> <p>14 DR. DABBS:</p> <p>15 A. I believe October of 2002, in the Fall, yeah.</p> <p>16 MR. SIMMONS:</p> <p>17 Q. You mentioned as well that there are some</p> <p>18 other texts and prior to your book in 2002,</p> <p>19 though, were there any other texts that</p> <p>20 addressed the technical aspects of</p> <p>21 immunohistochemical testing as comprehensively</p> <p>22 as the one which you've edited?</p> <p>23 DR. DABBS:</p> <p>24 A. There were texts that--I don't know that you</p> <p>25 would consider them textbooks per se, but they</p>

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<p>1 were more like manuals that were available 2 through certain publishers, but they were more 3 laboratory sort of basic science oriented and 4 not oriented towards the clinical laboratory. 5 So that's where my textbook differed, it was 6 more applicable to the clinical laboratory. 7 MR. SIMMONS: 8 Q. And I gather that part of the reason for you 9 preparing your textbook and initiating it was 10 the recognition of the need for just such a 11 text for immunohistochemical laboratories? 12 DR. DABBS: 13 A. Yes. 14 MR. SIMMONS: 15 Q. Which was not available before yours? 16 DR. DABBS: 17 A. Correct. 18 MR. SIMMONS: 19 Q. You've told us about--and I may jump around a 20 little bit here from topic to topic. You've 21 told us about H scores and Allred scores and 22 so on, and different means of reporting the 23 interpretation of an ER/PR test, and if I 24 understand correctly, there's at least four 25 different variations that I've heard mentioned</p>	<p>1 A. You may. 2 MR. SIMMONS: 3 Q. Choose to report that way. 4 DR. DABBS: 5 A. You may. 6 MR. SIMMONS: 7 Q. Was there a time when reporting as simply 8 negative or positive was not in the minority, 9 but maybe the predominant way of reporting 10 this test? 11 DR. DABBS: 12 A. I think that the majority--the most prevalent 13 method of reporting always had to do with some 14 sort of number. 15 MR. SIMMONS: 16 Q. Uh-hm. 17 DR. DABBS: 18 A. And I think the most common number at least 19 for the first ten years was probably the 20 cutoff at 10 percent that I mentioned. 21 MR. SIMMONS: 22 Q. Uh-hm. 23 DR. DABBS: 24 A. So that was not just a positive or negative 25 result. They would indicate that more than 10</p>
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<p>1 by you. One would be to simply report the 2 result as positive or negative. Another would 3 be to report the percentage of nuclei that have 4 stained positive that shown any staining. 5 Third would be the Allred score, which you've 6 explained how that works, and then the fourth 7 would be the H score which you use in your 8 institution. Are those primarily the four ways 9 in which these tests have been scored and 10 reported? 11 DR. DABBS: 12 A. Those are four common ways in which tests have 13 been reported, yes. 14 MR. SIMMONS: 15 Q. Do you know if simply reporting the tests as 16 positive or negative is still in use, or 17 whether that's now been discounted and no 18 longer accepted? 19 DR. DABBS: 20 A. I think if you survey probably in the States, 21 it would probably be a minority. 22 MR. SIMMONS: 23 Q. Uh-hm, but you would still find that some 24 institutions -- 25 DR. DABBS:</p>	<p>1 percent, and some laboratories went further 2 and broke it down, the percentage. 3 MR. SIMMONS: 4 Q. Uh-hm. 5 DR. DABBS: 6 A. That's why the consensus group felt that it 7 was more important to do a semi-quantisation 8 because semi-quantisation is important for 9 individual patients. 10 MR. SIMMONS: 11 Q. So do I understand then that if the percent is 12 to be reported, there may then be a couple of 13 variations on that. It could be reported as a 14 number; 8 percent, 25 percent, 60 percent, 80 15 percent, or do I understand you to say that 16 some practises may have been to say greater 17 than 10 percent or less than 10 percent 18 without defining it beyond that? 19 DR. DABBS: 20 A. There have been laboratories reporting as 21 such, yes. 22 MR. SIMMONS: 23 Q. Yes, okay. Your laboratory reports the H 24 score method? 25 DR. DABBS:</p>

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1 A. Yes.  
 2 MR. SIMMONS:  
 3 Q. And for how long has that been done at Magee?  
 4 DR. DABBS:  
 5 A. The H score method basically is derived from a  
 6 formula that shows the intensity and  
 7 proportion of cells.  
 8 MR. SIMMONS:  
 9 Q. Uh-hm.  
 10 DR. DABBS:  
 11 A. And we began reporting the intensity and  
 12 proportion of cells in 2002. About six months  
 13 ago, basically what we decided to add to that  
 14 was to do the math, if you will. If you do  
 15 the math from that proportion and intensity,  
 16 you derive the H score. So we decided to  
 17 revise our reporting method in sort of a  
 18 synoptic format. Basically, what we do is--  
 19 and it wasn't just about the H score. We use  
 20 proliferation indices, we use HER 2 score, and  
 21 we use the ER along with lymphatic space  
 22 invasion as a sort of synopsis on the  
 23 immunohistochemistry reporting form, and  
 24 decided to add the H score to give our  
 25 clinicians a quantitative number that would be

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1 an easy reference. In doing so, what we did  
 2 was we went back and looked back and looked at  
 3 30 months of our repots, converted them all to  
 4 H scores, and then looked at the median and  
 5 mode percent of cells staining for each  
 6 category. So, for example, if I see an H  
 7 score of 250, that means automatically to me  
 8 that the median number of cells staining in a  
 9 situation like that is greater than 75  
 10 percent, and we have those sort of little  
 11 mnemonics present on our reporting forms so  
 12 that when a clinician sees that, they look at  
 13 that and they say it's easily translatable,  
 14 they can use whatever they want. So that they  
 15 get used to it. So that an H score to them,  
 16 250, somewhere down the road as they get used  
 17 to it, they'll think more than 75 percent of  
 18 cell staining. So it's helpful in that  
 19 regard.  
 20 MR. SIMMONS:  
 21 Q. So you don't now actually report the  
 22 percentage of cells stained and the H score,  
 23 it's only the H score, that's the only number  
 24 that's given, is it?  
 25 DR. DABBS:

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1 A. No, we continue to report the percent of cells  
 2 staining as well as their intensity.  
 3 MR. SIMMONS:  
 4 Q. Yes.  
 5 DR. DABBS:  
 6 A. And the H score.  
 7 MR. SIMMONS:  
 8 Q. And the H score.  
 9 DR. DABBS:  
 10 A. Right, and we have these little mnemonics in  
 11 there that will show in bold brackets a mean  
 12 score, H score of 250, equals greater than 75  
 13 percent of cell staining.  
 14 MR. SIMMONS:  
 15 Q. Shorthand, okay. Now in 2002, can you give me  
 16 a quick example of how you would have actually  
 17 reported an ER/PR test in 2002?  
 18 DR. DABBS:  
 19 A. Yes, we - since 2002 and to date, we have a  
 20 statement on our ER/PR report that basically  
 21 is a cut and paste from the NIH Consensus  
 22 Conference that says that a negative result is  
 23 zero staining and a positive result is any  
 24 nuclear expression, and we say "and is semi-  
 25 quantitated as indicated below", and basically

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1 that shows the brackets with the percent of  
 2 cell staining, 1 plus, and percent, 2 plus,  
 3 and there's a percent, and 3 plus.  
 4 MR. SIMMONS:  
 5 Q. Yes.  
 6 DR. DABBS:  
 7 A. The only thing that we added five or six years  
 8 later was we did the math and applied that as  
 9 well.  
 10 MR. SIMMONS:  
 11 Q. Now prior to 2002, how were they reported?  
 12 DR. DABBS:  
 13 A. Prior to 2002, to some degree they were  
 14 reported by a H score method that was a little  
 15 bit different than what we used to use. There  
 16 are variations of an H score method. The one  
 17 that was in use was based on a scale of zero  
 18 to 500 and it was a little more tedious in  
 19 terms--the scoring method, instead of zero to  
 20 3 plus for intensity, it went zero to 4 plus,  
 21 and then there was a mathematical factor added  
 22 in of 100, so that's why the spread was  
 23 greater.  
 24 MR. SIMMONS:  
 25 Q. Uh-hm.

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1 DR. DABBS:  
 2 A. But the H score method as used, we did a  
 3 internal validation with what that meant in  
 4 terms of cell intensity and percent of cell  
 5 staining over that 30 month period, and the H  
 6 score, in general, you can use for any kind of  
 7 immunohistochemistry staining. Basically, what  
 8 it is, it's a combination of percent of cell  
 9 staining and the degree of intensity. So the  
 10 committee has been--one of the items we  
 11 discussed for some time was trying to add some  
 12 uniformity to how to report any  
 13 immunohistochemistry stain, and basically we  
 14 came down to a description that says we're  
 15 supposed to say what is staining, where it's  
 16 staining, and how is it staining.  
 17 MR. SIMMONS:  
 18 Q. Uh-hm, okay. So for ER/PR then, do I  
 19 understand correctly that the consensus  
 20 recommendation for how to report it is, in  
 21 fact, the method that you used at Magee from  
 22 2002 until a couple of months ago?  
 23 DR. DABBS:  
 24 A. Correct.  
 25 MR. SIMMONS:

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1 Q. Rather than the H score?  
 2 DR. DABBS:  
 3 A. Correct.  
 4 MR. SIMMONS:  
 5 Q. In your presentation, if we can bring up page  
 6 7, please, of P-2621. Dr. Dabbs, there's a  
 7 reference here on your slide to the Perchuck  
 8 et al ER ID5 study done in--published, anyway,  
 9 in 1996?  
 10 DR. DABBS:  
 11 A. Yes.  
 12 MR. SIMMONS:  
 13 Q. Now when you mentioned this yesterday, with my  
 14 note I may have this wrong, I understood you  
 15 to say that based on this study, it concluded  
 16 that a 10 percent report of ER staining was as  
 17 clinically effective as reporting the exact  
 18 percentage and the intensity of the staining.  
 19 Have I got that right?  
 20 DR. DABBS:  
 21 A. That's correct, that's what the paper by  
 22 Perchuck said.  
 23 MR. SIMMONS:  
 24 Q. So this would be one of the papers that would  
 25 support the proposition that there's little to

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1 be added to the clinical usefulness by  
 2 reporting the intensity versus just reporting  
 3 the percentage. Would that be correct?  
 4 DR. DABBS:  
 5 A. Strictly speaking in terms of the result of  
 6 the test, yes but there are other issues  
 7 associated with reporting staining intensity  
 8 which are of quality issues too.  
 9 MR. SIMMONS:  
 10 Q. Okay. So from the clinician's point of view  
 11 then, this study, and there may be others that  
 12 say the opposite, but this study would say  
 13 that the clinician using the result gets as  
 14 much value out of getting a percentage alone  
 15 as out of a percentage combined with an  
 16 intensity?  
 17 DR. DABBS:  
 18 A. Yes, that's correct, and if you--and there  
 19 have been several studies performed, including  
 20 whenever we looked at the 30 month period  
 21 where we converted our reporting method into H  
 22 score, that, yes, the answer is the percent of  
 23 cell staining does correlate with scoring  
 24 method of percent plus intensity.  
 25 MR. SIMMONS:

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1 Q. Uh-hm.  
 2 DR. DABBS:  
 3 A. And some people argue that there's some  
 4 subjectivity--more subjectivity in the  
 5 interpretation of intensity than there is  
 6 percent of cell staining.  
 7 MR. SIMMONS:  
 8 Q. Uh-hm.  
 9 DR. DABBS:  
 10 A. But the utility--the real utility of reporting  
 11 the intensity of staining is that your assay  
 12 shows a range of intensity of staining and  
 13 isn't all or none.  
 14 MR. SIMMONS:  
 15 Q. So it's--so the real usefulness of assessing  
 16 the intensity then is as a quality assurance  
 17 measure?  
 18 DR. DABBS:  
 19 A. At least--it is at least in part, but what it  
 20 also permits you to do is to generate an  
 21 actual quantitative number --  
 22 MR. SIMMONS:  
 23 Q. Uh-hm.  
 24 DR. DABBS:  
 25 A. That is reasonably reproducible in terms of

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1 the H score because clinicians are clinicians,  
 2 and clinicians everywhere, they like numbers,  
 3 and there are other testing modes available  
 4 for estrogen and progesterone receptor not by  
 5 immunohistochemistry that will give an actual  
 6 quantitative number. So what we do in our  
 7 reporting format in our institution is we  
 8 report raw scores of staining, percent plus  
 9 intensity, we report the actual numerical  
 10 number associated with that as well, and we  
 11 also cite as references points what that means  
 12 in terms of the median number of cell staining  
 13 for any particular case.

14 MR. SIMMONS:  
 15 Q. Okay. On page 8, there is a reference in the  
 16 slide in the bottom left there to a study  
 17 published in 2005 by Fisher, and I understood  
 18 you to describe this study as being one that  
 19 compared ER/PR results from the older  
 20 biochemical assay method to results using an  
 21 immunohistochemical method?

22 DR. DABBS:  
 23 A. Yes.

24 MR. SIMMONS:  
 25 Q. Is that correct? I was curious, this being

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1 2005, I had gathered from the early part of  
 2 your presentation that the biochemical assay  
 3 method had been pretty well displaced by the  
 4 IHC method by this time?

5 DR. DABBS:  
 6 A. Correct.

7 MR. SIMMONS:  
 8 Q. And I was wondering what the purpose was in  
 9 2005 of doing that comparison here in this  
 10 study?

11 DR. DABBS:  
 12 A. Oh, sure. Well, Dr. Fisher was the  
 13 pathologist for the NSABP and this clinical  
 14 trial was actually performed back in the 70s.  
 15 So basically what it was, it was a follow-up  
 16 cohort of those patients, about 400 patients  
 17 in that B-09 protocol. So he had the DCC  
 18 data. It wasn't like it had been generated  
 19 anew.

20 MR. SIMMONS:  
 21 Q. Uh-hm.

22 DR. DABBS:  
 23 A. Okay, that was archived data, and so he had  
 24 all the tissue blocks from those patients. So  
 25 he basically, said, okay, this is how we did

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1 our ER then, let's see how we can--the scoring  
 2 methods, and what that was basically was  
 3 scoring methods, it was any or none, it was  
 4 semi-quantitative with your eyeball, and there  
 5 was a group that did a more detailed analysis  
 6 with image analysis, and the conclusions of  
 7 that were that any of those modes were equal  
 8 in determining how patients outcome was with  
 9 regard--in five and ten years, which is a  
 10 really nice follow-up for that group of  
 11 patients, but what it did not say or attempt  
 12 to say was the importance of quantisation for  
 13 the individual patient, okay.

14 MR. SIMMONS:  
 15 Q. Uh-hm.

16 DR. DABBS:  
 17 A. Because as you know, you can have patients who  
 18 have 11 percent of cells or those who have 85  
 19 percent of cells, and I can tell you from my  
 20 experience in looking at all the data and  
 21 doing the cross-analysis, that someone with 80  
 22 percent of positive cells is virtually certain  
 23 to be ER positive and PR positive, and it's  
 24 that group of patients that respond best to  
 25 therapy. So if the clinician has a patient

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1 who is young and healthy, and has no contra-  
 2 indications to this medicine which can give  
 3 you--put you at increased risk of endometrial  
 4 cancer, it can give you strokes, it can give  
 5 you thromboembolism, not to mention some other  
 6 less than satisfactory side effects like hot  
 7 flashes and what not. For a patient who is  
 8 healthy like that, it should be no problem,  
 9 but if this patient has relative contra-  
 10 indications, medical contra-indications or is  
 11 elderly and frail, and their ER is 11 percent  
 12 or 5 percent compared to 80 percent, you look  
 13 at that and the clinician has to weigh, you  
 14 know, weighing the risk/benefit.

15 MR. SIMMONS:  
 16 Q. Uh-hm.

17 DR. DABBS:  
 18 A. Am I going to harm this patient more by giving  
 19 this medicine or am I going to be doing her  
 20 better by giving her this medicine, and that's  
 21 where quantisation for the individual patient  
 22 becomes important. It's not important for  
 23 populations.

24 MR. SIMMONS:  
 25 Q. Now you said that those that are ER positive

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<p>1 and PR positive are known to respond better to</p> <p>2 hormone treatment?</p> <p>3 DR. DABBS:</p> <p>4 A. Yes.</p> <p>5 MR. SIMMONS:</p> <p>6 Q. And that's based on clinical studies, is it?</p> <p>7 DR. DABBS:</p> <p>8 A. Yes, it is, multiple clinical studies.</p> <p>9 MR. SIMMONS:</p> <p>10 Q. Now the next piece of that, you said that a</p> <p>11 high ER score is usually also a high--a PR</p> <p>12 positive?</p> <p>13 DR. DABBS:</p> <p>14 A. That's correct.</p> <p>15 MR. SIMMONS:</p> <p>16 Q. Yes.</p> <p>17 DR. DABBS:</p> <p>18 A. Basically, it goes the best responders are ER</p> <p>19 positive and PR positive, and those ER scores</p> <p>20 are almost always more than 80 percent cells.</p> <p>21 MR. SIMMONS:</p> <p>22 Q. Has there been any clinical study looking at</p> <p>23 just the ER score and the intensity of the ER</p> <p>24 score, ignoring whether the PR is positive or</p> <p>25 negative and correlating that with clinical</p>	<p>1 outcomes associated with it, that includes</p> <p>2 either biochemical assay or IHC, have comments</p> <p>3 about the method, the response, if you will,</p> <p>4 the patients who have 1 percent of cells don't</p> <p>5 respond as well as patients who have 50</p> <p>6 percent. That's virtually in every paper that</p> <p>7 has an outcome associated with it. It was the</p> <p>8 paper by Harvey in 1999 that was sort of a</p> <p>9 seminal paper that took the barrier, if you</p> <p>10 will, down to greater than 1 percent of cells.</p> <p>11 MR. SIMMONS:</p> <p>12 Q. Right.</p> <p>13 DR. DABBS:</p> <p>14 A. But in the paper that actually was in the mid</p> <p>15 90s by Mascarelli, 1995, that's where they did</p> <p>16 the ID5 with the 10 percent and 5 percent</p> <p>17 cutoff and found the difference.</p> <p>18 MR. SIMMONS:</p> <p>19 Q. Yeah.</p> <p>20 DR. DABBS:</p> <p>21 A. That was sort of the telltale then that maybe</p> <p>22 we could go lower than 5 percent.</p> <p>23 MR. SIMMONS:</p> <p>24 Q. Uh-hm, okay. On the next page, page 9, you</p> <p>25 have a slide and I think this is in--there's a</p>
<p>1 outcome?</p> <p>2 DR. DABBS:</p> <p>3 A. Yes, there have been, and basically the</p> <p>4 hierarchy, if you will, would be--of course,</p> <p>5 the patients who respond best are ER positive,</p> <p>6 PR positive. The next group is ER positive,</p> <p>7 PR negative.</p> <p>8 MR. SIMMONS:</p> <p>9 Q. Uh-hm.</p> <p>10 DR. DABBS:</p> <p>11 A. The next group is ER negative, PR positive.</p> <p>12 MR. SIMMONS:</p> <p>13 Q. Yes.</p> <p>14 DR. DABBS:</p> <p>15 A. And the group that tends not to respond are</p> <p>16 the ones that are double negative.</p> <p>17 MR. SIMMONS:</p> <p>18 Q. I understand that, but has there been any</p> <p>19 study to take the ER score and compare scores</p> <p>20 of 1 percent, 10 percent, 20 percent, 50</p> <p>21 percent, 80 percent, and assess clinical</p> <p>22 outcome compared to the percentage on that</p> <p>23 basis that you know of?</p> <p>24 DR. DABBS:</p> <p>25 A. Yes, well, most of the papers that have</p>	<p>1 slide on the lower left here also headed</p> <p>2 "Different procedures intra and inter</p> <p>3 laboratory compromise standardization".</p> <p>4 DR. DABBS:</p> <p>5 A. Uh-hm.</p> <p>6 MR. SIMMONS:</p> <p>7 Q. Was that to be "intra" and "inter" laboratory?</p> <p>8 DR. DABBS:</p> <p>9 A. Yes, "inter" and "intra".</p> <p>10 MR. SIMMONS:</p> <p>11 Q. Inter and intra laboratory, and you've</p> <p>12 identified the preparation phase, the staining</p> <p>13 phase, and the interpretation phase there with</p> <p>14 arrows with a series of different steps in the</p> <p>15 procedure identified in each of those phases,</p> <p>16 a total of, if you add them up, I think</p> <p>17 there's 14 different steps there that you've</p> <p>18 categorized, and on the very bottom there</p> <p>19 you've got 3 to the power of 14 equals 4.8,</p> <p>20 and is that million?</p> <p>21 DR. DABBS:</p> <p>22 A. Yes.</p> <p>23 MR. SIMMONS:</p> <p>24 Q. Million procedures. So I may be interpreting</p> <p>25 this wrong, but do I take you to be saying</p>

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<p>1 here that if in each of those 14 steps there</p> <p>2 are three possible variations of the way to</p> <p>3 perform it, that step, that means that for the</p> <p>4 total process there's 4.8 million different</p> <p>5 variations in the whole process?</p> <p>6 DR. DABBS:</p> <p>7 A. Yes, potentially to sort of--it's a high</p> <p>8 impact slide that show that of these three</p> <p>9 particular phases, there are a total of 14</p> <p>10 different kinds of variations. So you could</p> <p>11 change one in there, you know, and change the</p> <p>12 next one, and change the next one. The point</p> <p>13 being that there are no two laboratories that</p> <p>14 may have the same exact fixation method or the</p> <p>15 exact same paraffin, or the same temperatures</p> <p>16 in their tissue processor and so forth. So</p> <p>17 the issue here was that--was an attempt at</p> <p>18 standardization.</p> <p>19 MR. SIMMONS:</p> <p>20 Q. Uh-hm.</p> <p>21 DR. DABBS:</p> <p>22 A. It's ideal to be able to get a control on all</p> <p>23 of these phases and that's what we attempted</p> <p>24 to do at the consensus conference was address</p> <p>25 the pre-analytic, analytic, and post-analytic</p>	<p>1 a group, put together and acknowledged that</p> <p>2 were probably most important in minimizing the</p> <p>3 impact of the--the high impact of the slide.</p> <p>4 MR. SIMMONS:</p> <p>5 Q. One of the things we've heard is that ER/PR</p> <p>6 testing has to be optimized within each lab</p> <p>7 that's doing it, and would that be because</p> <p>8 there has not been the kind of standardization</p> <p>9 which you're now promoting, that it had been</p> <p>10 necessary for each lab to separately optimize</p> <p>11 and validate its variation on these different</p> <p>12 steps?</p> <p>13 DR. DABBS:</p> <p>14 A. Yes, exactly.</p> <p>15 MR. SIMMONS:</p> <p>16 Q. And have there been any--it's one thing to say</p> <p>17 there's no standardization of the steps. Has</p> <p>18 there been any consensus or standardization of</p> <p>19 the way you go about validating your own</p> <p>20 testing even?</p> <p>21 DR. DABBS:</p> <p>22 A. Well, I think that the first paper that came</p> <p>23 out in the AIM Journal had a very nice</p> <p>24 description, and I think I alluded to some of</p> <p>25 these, how to do immunohistochemistry in</p>
<p>1 factors.</p> <p>2 MR. SIMMONS:</p> <p>3 Q. So aside from the standardization through the</p> <p>4 recommendations that were made, would it be</p> <p>5 fair to say that of these 14 step procedure,</p> <p>6 laboratories in the United States do employ</p> <p>7 variations in each of those steps from</p> <p>8 laboratory to laboratory?</p> <p>9 DR. DABBS:</p> <p>10 A. There are variations inherent in every</p> <p>11 laboratory. There are many devices, tissue</p> <p>12 processors, that vary between laboratories.</p> <p>13 MR. SIMMONS:</p> <p>14 Q. Uh-hm.</p> <p>15 DR. DABBS:</p> <p>16 A. There are tissue processors in--multiple</p> <p>17 tissue processors in a hospital, and, you</p> <p>18 know, there may be three different brands of</p> <p>19 them all operating differently. So what we</p> <p>20 try to do, though, what we've recognized over</p> <p>21 time is that fixation is absolutely key.</p> <p>22 Extreme temperatures are absolutely key. You</p> <p>23 don't want to overheat specimens during</p> <p>24 processing, and all of those features</p> <p>25 basically flowed from the evidence that we, as</p>	<p>1 general, especially for those cases that are</p> <p>2 not categorical like ER and PR testing, that</p> <p>3 you're supposed to take a certain number of</p> <p>4 cases --</p> <p>5 MR. SIMMONS:</p> <p>6 Q. Uh-hm.</p> <p>7 DR. DABBS:</p> <p>8 A. A certain number that are high expressors,</p> <p>9 certain ones that are low expressors, and</p> <p>10 certain ones that are intermediate, or</p> <p>11 negative, and use those as your optimization</p> <p>12 procedure. That information has been gleaned,</p> <p>13 if you will, from immunohistochemistry</p> <p>14 literature over the ages, but I think that</p> <p>15 this committee for the first time, you know,</p> <p>16 congealed it and put it in its first round of</p> <p>17 recommendations in the paper that came out</p> <p>18 last year.</p> <p>19 MR. SIMMONS:</p> <p>20 Q. In 2007.</p> <p>21 DR. DABBS:</p> <p>22 A. Yes.</p> <p>23 MR. SIMMONS:</p> <p>24 Q. Okay. There's been some discussion regarding</p> <p>25 training and qualification of laboratory</p>

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<p>1 technicians who perform immunohistochemistry, 2 and since you're here from another 3 jurisdiction, from the United States, it's an 4 opportunity to find out the way things are 5 done where you are. I presume there is some 6 formal type of licensing for laboratory 7 technicians in Pennsylvania, is there?</p> <p>8 DR. DABBS: 9 A. Yes, there is.</p> <p>10 MR. SIMMONS: 11 Q. Is that a state responsibility or US federal 12 government, or would you know?</p> <p>13 DR. DABBS: 14 A. It's a state responsibility, so they operate 15 under licensing in the local state, but they 16 also have to have qualifying exams and pass 17 those from their schools that they attend, be 18 it in histotechnology, you know, or whatever 19 area.</p> <p>20 MR. SIMMONS: 21 Q. Right. Is there any special licensing or some 22 set of licensing specifically for technicians 23 performing immunohistochemistry?</p> <p>24 DR. DABBS: 25 A. There isn't a specific licensing per se, but</p>	<p>1 organization is holding their meeting right 2 now in Pittsburgh, the National Society of 3 Histotechnologists.</p> <p>4 MR. SIMMONS: 5 Q. Yes.</p> <p>6 DR. DABBS: 7 A. They have lots of workshops, people who are 8 prominent in the field giving lectures.</p> <p>9 MR. SIMMONS: 10 Q. Okay. So it wouldn't be--the school where a 11 technologist would go as a student to learn 12 the basics of their profession, that wouldn't 13 be where you would go to do the 14 immunohistochemistry course? It would be 15 something offered by an organization like the 16 National Society of Histochemistry?</p> <p>17 DR. DABBS: 18 A. Yes.</p> <p>19 MR. SIMMONS: 20 Q. Yes, okay. More in the line of continuing 21 education?</p> <p>22 DR. DABBS: 23 A. That's true. Now I can tell you that we--in 24 as far as histotechnology schools go, we have 25 a school at our institution and those students</p>
<p>1 there is an examination that one can sit for 2 that shows sort of a special qualification, if 3 you will, in immunohistochemistry.</p> <p>4 MR. SIMMONS: 5 Q. And who sponsors that examination or who makes 6 it available?</p> <p>7 DR. DABBS: 8 A. That examination, as I recall, is sponsored by 9 the ASCP.</p> <p>10 MR. SIMMONS: 11 Q. Okay.</p> <p>12 DR. DABBS: 13 A. I believe it's the ASCP. I'm not 100 percent 14 certain on that.</p> <p>15 MR. SIMMONS: 16 Q. Okay. To your knowledge, is there, are there 17 any special courses of training available for 18 technicians in immunohistochemistry? We know 19 that there's some schools that technologists 20 can go to to learn histochemistry, but are 21 there--is there specialized training available 22 for immunohistochemistry?</p> <p>23 DR. DABBS: 24 A. There are courses available, sponsored by 25 various organizations and probably the largest</p>	<p>1 are exposed to immunohistochemistry, just like 2 they are everything else in the laboratory, as 3 part of their training program.</p> <p>4 MR. SIMMONS: 5 Q. Their basic program?</p> <p>6 DR. DABBS: 7 A. Yes.</p> <p>8 MR. SIMMONS: 9 Q. Okay. You'd mentioned that there's--I think 10 you have a research lab at your institution as 11 well?</p> <p>12 DR. DABBS: 13 A. Yes.</p> <p>14 MR. SIMMONS: 15 Q. As well as a clinical lab. Do you, in your 16 position, play any role in the management of 17 the technologists and technicians, staffing 18 issues, filling positions, that sort of thing?</p> <p>19 DR. DABBS: 20 A. Well, I work closely with our laboratory 21 administrator and the person who works closely 22 with her is our manager for surgical 23 pathology. So when there are staffing issues, 24 I hear about them, whether people are leaving 25 or have been hired. We have a rather</p>



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<p>1 extensive checklist of competencies that 2 people are made to go through and sign off, 3 whether they be histotechs or people doing 4 immunohistochemistry or path assistants or 5 whatever. There's a competency for everything 6 that they need to sign off.</p> <p>7 MR. SIMMONS: 8 Q. Are you able to offer us any comment or 9 observations regarding the availability of 10 appropriately trained people, technologists 11 for immunohistochemistry?</p> <p>12 DR. DABBS: 13 A. Yes. Generally speaking, if people are going 14 to be--if histotechnologists are going to be 15 doing immunohistochemistry, it comes from a 16 desire from them from within to want to do 17 this, and we train them on it. Again, I say 18 we, you know, we document all of their 19 competencies. We don't force anyone to do 20 that. We have a select group of people who do 21 that and they rotate whenever. It's their 22 responsibility through that particular, you 23 know, service arm of the laboratory. Is it 24 difficult to get qualified people? I would 25 say in general it's difficult to get</p>	<p>1 those being SP1, and at this point in your 2 presentation, I have a note that you mentioned 3 a study performed in 2006 concerning SP1, and 4 my note was that it compared ER results to 5 testing performed using the 1D5 antibody.</p> <p>6 DR. DABBS: 7 A. Correct.</p> <p>8 MR. SIMMONS: 9 Q. Does that sound familiar? And I'd noted that 10 you'd said that using the SP1 clone, there 11 were eight to ten more positive cases than 12 there were using the 1D5?</p> <p>13 DR. DABBS: 14 A. Correct.</p> <p>15 MR. SIMMONS: 16 Q. All right. So out of 100 samples run in that 17 study, there would be eight to ten samples 18 that would have been reported negative using 19 1D5 and positive using SP1?</p> <p>20 DR. DABBS: 21 A. I believe that was the conclusions of the 22 author in that particular study, where I think 23 they used the one--greater than one percent of 24 cells cut off.</p> <p>25 MR. SIMMONS:</p>
<p>Page 129</p> <p>1 histotechnologists where we are, and that's 2 why we created our own school.</p> <p>3 MR. SIMMONS: 4 Q. Yes.</p> <p>5 DR. DABBS: 6 A. So that sort of helps us out in the long term. 7 Yes, it is difficult to get qualified people 8 who are interested in that, and you know, it 9 sort of goes back to what I was saying earlier 10 when I was giving the presentation about the 11 Dextran-coated Charcoal method were done by 12 technicians who are very heavily versed with 13 laboratory science, you know, chemical 14 columns, all sorts of very complex aspects of 15 a scientific laboratory, not a hospital 16 laboratory, and one of the reasons why that 17 never really took on in hospitals, because 18 those people just generally didn't work in 19 hospitals, nor could hospitals afford that, 20 you know, complex equipment.</p> <p>21 MR. SIMMONS: 22 Q. In your presentation, page 17, please? 23 There's a mention here, on the right-hand 24 side, in recommendation 11, of the three 25 antibody clones that are recommended. One of</p>	<p>Page 131</p> <p>1 Q. Yes.</p> <p>2 DR. DABBS: 3 A. And I think the cases that became positive 4 were all weakly positive.</p> <p>5 MR. SIMMONS: 6 Q. Okay. So there were--out of 100 tests, there 7 would have been eight or ten that went from 8 zero with 1D5 to weakly positive with SP1?</p> <p>9 DR. DABBS: 10 A. Yes.</p> <p>11 MR. SIMMONS: 12 Q. Which, by your definition, would be moving 13 from negative to positive?</p> <p>14 DR. DABBS: 15 A. Yes.</p> <p>16 MR. SIMMONS: 17 Q. Have any--are you aware of any similar studies 18 comparing the SP1 clone to the 6F11 clone?</p> <p>19 DR. DABBS: 20 A. To the SP1 versus the 6F11 clone?</p> <p>21 MR. SIMMONS: 22 Q. Yes.</p> <p>23 DR. DABBS: 24 A. Just an in-house study that I looked at 25 because we were using the 6F11, and the 6F11,</p>

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1 according to the literature, is slightly more  
 2 sensitive than the 1D5.  
 3 MR. SIMMONS:  
 4 Q. Okay.  
 5 DR. DABBS:  
 6 A. Okay, so when we were--when I was looking at  
 7 converting to the SP1 clone, I took 20 or 25,  
 8 I can't remember which, of our negative cases  
 9 with 6F11 and came up with three that were  
 10 weakly positive. They were actually--they  
 11 were less than one percent of positive cells,  
 12 but if you're including any cases that are--  
 13 rather a positive result is any nuclear  
 14 expression, then they would be considered very  
 15 weakly positive. So in essence, by looking at  
 16 our select group of negatives with the SP1,  
 17 according to a very comparable protocol from  
 18 what was published in JCAHO 2006, I was able  
 19 to reproduce the exact number of cases that  
 20 became weakly positive with that.  
 21 MR. SIMMONS:  
 22 Q. Okay. So if I understand correctly, of the 20  
 23 to 25 cases you tested using 6F11 that were  
 24 negative, meaning zero, on retesting with SP1,  
 25 there were three that were now weakly

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1 positive, although very weakly positive?  
 2 DR. DABBS:  
 3 A. Um-hm.  
 4 MR. SIMMONS:  
 5 Q. So had those cases first been tested after the  
 6 introduction of SP1, they would have been  
 7 reported as positive cases in your  
 8 institution?  
 9 DR. DABBS:  
 10 A. They would have been reported as weakly  
 11 positive, less than one percent of cells.  
 12 MR. SIMMONS:  
 13 Q. Okay, and would that have been any cause at  
 14 all for any concern for you to look back at  
 15 any other negative cases that had been done  
 16 using 6F11, out of any concern for the  
 17 clinical treatment of the patients?  
 18 DR. DABBS:  
 19 A. I don't think so. Basically, the  
 20 investigation there was to look and see if the  
 21 study that was published could be reproduced  
 22 in my laboratory, and it was, and I think that  
 23 just as these antibody clones become available  
 24 and evolve, that the 1D5 is a little bit less  
 25 sensitive than the 6F11, which apparently is a

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1 little less sensitive than the SP1, and but  
 2 the key thing is that they're all very robust  
 3 antibodies and that they give solid,  
 4 reproducible and accurate results. You have  
 5 to keep in mind that every--since they are  
 6 monoclonal antibodies, they have a very  
 7 limited range of specificity. So that where  
 8 you may see one being positive weakly, another  
 9 one may well be negative, because when these  
 10 antibodies are generated, the antibodies that  
 11 are generated are generated against specific  
 12 areas of the estrogen receptor molecule and  
 13 they're that specific. So while the 1D5 may  
 14 see epitope A, 6F11 may see a part of A and  
 15 most of B, epitope B, and SP1 might see A, B  
 16 and part of epitope C. Okay. So you really  
 17 don't know until you begin testing these on  
 18 tissue. But they all show very comparable  
 19 results, in terms of immunostaining.  
 20 MR. SIMMONS:  
 21 Q. So there are base scientific reasons why you  
 22 would see some differences among the three  
 23 antibodies, in recognition of positivity?  
 24 DR. DABBS:  
 25 A. Based on the clone, yes.

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1 MR. SIMMONS:  
 2 Q. So then, as a clinician or as a pathologist  
 3 who's selecting an antibody here, how do you  
 4 determine which one is best? How do you  
 5 determine in any particular case which one is  
 6 producing the right result, when you have one  
 7 saying a positive and one saying a negative?  
 8 DR. DABBS:  
 9 A. Well, I think what you have to look at is with  
 10 the outcome studies that have been performed  
 11 with each one of these clones, and they all  
 12 show very good correlation with endocrine  
 13 response in outcomes of large numbers of  
 14 patients, thousands of patients, and that's  
 15 really the proof that the antibody and that  
 16 testing measure works. We all know that  
 17 whenever we have some of these conversions  
 18 from negative to weakly positive, like in  
 19 example from 6F11 to SP1, that there are many  
 20 clinicians for a select group of patients  
 21 where a weak, you know, changing to one  
 22 percent or less than five percent, whatever  
 23 cut offs that they would use clinically may  
 24 have no impact. A patient who is very weakly  
 25 positive, they think might not get much of a

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1 bang out of the therapy and think, you know  
2 what, I don't think that this individual  
3 patient is going to benefit by this. But if  
4 you look at the overall outcome studies and  
5 response, yes, patients who are high  
6 expressors are going to respond best. The  
7 ones who are low expressors, no matter whether  
8 they're SP1 weak or 6F11 weak or 1D5 weak, and  
9 in fact, if you look back at the consensus  
10 statement from the NIH that I showed, if you  
11 read into further areas which I did not show,  
12 it will say--it says that if tissue is not  
13 available or the result is uncertain that the  
14 patient should be treated as though they're ER  
15 positive.

16 MR. SIMMONS:  
17 Q. That was the 2000 NIH consensus statement?  
18 DR. DABBS:  
19 A. Yes. So you know, while there apparently is  
20 some subjectivity in terms of testing method,  
21 there also is subjectivity from the clinician,  
22 in terms of who are they going to treat with a  
23 given result. It's not all cut and dry and  
24 black and white.

25 MR. SIMMONS:

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1 Q. Okay. Just to go back for a second then to  
2 that 2006 study, comparing SP1 to 1D5 with the  
3 eight to ten percent difference. Just  
4 presuming now that you had a laboratory that  
5 was switching from 1D5 to SP1 and their own  
6 concordant study matched the results of this  
7 2006 study that you referred to.

8 DR. DABBS:  
9 A. Yes.

10 MR. SIMMONS:  
11 Q. They would have a situation where the clone  
12 they're using tomorrow, the SP1, was going to  
13 find eight to ten percent more positives than  
14 the one they used yesterday, the 1D5. In your  
15 experience, would that be any cause for  
16 consideration of reexamining your recent  
17 negatives under the 1D5? Because presumably,  
18 you'd find eight to ten percent of those that  
19 were now positive and patients who presumably  
20 could benefit from that information.

21 DR. DABBS:  
22 A. I think really, the answer there revolves  
23 around what clinicians do with these extremely  
24 low expressors and I think, in general, that  
25 doesn't really do very much for clinicians.

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1 Whenever they see a very low expressor like  
2 that one percent or less or something where  
3 there's just, you know, one positive cell,  
4 that doesn't do too much for their clinical  
5 decision making.

6 MR. SIMMONS:  
7 Q. Okay. You gave some evidence regarding  
8 dilutions of antibodies and in conjunction  
9 with the optimization of an antibody, such as  
10 the ER antibody, and I believe I either saw  
11 reference or heard you say that the process  
12 you'd use for introducing a new antibody would  
13 be to start with the manufacturers  
14 specifications sheet and see the dilution that  
15 was recommended on it, and then try probably a  
16 dilution one above and one below, and you'd  
17 run some test slides and see which, and I'm  
18 not sure if you said this or if I read this in  
19 your book now.

20 DR. DABBS:  
21 A. Yes.

22 MR. SIMMONS:  
23 Q. But does that sound right?  
24 DR. DABBS:  
25 A. Yes. That was part of the actual first paper

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1 that came out, the recommendations, yes.

2 MR. SIMMONS:  
3 Q. Okay, yes. Now when you say one above and one  
4 below, just to take a concrete example, if the  
5 manufacturer's recommendation is a dilution of  
6 one in 50, one part of antibody to 50 parts  
7 of, is it dilutant?

8 DR. DABBS:  
9 A. Yes.

10 MR. SIMMONS:  
11 Q. Yes, okay, what would the one above be and  
12 what would the one below be?

13 DR. DABBS:  
14 A. Okay. So if you have one in 50, then the one  
15 below would be one in 100 and the one above  
16 would be one in 25.

17 MR. SIMMONS:  
18 Q. Okay. So they would be -  
19 DR. DABBS:  
20 A. A stronger and a weaker dilution.

21 MR. SIMMONS:  
22 Q. So the one above would be half the recommended  
23 dilution?  
24 DR. DABBS:  
25 A. Right.

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1 MR. SIMMONS:  
 2 Q. And the one--and the next one would be double  
 3 the recommended dilution, and you would  
 4 compare these, results of each of those, and  
 5 you would select among one in 25, one in 50 or  
 6 one in 100, as the dilution that you would  
 7 use?  
 8 DR. DABBS:  
 9 A. Correct.  
 10 MR. SIMMONS:  
 11 Q. Okay. Now if you are comparing--well, you  
 12 also spoke about a potential source of error  
 13 in the testing being variations in the  
 14 dilution that's actually used, maybe as a  
 15 result of pipette calibration, for example, or  
 16 technologist error in the preparation of the  
 17 dilutions. If you were working with a one in  
 18 50 dilution, would it be fair to say that the  
 19 type of error that would result from pipettes  
 20 or technologist error would probably be much  
 21 less of a difference from one in 50 than the  
 22 alternatives that you've chosen when you've  
 23 done your validation? I didn't put that very  
 24 well. If you want to achieve a one in 50,  
 25 what sort of error would you expect to find if

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1 there's not appropriate attention being paid  
 2 to issues like calibration and technical  
 3 control of the dilution?  
 4 DR. DABBS:  
 5 A. I find that impossible to answer, because if  
 6 the technician really doesn't--isn't well  
 7 versed in using the pipette and/or calibrating  
 8 it, then they could be off on both parts.  
 9 They could be off on the antibody  
 10 concentration, as well as the dilutant. So  
 11 you could end up with--I have no idea what  
 12 that titre ends up being.  
 13 MR. SIMMONS:  
 14 Q. Okay. Mr. Coffey asked you about a  
 15 possibility of there being false positives in  
 16 ER and PR testing and one of the--you  
 17 mentioned that there's two ways in which that  
 18 might occur, and one of them you said was that  
 19 if there was too much antigen retrieval when  
 20 using the avidin biotin method, the ABC  
 21 method, that there could be an effect on the  
 22 slide which I understood you to say could be  
 23 mistaken for positivity?  
 24 DR. DABBS:  
 25 A. Correct.

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1 MR. SIMMONS:  
 2 Q. Right. Would that same concern apply to the  
 3 peroxidase, anti-peroxidase method?  
 4 DR. DABBS:  
 5 A. Probably not.  
 6 MR. SIMMONS:  
 7 Q. Okay. You've spoken about internal controls.  
 8 Is it correct to say that you can interpret an  
 9 ER or PR result without an internal control,  
 10 that the presence of an internal control is  
 11 not a mandatory element to be able to  
 12 interpret the result?  
 13 DR. DABBS:  
 14 A. And to that I was speaking, if you have a core  
 15 biopsy which is 100 percent tumour and doesn't  
 16 have any normal tissue and you have a proper  
 17 external control that's placed on the same  
 18 slide -  
 19 MR. SIMMONS:  
 20 Q. Yes.  
 21 DR. DABBS:  
 22 A. - and you have a positive result, that would  
 23 be an acceptable result. That would be no  
 24 cause to reject the specimen. On the other  
 25 hand, if the result, in the same situation, if

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1 the external control was negative on the slide  
 2 and the test tissue was negative, that's a  
 3 cause for concern. That's saying that most  
 4 likely the antibody wasn't dispensed or  
 5 something else went drastically wrong to give  
 6 you a negative result times two. And again, a  
 7 safe measure for a situation where you have  
 8 tumour with a positive external control on the  
 9 same slide and a negative tumour result still  
 10 means that it should be repeated on the  
 11 resected specimen to assure that that negative  
 12 result wasn't due to sampling alone.  
 13 MR. SIMMONS:  
 14 Q. Okay. You were shown a memo prepared by Dr.  
 15 Khalifa here back in 1998 at the time when  
 16 what was then the Health Care Corporation here  
 17 was switching, the laboratory was switching to  
 18 ER/PR testing from the biochemical assay  
 19 method to the immunohistochemistry method.  
 20 And in the course of some questions that you  
 21 were asked then, including by the  
 22 Commissioner, I think you were asked to  
 23 describe what would be the appropriate way to  
 24 validate the introduction of the IHC method in  
 25 those circumstances. And I'm not sure I

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<p>1 gathered from your answer, I'm not sure I</p> <p>2 understood if you actually explained what</p> <p>3 would have been the ideal way to do that. And</p> <p>4 I'm wondering if maybe you could try that</p> <p>5 again for me?</p> <p>6 DR. DABBS:</p> <p>7 A. Okay. You mean moving from the -</p> <p>8 MR. SIMMONS:</p> <p>9 Q. Yes.</p> <p>10 DR. DABBS:</p> <p>11 A. - biochemical assay to immunohistochemistry?</p> <p>12 MR. SIMMONS:</p> <p>13 Q. Yes. What would a lab do, what would be the</p> <p>14 way for a lab to tackle that in '97, 1998</p> <p>15 based on what was known at the time?</p> <p>16 DR. DABBS:</p> <p>17 A. Based on what was known at the time?</p> <p>18 MR. SIMMONS:</p> <p>19 Q. Yes.</p> <p>20 DR. DABBS:</p> <p>21 A. Basically in '97 and so forth the papers by</p> <p>22 Mascarelli and Perchuck were out there</p> <p>23 regarding 1D5. So I think by using that</p> <p>24 methodology for the 1D5 that was published,</p> <p>25 and I think at that time the 1D5 was probably</p>	<p>1 followed to the letter.</p> <p>2 MR. SIMMONS:</p> <p>3 Q. Um-hm. Pretty well all labs in North America</p> <p>4 at some point made the switch from biochemical</p> <p>5 assay to IHC for ER/PR testing.</p> <p>6 DR. DABBS:</p> <p>7 A. Yes.</p> <p>8 MR. SIMMONS:</p> <p>9 Q. From your experience and your knowledge do you</p> <p>10 know if that was a commonly followed approach</p> <p>11 exactly as you set out here or do you know</p> <p>12 what other labs have done when they've made</p> <p>13 that switch -</p> <p>14 DR. DABBS:</p> <p>15 A. I do not know what other laboratories have</p> <p>16 done.</p> <p>17 MR. SIMMONS:</p> <p>18 Q. Um-hm.</p> <p>19 DR. DABBS:</p> <p>20 A. I do know that the best practice and one of</p> <p>21 the items that we tried to get across through</p> <p>22 the consensus recommendations is that, you</p> <p>23 know, we looked at what was out there</p> <p>24 validated, not only technically, but also</p> <p>25 clinically.</p>
<p>Page 145</p> <p>1 the only ER antibody that was available and</p> <p>2 the 6F11 came, I think, a little bit later.</p> <p>3 MR. SIMMONS:</p> <p>4 Q. Um-hm.</p> <p>5 DR. DABBS:</p> <p>6 A. And the SP1 until recently. So it would have</p> <p>7 been acceptable to recapitulate the</p> <p>8 methodology that Perchuck et al used and</p> <p>9 Mascarelli and in the process of working that</p> <p>10 up, verifying the optimization and the</p> <p>11 conditions for that. Then doing comparative</p> <p>12 studies with your data that you have with the</p> <p>13 dextran-coated charcoal method like the paper</p> <p>14 by Fisher and comparing them, cross comparing</p> <p>15 them, they came up with a ten percent cutoff,</p> <p>16 ideally, if it was available locally to have</p> <p>17 outcome studies associated with those patients</p> <p>18 who had the biochemical assay. Then you would</p> <p>19 have a clinical validation, as well. But my</p> <p>20 point is since Perchuck did a clinical</p> <p>21 validation with that test, then it would be</p> <p>22 acceptable for the setting up the assay to set</p> <p>23 up the assay exactly as they did using the</p> <p>24 same cutoffs and expecting the same sort of</p> <p>25 outcome result. But it would have to be</p>	<p>Page 147</p> <p>1 MR. SIMMONS:</p> <p>2 Q. Um-hm.</p> <p>3 DR. DABBS:</p> <p>4 A. And that's why we cite the paper by Harvey et</p> <p>5 al from 1999, that was the paper that Allred</p> <p>6 was also on, where they discovered that it was</p> <p>7 the one percent, patients who had one percent</p> <p>8 or more did have an outcome that was</p> <p>9 associated with endocrine manipulation. So</p> <p>10 whether people utilized that information, per</p> <p>11 se, is beyond me, I don't know for sure. But</p> <p>12 what we wanted to do was at least point in the</p> <p>13 direction that if this is clinical validation</p> <p>14 that you're looking for, these are the</p> <p>15 conditions that you have to have to use and</p> <p>16 you have to use this scoring method, this</p> <p>17 antibody, under these conditions. You can't</p> <p>18 just--you cannot just obtain an antibody, work</p> <p>19 it up your own way and say this guy used ten</p> <p>20 percent, I'm going to use ten percent. That's</p> <p>21 not a clinical validation.</p> <p>22 MR. SIMMONS:</p> <p>23 Q. So aside from going to the literature and</p> <p>24 doing that kind of review and finding those</p> <p>25 studies, back in '97, '98, do I take it then</p>

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1 that there was nothing equivalent to a  
 2 consensus recommendation about what the  
 3 process should be to introduce ER/PR by IHC?  
 4 DR. DABBS:  
 5 A. Well, I think that the papers, there may not  
 6 have been a consensus statement, per se, but  
 7 the papers by Perchuck, by Mascarelli and then  
 8 a few years later by Harvey, clearly  
 9 demonstrated that this is the process that  
 10 they followed. And I think that, you know, a  
 11 reasonable pathologist knowing the vagaries of  
 12 individual testing should be aware that they  
 13 can't pick an antibody out of the sky and work  
 14 it up and expect to have the same outcome as  
 15 something that was published and validated  
 16 clinically.  
 17 MR. SIMMONS:  
 18 Q. A few other specific things coming out of your  
 19 examination this morning. You were asked some  
 20 questions about, by Mr. Coffey, about  
 21 refrigeration of specimens once placed in  
 22 formalin. And if I understood you correctly  
 23 to say, what I gathered from what you'd said  
 24 was that the important thing is to get the  
 25 specimen sliced within an hour of when it was

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1 removed from the--of surgical removal, and  
 2 that whether it goes in formalin before or  
 3 after that would not--I'm sorry, I'm confused  
 4 now. The important thing was the slicing and  
 5 if it had to wait before being sliced,  
 6 refrigeration maybe might be of some  
 7 advantage. But once it makes it into the  
 8 formalin, refrigerating it in formalin isn't  
 9 going to add anything to the fixation of the  
 10 specimen?  
 11 DR. DABBS:  
 12 A. Refrigeration in formalin will not add  
 13 anything to the specimen, no.  
 14 MR. SIMMONS:  
 15 Q. Is it possible that refrigeration in formalin  
 16 would actually slow the effect of the  
 17 penetration of the formalin?  
 18 DR. DABBS:  
 19 A. That's certainly conceivable since we know  
 20 that heating formalin will accelerate fixation  
 21 and penetration, in fact, yes.  
 22 MR. SIMMONS:  
 23 Q. Okay. You discussed reprocessing of tissue  
 24 this morning. Do I gather from your evidence  
 25 that reprocessing is something that does

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1 happen on occasion in your laboratory at  
 2 McGee?  
 3 DR. DABBS:  
 4 A. It happens in our laboratory; I'm sure it  
 5 happens in every laboratory to some degree.  
 6 MR. SIMMONS:  
 7 Q. Sure, right. And you've told us that  
 8 reprocessing, if a specimen is adequately  
 9 fixed, reprocessing should have no effect on  
 10 it?  
 11 DR. DABBS:  
 12 A. Correct.  
 13 MR. SIMMONS:  
 14 Q. I gather that. If it's inadequately fixed,  
 15 reprocessing won't improve the specimen?  
 16 DR. DABBS:  
 17 A. Correct.  
 18 MR. SIMMONS:  
 19 Q. Now, if the reason for reprocessing is that  
 20 the specimen had not been adequately  
 21 dehydrated during the tissue processing phase,  
 22 would reprocessing have some positive effect  
 23 then?  
 24 DR. DABBS:  
 25 A. Well, it would have a positive effect on

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1 allowing the technician to cut an adequate  
 2 section.  
 3 MR. SIMMONS:  
 4 Q. Yes.  
 5 DR. DABBS:  
 6 A. But it wouldn't have an effect on  
 7 immunohistochemistry.  
 8 MR. SIMMONS:  
 9 Q. And would have no effect on IHC. So in  
 10 essence then fixation will have an effect on  
 11 the IHC, but whether the tissue is  
 12 reprocessed, well fixed or not, is not going  
 13 to have any particular effect on the  
 14 performance of the IHC test?  
 15 DR. DABBS:  
 16 A. Correct.  
 17 MR. SIMMONS:  
 18 Q. Now you've told us about the metrics that you  
 19 gather in your lab. Can you give some  
 20 indication of how long your lab has been  
 21 gathering this sort of information?  
 22 DR. DABBS:  
 23 A. Sure. Think for a second. This information  
 24 has been gathered since 2000--in the form that  
 25 I'm familiar with.

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<p>1 MR. SIMMONS: 2 Q. Yes. 3 DR. DABBS: 4 A. Since I became chief and that would have been 5 in 2003. 6 MR. SIMMONS: 7 Q. Okay. And do you have any idea how common a 8 practice that is among immunohistochemistry 9 laboratories you're familiar with, to track 10 these sorts of metrics that you're tracking in 11 your lab? 12 DR. DABBS: 13 A. I do not know how frequent that is. I think 14 that one of the items, you know, the sort of 15 new paradigm for complex testing, this 16 includes ER/PR and HER2, HER2 has been a lot 17 more visible in many respects and people, you 18 know, would say, well, what's your positive 19 rate for HER2. 20 MR. SIMMONS: 21 Q. Um-hm. 22 DR. DABBS: 23 A. Because in the literature there are many 24 papers that say, you know, 20 to 30 or 25 to 25 35 percent, and that's not what--those numbers</p>	<p>1 DR. DABBS: 2 A. Yes. 3 MR. SIMMONS: 4 Q. And I think I understand what you mean by 5 that, but can you explain to me a little more 6 just what exactly you mean when you refer to 7 controlled fixation? 8 DR. DABBS: 9 A. Sure. The controlled fixation basically is 10 documenting how long the specimens are sitting 11 in formalin. 12 MR. SIMMONS: 13 Q. That's the documentation? 14 DR. DABBS: 15 A. That's the documentation. 16 MR. SIMMONS: 17 Q. Um-hm. And when was that introduced in your 18 laboratory? 19 DR. DABBS: 20 A. That was introduced in our laboratory right in 21 January of 2007. That was right after our, 22 one of our meetings. 23 MR. SIMMONS: 24 Q. Okay. Do you know how common a practice that 25 is in other immunohistochemistry laboratories?</p>
<p style="text-align: right;">Page 153</p> <p>1 have been tossed around without qualification. 2 If you look at the original clinical trials 3 where they considered patients who were two 4 plus and three plus - 5 MR. SIMMONS: 6 Q. And this is the HER2 now, you - 7 DR. DABBS: 8 A. Yeah, the HER2, right. 9 MR. SIMMONS: 10 Q. Yes, okay. 11 DR. DABBS: 12 A. That number may hold up, but if you look at 13 patients who are actually three plus, the 14 number is closer to 15 percent and probably 15 doesn't rise beyond 18 percent. 16 MR. SIMMONS: 17 Q. Okay. 18 DR. DABBS: 19 A. In a laboratory that's performing the test 20 correctly. 21 MR. SIMMONS: 22 Q. Okay. This morning also that in discussing 23 that same topic you mentioned that your 24 laboratory had moved to what you called 25 controlled fixation?</p>	<p style="text-align: right;">Page 155</p> <p>1 DR. DABBS: 2 A. I know that it's becoming more common just in 3 chatting with various people and getting phone 4 calls and whatnot. I have, you know, given 5 talks at various national organization 6 meetings since then and people are on board 7 with that and it's becoming a part of the CAP 8 checklist that they use to accredit 9 laboratories. 10 MR. SIMMONS: 11 Q. In talking about the change to the SP 1 12 antibody this morning you also said, or I 13 noted that you said that your rate of cases 14 that were ER negative, PR positive prior to 15 the SP1 was 5.7 percent? 16 DR. DABBS: 17 A. Well, the SP1 antibody, that's the ER 18 antibody. 19 MR. SIMMONS: 20 Q. Oh, the ER antibody, that's right, yes. 21 DR. DABBS: 22 A. Yeah, that's - 23 MR. SIMMONS: 24 Q. Yes, SP1 is the ER antibody, right. So using 25 the SP1 for the ER antibody you had 5. 7</p>

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<p>1 percent of your cases that were ER negative 2 and PR positive? 3 DR. DABBS: 4 A. Correct. 5 MR. SIMMONS: 6 Q. And after introduction of the SP1 that went to 7 one percent? 8 DR. DABBS: 9 A. Well, it wasn't the SP1, the introduction of 10 the SP1. It was the PR clone 1E2. 11 MR. SIMMONS: 12 Q. Oh, okay. So the PR clone changed, also? 13 DR. DABBS: 14 A. The PR clone changed also, right, also to a 15 rabbit monoclonal, correct. 16 MR. SIMMONS: 17 Q. So you had fewer cases that were ER negative, 18 PR positive. Was that because you now had 19 more ER negative, PR negative or more ER 20 positive, PR positive? 21 DR. DABBS: 22 A. There's more ER positive, PR negative. 23 MR. SIMMONS: 24 Q. Okay. Is there any clinical significance to 25 that change in proportion?</p>	<p>1 for example, going back and looking back at 2 any of the patients who had been in a category 3 that you now know to be reported differently? 4 DR. DABBS: 5 A. Correct. The only issue there would be if, 6 you know, if your ER positive rate was somehow 7 not within the realm of what's been published, 8 that would be the concern. But other than 9 that, no. 10 MR. SIMMONS: 11 Q. Okay. By the way, are you aware of any 12 circumstance where any laboratory in the 13 United States or elsewhere has used their 14 metrics and found that their positivity rate 15 was out of line and then have then gone back 16 to look at previous cases to determine if 17 there should be any treatment changes or 18 clinical consequences? 19 DR. DABBS: 20 A. I am not aware of any literature to that 21 effect. 22 MR. SIMMONS: 23 Q. Um-hm. Or anecdotally of any circumstances 24 where that's happened? 25 DR. DABBS:</p>
<p>Page 157</p> <p>1 DR. DABBS: 2 A. Most likely not, and the reason for that is 3 the literature, if you look at that, 4 clinicians are uncertain what to do in many 5 respects with the ER negative, PR positive 6 group. 7 MR. SIMMONS: 8 Q. Um-hm. 9 DR. DABBS: 10 A. They tend to respond at least in the small 11 amount of information that is out there, it's 12 a pretty small group of patients. The most 13 recent paper, I believe, was in JCAHO, and I 14 think Dr. Ellis', Ian Ellis' name was on it. 15 They had a small number, they actually came 16 out with an uncertain result but they tended, 17 they looked like they were maybe slightly 18 responders like a very weak ER. Other 19 clinicians believe that they act like a double 20 negative, an ER negative, PR negative. But, 21 so when you take into amount the small amount 22 of information that's out there, it looks like 23 it's sort of equivocal in terms of response. 24 MR. SIMMONS: 25 Q. So no clinically significant enough to merit,</p>	<p>Page 159</p> <p>1 A. No, no. 2 MR. SIMMONS: 3 Q. Okay. Mr. Coffey asked you about false 4 positives this morning. And you told us 5 personally you haven't seen a false positive 6 result. And you said it was possible or 7 theoretically possible to get a false positive 8 if something had been primarily fixed in 9 alcohol after very minimal exposure to 10 formalin. Now, I think I've got that right. 11 DR. DABBS: 12 A. Correct. 13 MR. SIMMONS: 14 Q. I think I got that right. When you say very 15 minimal exposure to formalin, what would that 16 be, how minimal would that be, can you give us 17 some indication of what we're talking about 18 there when we say minimal exposure to 19 formalin? 20 DR. DABBS: 21 A. Probably less than an hour or two. 22 MR. SIMMONS: 23 Q. So it would have to be less than an hour 24 exposure to formalin for the later exposure to 25 alcohol to theoretically have the effect of</p>



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1 producing a false positive?  
 2 DR. DABBS:  
 3 A. Correct.  
 4 MR. SIMMONS:  
 5 Q. Right. And you say theoretically. Is there  
 6 any kind of clinical evidence of false  
 7 positives being produced in that way?  
 8 DR. DABBS:  
 9 A. Only in the regard whenever I had the--was  
 10 looking at primary alcohol fixation that was  
 11 this molecular friendly fixative.  
 12 MR. SIMMONS:  
 13 Q. Yes.  
 14 DR. DABBS:  
 15 A. What I would do is I would take the biopsies  
 16 and divide them and part would go to our  
 17 standard processing and start to--and others  
 18 to alcohol. And that's where I noticed some  
 19 weak positivity show up, weak to moderate  
 20 positivity and it was really erratic, you  
 21 couldn't predict when it would happen.  
 22 MR. SIMMONS:  
 23 Q. And in that case the biopsies going to the  
 24 alcohol, had they ever been in formalin?  
 25 DR. DABBS:

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1 A. No.  
 2 MR. SIMMONS:  
 3 Q. No?  
 4 DR. DABBS:  
 5 A. They never saw formalin.  
 6 MR. SIMMONS:  
 7 Q. Okay. You spoke about FDA approved testing  
 8 kits as being a recommendation that if  
 9 possible that it's a good idea to use those.  
 10 And this may be a technical question, you may  
 11 not know this, may have to get this from  
 12 someone else. Do you know if the Ventana  
 13 benchmark automated tester is an FDA approved  
 14 piece of equipment?  
 15 DR. DABBS:  
 16 A. Yes. I think the brand name that they give to  
 17 that is Pathway or something like that.  
 18 MR. SIMMONS:  
 19 Q. Well, the one we're familiar with the Ventana  
 20 Benchmark XT.  
 21 DR. DABBS:  
 22 A. The XT, yes, that's the machine. And the  
 23 product that they use for that is, I believe,  
 24 the marketed name is Pathway.  
 25 MR. SIMMONS:

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1 Q. Um-hm.  
 2 DR. DABBS:  
 3 A. It's a trademark for that line of FDA approved  
 4 products.  
 5 MR. SIMMONS:  
 6 Q. Okay, so that line of approved products, would  
 7 that include the pre-dilute antibodies meant  
 8 for use in that machine and the detection  
 9 kits, the other reagents used in the testing  
 10 process in that machine?  
 11 DR. DABBS:  
 12 A. Yes.  
 13 MR. SIMMONS:  
 14 Q. Yeah. So when you refer to an FDA approved  
 15 kit, would the Ventana Benchmark XT with those  
 16 antibodies and reagents meet what you're  
 17 suggesting in your recommendation there?  
 18 DR. DABBS:  
 19 A. That's correct, that would be one particular  
 20 marketed line by a specific vendor. There are  
 21 other vendors.  
 22 THE COMMISSIONER:  
 23 Q. Dr. Dabbs, how long has this process of FDA  
 24 approved kits been going on?  
 25 DR. DABBS:

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1 A. Well, I think that there's been a move to that  
 2 ever since the Hercept test for HER2 testing  
 3 came about. There was a move to that to have  
 4 more uniformity and a move away from analyte  
 5 specific reagents in hospital laboratories  
 6 because of potential internal, you know,  
 7 variations. When was that, I would say it  
 8 became more prominent for the hormone receptor  
 9 at the turn of the century, earlier this  
 10 decade.  
 11 THE COMMISSIONER:  
 12 Q. Thank you.  
 13 MR. SIMMONS:  
 14 Q. Thank you, very much, Dr. Dabbs. That's all  
 15 my questions.  
 16 THE COMMISSIONER:  
 17 Q. Thank you, Mr. Simmons. Mr. Browne, it's  
 18 getting near to the lunch hour, so I suggest  
 19 we have the break for lunch and then we'll  
 20 continue. But could you give me your  
 21 estimate?  
 22 MR. BROWNE:  
 23 Q. I'll be 15 or 20 minutes. Mr. Simmons has  
 24 covered a lot of the areas, so I'm just going  
 25 to go back over (inaudible).

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1 THE COMMISSIONER:  
 2 Q. All right. Mr. Pritchett?  
 3 MR. PRITCHETT:  
 4 Q. We don't anticipate any questions,  
 5 Commissioner.  
 6 THE COMMISSIONER:  
 7 Q. Ms. Newbury?  
 8 MS. NEWBURY:  
 9 Q. I'll be about 15 minutes or so.  
 10 THE COMMISSIONER:  
 11 Q. Mr. Crosbie?  
 12 CROSBIE, Q.C.:  
 13 Q. Not more than 30 minutes.  
 14 THE COMMISSIONER:  
 15 Q. Mr. Pike?  
 16 MR. PIKE:  
 17 Q. No questions. Thank you.  
 18 THE COMMISSIONER:  
 19 Q. All right. I guess we can govern ourselves  
 20 accordingly for the next witness who is in the  
 21 lineup. Thank you, we'll break for lunch and  
 22 reconvene at five after two.  
 23 (LUNCH BREAK)  
 24 THE COMMISSIONER:  
 25 Q. Please be seated. Mr. Browne.

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1 DR. DAVID DABBS, EXAMINATION BY MR. PETER BROWNE  
 2 MR. BROWNE:  
 3 Q. Good afternoon, Dr. Dabbs. My name is Peter  
 4 Browne, we met yesterday. I represent  
 5 individual physicians, mainly pathologists and  
 6 oncologists who have been called before the  
 7 Inquiry. I just want to cover some of the  
 8 areas, actually, just go back, Mr. Simmons  
 9 covered with you in his cross-examination.  
 10 But before I do that I just want to have a  
 11 point of clarification. If we could,  
 12 Registrar, have Exhibit P-2622. This is Dr.  
 13 Dabb's curriculum vitae. And, Doctor, it may  
 14 be my misunderstanding of--and if we could  
 15 just scroll down here? Here we go. Doctor,  
 16 your training here, it says July, 1976 to  
 17 July, 1981, Medical College of Ohio. I take  
 18 it that's your MD training?  
 19 DR. DABBS:  
 20 A. Correct.  
 21 MR. BROWNE:  
 22 Q. And then May, 1978 to May, 1979, pathology  
 23 fellow. Did you do your fellowship during your  
 24 undergraduate training or -  
 25 DR. DABBS:

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1 A. That's a good question. Actually, that's a  
 2 good pick-up. In the States there was  
 3 initiated, I think, a few years before this,  
 4 probably, I'm going to say around 1975, a  
 5 program called a Post-Sophmore Fellowship  
 6 year. And what it was was it was created by  
 7 pathology societies to attempt to increase the  
 8 influx of people from medical school and  
 9 garner an interest in them so that perhaps  
 10 they might go into pathology. It was a  
 11 recruiting method. So what I did in medical  
 12 school, at the end of my sophomore year, which  
 13 I think would have been 1978, I technically  
 14 dropped out of medical school for a year and  
 15 stayed at the Medical College of Ohio Hospital  
 16 and did a fellowship in pathology and  
 17 basically I did everything that a first-year  
 18 pathologist in training would do during that  
 19 year. And then at the end of that I reentered  
 20 medical school, finished my clinical  
 21 clerkships and graduated. And that year  
 22 actually counted towards my residency  
 23 requirements from the American Board of  
 24 Pathology.  
 25 MR. BROWNE:

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1 Q. You admit that that's not the normal path that  
 2 most pathologists follow?  
 3 DR. DABBS:  
 4 A. That's not the normal path, correct. It was  
 5 something that the American Board and  
 6 pathology organizations wanted to use to  
 7 increase the interest of medical students in  
 8 the realm of pathology.  
 9 MR. BROWNE:  
 10 Q. Okay. And you also mentioned, as well, that  
 11 during your residency training you received a  
 12 lot of attention and training in IHC, is that  
 13 correct?  
 14 DR. DABBS:  
 15 A. Correct.  
 16 MR. BROWNE:  
 17 Q. Was that unique to your particular residency?  
 18 Because we've heard, the Commissioner has  
 19 heard a lot of evidence from several  
 20 pathologists who have testified before her  
 21 that depending on where you trained, your  
 22 residency, the focus may be different. We've  
 23 heard about training in anatomical pathology,  
 24 general pathology and the different focuses  
 25 there. So again, was that sort of a unique

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1 experience that you had as opposed to just  
 2 general pathologists?  
 3 DR. DABBS:  
 4 A. I think it was probably more heavily weighted  
 5 to immunohistochemistry in the residency where  
 6 I was, yes.  
 7 MR. BROWNE:  
 8 Q. Okay. And I think you also mentioned in  
 9 response to one of the questions of Mr. Coffey  
 10 that between 1980 and 1984 where you did your  
 11 residency, that was sort of the epicentre for  
 12 immunohistochemistry?  
 13 DR. DABBS:  
 14 A. Yes, pretty much.  
 15 MR. BROWNE:  
 16 Q. And also again, just sticking with some sort  
 17 of unique characteristics, if I may, and maybe  
 18 I'm misinterpreting this, but you also had a  
 19 fellowship in cytology, is that correct?  
 20 DR. DABBS:  
 21 A. There was--no, I did not have a fellowship in  
 22 cytopathology.  
 23 MR. BROWNE:  
 24 Q. Sorry -  
 25 DR. DABBS:

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1 A. The last, towards the end of my residency I  
 2 did a fellowship actually in diagnostic  
 3 electron microscopy and surgical pathology.  
 4 MR. BROWNE:  
 5 Q. Okay.  
 6 DR. DABBS:  
 7 A. Now, you'll see under the -  
 8 MR. BROWNE:  
 9 Q. The certification, that, sorry, that's where I  
 10 was -  
 11 DR. DABBS:  
 12 A. That was the certification, correct. And you  
 13 know what, that examination was the very first  
 14 time that examination was given and I think up  
 15 until the year of, I want to say sometime in  
 16 the 1990s a fellowship to sit for that  
 17 examination was not necessary, but then it  
 18 became necessary, I think, in the mid '90s,  
 19 somewhere around that that you had to take a  
 20 fellowship in cytology in order to sit for  
 21 that examination.  
 22 MR. BROWNE:  
 23 Q. Okay. And just focusing on the cytopathology  
 24 certification. I got the impression from your  
 25 answer yesterday that that gave you another

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1 sort of additional advantage with the fact  
 2 that this training helped you look at cellular  
 3 formation as opposed to again the broader  
 4 pathology residency. Is that a fair  
 5 encapsulation of what I understood you to say?  
 6 DR. DABBS:  
 7 A. It is a fair, I think, analogy. It's just  
 8 another tool, a different tool to look at  
 9 cells. And you know, another aspect of that  
 10 was electron microscopy, which is not in use  
 11 nowadays very much, it's been supplanted by  
 12 immunohistochemistry. So, you know, the tools  
 13 in anatomic pathology, they vary with regards  
 14 to how you examine tissues and cells and they  
 15 all compliment each other.  
 16 MR. BROWNE:  
 17 Q. Would the cytopathology, though, help you, I  
 18 guess, more in the--dovetail more with the  
 19 immunohistochemistry interpretation?  
 20 DR. DABBS:  
 21 A. Not necessarily. I think cytology, the  
 22 applications of immunohistochemistry and  
 23 cytology, it helped in that particular area,  
 24 yes.  
 25 MR. BROWNE:

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1 Q. Okay. Now, I understood you to say that by  
 2 1997, I think I got the quote correctly, that  
 3 you got frustrated by lack of references there  
 4 were and there were very few textbooks around  
 5 the subject matter of immunohistochemistry.  
 6 Is that--did I capture that statement  
 7 correctly?  
 8 DR. DABBS:  
 9 A. Yes.  
 10 MR. BROWNE:  
 11 Q. Okay. And then as a result of that you  
 12 approached publishers and then in 2002 the  
 13 first version of your textbook came out?  
 14 DR. DABBS:  
 15 A. Correct.  
 16 MR. BROWNE:  
 17 Q. And, Registrar, if we could have P-1767?  
 18 Doctor, this, Mr. Simmons, I think you spoke  
 19 to this quite extensively this morning. This,  
 20 in fact, is the document that we were talking  
 21 about in terms that it came out of the Florida  
 22 conference in 2006--or, sorry, it started in  
 23 Santa Barbara and then Florida in 2007, is  
 24 that right?  
 25 DR. DABBS:

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1 A. Correct.

2 MR. BROWNE:

3 Q. And this is the document that the authors

4 Goldstein--so this was the ad hoc committee of

5 which you're a member, I see down -

6 DR. DABBS:

7 A. Yes.

8 MR. BROWNE:

9 Q. Several people listed down in the lower right-

10 hand corner.

11 DR. DABBS:

12 A. Yes, and there are--right, exactly.

13 MR. BROWNE:

14 Q. And I just wanted to sort of just focus on

15 his, if I could, for a second and just have

16 you sort of comment further, if it's

17 necessary. But in the paragraph on the

18 screen, just above "Preanalytical Factors" it

19 begins, "Despite the improvements of reagents,

20 automation, authors over the years have

21 consistently noted the inconsistent quality of

22 IHC assays. Unlike previous IHC epochs, most

23 of the causative responsibility rests with the

24 individual laboratory performing IHC." And

25 then--and it goes on "and specifically the

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1 lack of standardization, attention to quality

2 assurance programs." So by this time, it was

3 evident to those gathered around the table

4 about these meetings that there was a, can I

5 say, human cry to move people in this

6 direction?

7 DR. DABBS:

8 A. There was more of a concerted effort to

9 acknowledge that there were variations that

10 people saw in the published literature that

11 needed to be addressed in a more focused

12 manner that would have more of a global impact

13 on the community.

14 MR. BROWNE:

15 Q. Okay. And then further on down it says,

16 "Unfortunately, laboratories often do not

17 appreciate the negative impact on their

18 specimens and the validity of IHC performed on

19 them by diverging away from these

20 recommendations." So while all this

21 information, I think if we look at the back--

22 there's close to 100 references that are cited

23 as the basis for these recommendations. But

24 the observation was made, look, we need to

25 bring all this literature together and develop

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1 these consensus statements, is that what I

2 understand to be -

3 DR. DABBS:

4 A. Yes, that was the call.

5 MR. BROWNE:

6 Q. Okay. In the period that's under sort of

7 review by the Commission, 1997, 2005, did your

8 lab change its practice in respect of, say,

9 the antibodies that it used?

10 DR. DABBS:

11 A. The laboratory changed, let's see. Well, I

12 arrived on the scene in 2001 and I know that

13 one of the things that we changed was we

14 changed our HER2 antibody kit. We were, I

15 believe, with the 1D5 antibody. We migrated

16 to 6F11 and I'm trying to think of the date

17 when that might have been. That might have

18 been somewhere between 2003 and 2005. And

19 then more recently to the SP1.

20 MR. BROWNE:

21 Q. Okay, so you have changed antibodies. What

22 about the nature of your antigen retrieval,

23 we've heard various evidence about the various

24 approaches to antigen retrieval. The time

25 that you at Mcgee, I guess is what you can

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1 speak of now. Have you changed the approach,

2 your approach to antigen retrieval?

3 DR. DABBS:

4 A. The approach to antigen retrieval has been

5 changed according to the protocols that have

6 been established for these FDA approved kits

7 that we use, yes.

8 MR. BROWNE:

9 Q. And you spoke yesterday about fixation times

10 and I sort of want to draw this into, make a

11 comment that you made, that there have been

12 changes in fixation times based on ASCO and

13 CAP recommendations. I didn't quite capture

14 when those recommendations came out. Is this

15 referring to this document or prior to that?

16 DR. DABBS:

17 A. No, it doesn't refer to this document. The

18 CAP, ASCO guidelines which came out

19 approximately two years ago, that was

20 regarding HER2 testing and the recommendation

21 there was that tissues had to be fixed for at

22 least six hours for tissues that were going to

23 have HER2 testing.

24 MR. BROWNE:

25 Q. Okay. Prior to, I guess, this document, were

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1           there any recommendations or guidelines by  
2            ASCO and CAP with regard to ER/PR?

3       DR. DABBS:

4           A. No, not at all.

5       MR. BROWNE:

6           Q. Okay. So there was no standard guidelines in  
7            terms of fixation?

8       DR. DABBS:

9           A. Correct.

10       MR. BROWNE:

11          Q. Okay. So we can take it that up to this point  
12          in time most--we could not be certain as to  
13          what fixation times any lab was following  
14          throughout the United States?

15       DR. DABBS:

16          A. Well, there are multiple papers that have been  
17          published ever since the ER by IHC became  
18          prevalent. Some of the authors in those  
19          papers were Hector Battifora, for example. He  
20          clearly--well, he did some studies that  
21          clearly demonstrated that fixation--that  
22          results were dependent upon fixation time and  
23          so they had recommended sort of time windows.  
24          I don't know that there was necessarily a  
25          minimum time recommended as strongly as were

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1           maximum times for that. But there are papers  
2           that do tangentially address fixation and the  
3           importance of fixation for ER testing.

4       MR. BROWNE:

5           Q. And do these papers address like various, like  
6           we see with Rhodes paper and so on, sort of  
7           the cause and effect of various lengths of  
8           fixation time?

9       DR. DABBS:

10          A. Yes.

11       MR. BROWNE:

12          Q. You spent a bit of time yesterday and again  
13          today talking about, I think, the importance  
14          of reporting intensity. And I understand your  
15          views and you've explained to the Commissioner  
16          how you view it as an important tool for  
17          clinicians. We spoke about this, actually,  
18          yesterday, as well. And what prompted that  
19          discussion was your reference to Dr. Nadji,  
20          Professor Nadji in Florida. And is Dr. Nadji  
21          a member of this consensus group?

22       DR. DABBS:

23          A. He never attended any of the meetings, so the  
24          answer to that would be no.

25       MR. BROWNE:

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1           Q. Okay. Nevertheless, Dr. Nadji, and we have,  
2           Registrar, if we could put up on the screen  
3           Exhibit 2630? Has that been entered? Okay.  
4           Dr. Nadji is recognized in the area, he's  
5           published extensively in the area of  
6           immunohistochemistry, has he not?

7       DR. DABBS:

8           A. Yes.

9       MR. BROWNE:

10          Q. Okay. And this article is entitled,  
11          "Quantitative Immunohistochemistry, Estrogen  
12          Receptor in Breast Cancer, Much Do About  
13          Nothing." And if we look--I'm sure if that's  
14          my highlighted--it is my highlighted copy.  
15          But it says in the bottom paragraph of the, I  
16          guess, the abstract of this paper, he says,  
17          "In this review I attempt to prevent"--excuse  
18          me, "present an argument that is based on our  
19          current information, quantitation of ER IHC is  
20          neither technically reliable nor clinically  
21          relevant." Now, I know that you've, in fact,  
22          you indicated to me yesterday that you've  
23          written response to this. Is that correct?

24       DR. DABBS:

25          A. We wrote a paper that was aimed at addressing

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1           issues associated with this, yes.

2       MR. BROWNE:

3           Q. Okay. But I guess the point I'm drawing upon  
4           here is that there are people--there are two  
5           schools of thought on this, are there not, and  
6           that Professor Nadji represents the argument,  
7           at least in this paper, presents the argument  
8           against quantification, whereas you put forth  
9           the argument for quantification. Is that a  
10          fair synopsis?

11       DR. DABBS:

12          A. Yes. And I think, you know, basically if you  
13          put it in perspective, I don't know that there  
14          are two camps, necessarily. I think that the  
15          recommendations from the consensus group are  
16          clear and clearly represent the majority. I  
17          think that Dr. Nadji in his experience and  
18          perhaps with one other person who has  
19          published on this topic are in the distinct  
20          minority. If you look at the literature on  
21          Ligand Binding method throughout its entire  
22          history, you will find out that they  
23          quantitate that and the clinicians used those  
24          quantitative results to determine if they were  
25          going to give patients endocrine therapy.

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1 Whenever you take a test that is a continuous  
 2 variable like that and you want to change the  
 3 testing format, the onus is upon the  
 4 laboratory director to see to it that that,  
 5 the change or the translation of that test  
 6 into a different format is properly optimized  
 7 and validated. In other words, if we were  
 8 talking about serum potassium and the range by  
 9 this machine over here is 3.5 to 5.6, okay,  
 10 and I decided to try a new test and I'm going  
 11 to report is as positive or negative, okay,  
 12 people are going to die because potassium is a  
 13 very crucial analyte. Well, I don't consider  
 14 that estrogen receptor and progesterone  
 15 receptor are any less crucial because patient  
 16 management and patient outcomes are based on  
 17 therapy, and so, therefore, in my mind, and in  
 18 the minds of the consensus group, we all fully  
 19 acknowledge that if you even look at the  
 20 immunohistochemistry literature--in fact, one  
 21 of the very first paper that attempted  
 22 translation that I cited where they looked at  
 23 immunofluorescence of cells with antibodies to  
 24 estradiol and determined that there was a  
 25 heterogeneity of cellular staining. If you

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1 look at the immunohistochemistry literature  
 2 throughout the decades, you will find that  
 3 every paper discusses at least that. So I  
 4 reject outright any assay that tells me that  
 5 it's all or none immunostaining. That's not a  
 6 properly validated assay, in my opinion, or  
 7 the opinion of the people of this group, of  
 8 the opinion of UK NEQAS people. So that's how  
 9 I view that. I think this paper is a  
 10 minority. I felt that it needed to be  
 11 responded to, and that's why we put together  
 12 our experience in our argument based on  
 13 information that a properly validated  
 14 immunochemistry assay is in a select group of  
 15 percentage of cases going to show strong  
 16 positive cells, negative cells, weakly  
 17 positive cells, and intermediate positive  
 18 cells, just like that slide--that single slide  
 19 that I showed you, that picture, at the  
 20 beginning.  
 21 MR. BROWNE:  
 22 Q. But, I guess, after getting these sort of  
 23 divergent views, I guess you recognize--you  
 24 would put Dr. Nadji in the minority, doesn't  
 25 that heighten the necessity to have, as we now

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1 have with the 2007 and now the 2008, the need  
 2 for consensus because of these sort of  
 3 differing views?  
 4 DR. DABBS:  
 5 A. That's correct, and I'm certain that Dr. Nadji  
 6 knew of these meetings. In fact, one of them  
 7 was in his own back yard and he didn't attend.  
 8 No one on this committee had any influence  
 9 over him, it was his choice to attend or not,  
 10 but I can tell you that an all or none assay  
 11 for immunohistochemistry ER, all or none, does  
 12 not exist in my mind, and it's not a properly  
 13 validated translated assay.  
 14 MR. BROWNE:  
 15 Q. We--in your presentation yesterday, you dealt  
 16 with the issue of--we can--I think it's P-  
 17 2629. Oh, no, your PowerPoint, my apologies.  
 18 Yes, sorry, actually let's just deal with  
 19 that. I think, if I made a note to myself  
 20 correctly yesterday, Doctor, you mentioned I  
 21 think it's recommendations 11 and 12, that  
 22 some labs are still using 10 percent. Is that  
 23 --  
 24 DR. DABBS:  
 25 A. Yes.

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1 MR. BROWNE:  
 2 Q. Did I--okay, and this is why I wanted to sort  
 3 of cover this off with you. In the paragraph  
 4 --this is the article you put into evidence  
 5 yesterday, comparison of evaluations for  
 6 hormone receptor in breast carcinoma. The  
 7 notion here, and I'm looking at the paragraph,  
 8 "In particular, endocrine response uncertain  
 9 was to find some expression of steroid hormone  
 10 receptors quantitatively low, usually  
 11 considered less than 10 percent of cells  
 12 positive are qualitatively insufficient to  
 13 indicate a substantial change in response".  
 14 This notion, has that been talked about for a  
 15 number of years, and, in particular, I would  
 16 just--you dealt with this to some extent with  
 17 Mr. Simmons this morning. In England, and we  
 18 have--I think I put it in as an exhibit, P-  
 19 2619, Doctor. Registrar, can we enter P-2619.  
 20  
 21 DR. DABBS:  
 22 A. While that paper goes up there, the paper that  
 23 was up here, if I can just sort of scroll down  
 24 to a particular place where I wanted to  
 25 illustrate something--okay, under the

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1 discussion that I have up here, "As for ER,  
 2 the bimodal distribution of the ER score by  
 3 DAKO manual staining using antibody 1D5 was  
 4 pointed out. That is in more than 94 or 90  
 5 percent of cases the tumours were completely  
 6 ER negative or unequivocally ER positive.  
 7 These results suggested that DAKO  
 8 immunohistochemistry assay is too sensitive  
 9 and perhaps not sufficiently specific". So  
 10 they're citing basically results that are  
 11 similar to Nadji as published in the past,  
 12 which another group out of Boston has  
 13 published in the past regarding the conditions  
 14 of that test. So they're acknowledging here  
 15 that they too experienced bimodal  
 16 distribution, but noticed it's only with that  
 17 one --

18 MR. BROWNE:  
 19 Q. Particular --

20 DR. DABBS:  
 21 A. Yes, which is the one that Nadji and the group  
 22 in Boston had published on, correct.

23 MR. BROWNE:  
 24 Q. Sorry, Doctor, if we could enter P-2619, and I  
 25 just want to--there's a comment here, Doctor,

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1 I'll get you to comment on or respond to, and  
 2 I think you spoke to this to some extent in  
 3 response to a question from Mr. Simmons this  
 4 morning and that's the importance of these  
 5 values for clinicians and the subjectivity  
 6 surrounding that for oncologist, in  
 7 particular, and this was a 1998 article and it  
 8 talks about the cutoffs at 1 percent, I think,  
 9 out of the literature out of the United States  
 10 and so on, but this paragraph right here says,  
 11 "Perhaps different cutoffs should be used,  
 12 depending on the clinical situation, i.e., in  
 13 the adjuvant or metastatic setting. It is the  
 14 aim to identify patients who will respond to a  
 15 particular regime or those who will not", and  
 16 it goes on and talks about, for example, in a  
 17 woman who's node negative and has a small low  
 18 grade tumour, should have little impact, and  
 19 again using--again responding to the 1  
 20 percent. If you look up above here, just  
 21 right here, "A recent editorial in the British  
 22 Medical Journal advocates a very low cutoff  
 23 for selection of patients for adjuvant  
 24 endocrine treatment, the San Antonio group  
 25 having found significant benefit in women with

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1 tumours containing only 1 percent positive  
 2 cells". So is this sort of paragraph speaking  
 3 to what you talk about, you know, that in that  
 4 1 to 10 percent category, it's important for  
 5 clinicians to weigh all the various factors  
 6 and I think they talk about here, and some of  
 7 those examples: tumours size, lymph node  
 8 involvement, distant metastatic spread and so  
 9 on. So there are other considerations  
 10 especially are significant in that 1 to 10  
 11 percent. Is that what I understand these  
 12 authors in the literature to be saying?

13 DR. DABBS:  
 14 A. I agree, and I think that this paper actually  
 15 demonstrates that pretty nicely. If I could  
 16 just scroll up here and show you this  
 17 particular graph right here, which is a graph  
 18 of ER predictive score versus the percent of  
 19 patients responding, you know, their scoring  
 20 method--basically, UK NEQAS uses a combination  
 21 of proportion of cells plus intensity.

22 MR. BROWNE:  
 23 Q. Uh-hm.

24 DR. DABBS:  
 25 A. And they came up with the scoring method here

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1 which is not too dissimilar to any other  
 2 scoring method, whether it be Allred or H  
 3 score or whatever, but if you look at the  
 4 highest score here which is 9, you have close  
 5 to 80, you know, 75 percent of patients  
 6 responding, but I will point out here that at  
 7 a score of zero, 10 percent of patients are  
 8 responding, and, you know, that's a--that  
 9 number is a significant number in the States,  
 10 I can tell you. If you tell a patient that  
 11 they have a 10 percent chance of having  
 12 metastatic tumour in their axilla from their  
 13 breast tumour, I would bet you that the vast  
 14 majority of them are going to want to have  
 15 surgery to have that axilla--an axillary  
 16 dissection. I think if you tell certain  
 17 patients that they have--even though their  
 18 test result was negative, they have a 1 in 10  
 19 chance of responding to a therapy, you know,  
 20 it's easy for us to all sit in this room and  
 21 talk about what if's, but if a patient who has  
 22 cancer is looking for some straw to grasp,  
 23 that 10 percent becomes 100 percent, and  
 24 that's why, just as you pointed out, and I  
 25 indicated earlier, when you get down to these

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1 real small, you know, between 1 and 10  
2 percent, it really matters on an individual  
3 basis and that's why quantisation is important  
4 and this shows it right here.  
5 MR. BROWNE:  
6 Q. And I guess quantisation, plus the other  
7 factors that are involved --  
8 DR. DABBS:  
9 A. Exactly.  
10 MR. BROWNE:  
11 Q. And that leads to that discussion between the  
12 oncologist and the patient to come to that  
13 decision as to whether or not this treatment  
14 is appropriate?  
15 DR. DABBS:  
16 A. Correct.  
17 MR. BROWNE:  
18 Q. Risk/benefit analysis.  
19 DR. DABBS:  
20 A. Right.  
21 MR. BROWNE:  
22 Q. Doctor, I'm not sure if it's Professor or Dr.  
23 Lester Layfield, are you familiar with any of  
24 his --  
25 DR. DABBS:

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1 A. Yes, I know Lester, yeah.  
2 MR. BROWNE:  
3 Q. He did some studies in 2000, a survey of labs  
4 across the United States.  
5 DR. DABBS:  
6 A. Uh-hm.  
7 MR. BROWNE:  
8 Q. Are you familiar with that particular --  
9 DR. DABBS:  
10 A. Yes, I am.  
11 MR. BROWNE:  
12 Q. And in that, if I'm correct, there were some  
13 labs using a 30 percent cutoff at that time?  
14 DR. DABBS:  
15 A. Well, there was a lab, and I wasn't sure which  
16 one it was, and I don't know if it was the one  
17 in St. John's or wherever that was, I wasn't  
18 familiar with it, it wasn't actually  
19 elucidated in that paper.  
20 MR. BROWNE:  
21 Q. I think they were US labs that were involved  
22 in that. Were there Canadian labs involved in  
23 that as well?  
24 DR. DABBS:  
25 A. I thought it was done in North America. It

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1 was a survey.  
2 MR. BROWNE:  
3 Q. Okay. You spoke to tumour --  
4 THE COMMISSIONER:  
5 Q. Can you find that paper that you --  
6 DR. DABBS:  
7 A. I do, and I can find it. I'll now provide it  
8 to you, Commissioner. Tumour Hetrogenicity.  
9 Doctor, you spoke to this as well, and I  
10 understand--and I want to make sure I  
11 understand correctly. Given a tumour which is  
12 five to six centimetres in size, and I think  
13 the recommended sectioning is five microns in  
14 terms of when you create the slides, do I  
15 understand that you should--the variability of  
16 that tumour should only be around 1 percent in  
17 terms of if you were to take various sections,  
18 a change of between--the risk of change  
19 between ER positive and ER negative? Probably  
20 I haven't said that correctly, but you spoke  
21 to that yesterday and I wasn't quite sure, you  
22 wouldn't expect differences of more than 1  
23 percent.  
24 DR. DABBS:  
25 A. Right, and by that, I meant, you know, using

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1 the criteria that a negative result is 100  
2 percent negative. I think by doing further  
3 sections on that, the likelihood of finding  
4 focal staining would probably be not more than  
5 1 percent.  
6 MR. BROWNE:  
7 Q. Okay. I made a note yesterday--I'm not sure  
8 if Mr. Coffey framed the question in this  
9 fashion or not or I wrote it down that way,  
10 but you spoke to the expected rate of 2  
11 percent in your lab, which if you get above 2  
12 percent, you get concerned?  
13 DR. DABBS:  
14 A. And that referred to repeats of  
15 immunohistochemistry tests in general.  
16 MR. BROWNE:  
17 Q. In general. I'm not sure if it was in terms  
18 of error rate or anything like that described  
19 in that manner, but is there a discussion  
20 about error rates in general in  
21 immunohistochemistry in the literature?  
22 DR. DABBS:  
23 A. When you say error rates, do you mean --  
24 MR. BROWNE:  
25 Q. Changes in results. We talk about the NEQAS



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1 variability between labs and so on.

2 DR. DABBS:

3 A. I am not aware of any. I think the most

4 exhaustive studies that have been done were

5 probably UK NEQAS showing variability, but

6 conversions, I'm not aware of.

7 MR. BROWNE:

8 Q. Okay. The Royal College of Pathologists of

9 Australia did a quality assurance review. Did

10 they touch on that in any way in 2006, or did

11 they compare variability?

12 DR. DABBS:

13 A. I think that was more of a variability

14 comparison as well.

15 MR. BROWNE:

16 Q. Were the results similar to what NEQAS found

17 in terms of the lab?

18 DR. DABBS:

19 A. They weren't too dissimilar.

20 MR. BROWNE:

21 Q. Registrar, if we could see Exhibit P-0113,

22 please. Doctor, this is the exhibit you were

23 shown, Dr. Ejeckam's memo, and if you recall

24 in the second memo, you were asked about core

25 biopsies. I'll just get it up here, "ER false

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1 negative results increase in core biopsies.

2 Therefore, where possible, restrict requests

3 to excisional biopsies", and you spoke to that

4 yesterday. Is it possible--you said, in fact,

5 it's the exact opposite?

6 DR. DABBS:

7 A. Correct.

8 MR. BROWNE:

9 Q. Is it possible that this may be speaking to

10 the problem of getting enough representative

11 tissue and tumour on the slide? I mean, that

12 is a known problem with core biopsy.

13 DR. DABBS:

14 A. Well, it's a known problem in that there can

15 be a variation. For example, you know, a

16 negative core biopsy result, but then you

17 should repeat that on the resected specimen.

18 However, that's a real distinct minority

19 compared to what should be positive. So, you

20 know, your positive for ER should be, you

21 know, 75 to 80 percent. That's an unusual

22 statement there.

23 MR. BROWNE:

24 Q. There was some discussion about slides. In

25 your lab, do you use particular slides for

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1 immunohistochemistry?

2 DR. DABBS:

3 A. We do use slides that are basically

4 constructed to maximize adherence of tissue

5 sections to them.

6 MR. BROWNE:

7 Q. And what type of--we've heard about positive

8 charged slides and there was another--histo

9 grip was another example.

10 DR. DABBS:

11 A. Yeah, there's a variety of brands out there,

12 and we use something that basically has

13 something akin to a positive charge on it. I

14 don't remember the precise brand name of it,

15 but, yes, that's an important aspect of it,

16 along with--the really critical aspect is

17 baking the sections and making sure that

18 they're water free before they go for IHC.

19 MR. BROWNE:

20 Q. So the two go hand in hand.

21 DR. DABBS:

22 A. Very much so.

23 MR. BROWNE:

24 Q. But it--I guess, you don't use normal slides

25 that you would, say, use for other routine

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1 pathology?

2 DR. DABBS:

3 A. Correct, exactly.

4 MR. BROWNE:

5 Q. Doctor, the Commission has heard a lot of

6 evidence about resources and funding for

7 immunohistochemistry programs. I'm sure--I'm

8 not sure how much you about the Canadian

9 system and how it is funded through government

10 and so on. It's much different than the

11 United States. It is akin to the National

12 Health Care Program in the United Kingdom, so

13 there are some similarities there. I

14 recognize that your experience may be limited

15 in that regard, but just generally, do you

16 have an particular views on the importance of

17 having appropriate funding irrespective of the

18 source for carrying out an

19 immunohistochemistry program?

20 DR. DABBS:

21 A. Uh-hm. Well, I think that education in

22 immunohistochemistry is part of anatomic

23 pathology, and I think that that's where the

24 training really should take place so there's

25 an equal exposure of all trainees who are

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1 being trained to be pathologists, and so,  
 2 therefore, it would follow, in my way of  
 3 thinking, that if a program is going to have--  
 4 be training pathologists to be board certified  
 5 in anatomic pathology, that they should have  
 6 all the wherewithal and the resources to train  
 7 anatomic pathologists in the discipline of  
 8 immunohistochemistry, the importance of the  
 9 nuances, and the technical aspects and how to  
 10 interpret and so forth, just like any other  
 11 aspect of surgical pathology.

12 MR. BROWNE:  
 13 Q. And in terms of the clinical application there  
 14 as well in terms of sufficient funding, are  
 15 you talking continuing medical education as  
 16 you go through or are you talking about the  
 17 sort of lead up into being certified as?

18 DR. DABBS:  
 19 A. Sure. I think that the training program is a  
 20 starting place, starting point. From then on,  
 21 pathologists go have a wide variety of choices  
 22 at national meetings. There's lots of  
 23 national meetings that occur where there are  
 24 lots of speakers who speak to different  
 25 aspects of immunohistochemistry with different

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1 levels of orientation. For example, let's  
 2 see, this will be the third annual course on  
 3 immunohistochemistry. The course is conducted  
 4 by Yazidjee. He is one of the people on this  
 5 paper. Last year, it was held in Santa  
 6 Barbara. The year before that, it was held in  
 7 Marathon, Florida. It's coming back to  
 8 Marathon, Florida for this January. So it's a  
 9 week-long course. It's everything you could  
 10 possibly know about the technical aspects of  
 11 IHC. I think he markets it fairly well.  
 12 Everyone that I know in my department got an  
 13 e-mail and they said "well, what's this?" So  
 14 the word is out there. I think that there's  
 15 been a need for this.

16 Some years back, in the mid 80s to early  
 17 90s, the Society for Applied  
 18 Immunohistochemistry, which is actually  
 19 sponsoring this course that I just described,  
 20 was more active on a local level. They would  
 21 have quarterly meetings in New York City and  
 22 people would travel there and look at  
 23 interesting cases and whatnot. There were a  
 24 fair number of pathologists interested in  
 25 that. That sort of atrophied, to some degree,

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1 and now things are starting to pick up, at  
 2 least specifically oriented to IHC.

3 Again, there are plenty of organizations.  
 4 There's plenty of speakers at the U.S. and  
 5 Canadian Academy of Pathology meeting, which  
 6 is either held in the U.S. or in Canada. The  
 7 American Society of Clinical Pathologists has  
 8 lots of courses, didactic, presentation, on  
 9 the subject, and there are other local and  
 10 national speakings at State levels and  
 11 whatnot. So there's ample opportunity for  
 12 CME, continuing medical education, in  
 13 immunohistochemistry.

14 MR. BROWNE:  
 15 Q. But in order to do that, you need to have  
 16 proper funding to allow people to go to that,  
 17 would you agree?

18 DR. DABBS:  
 19 A. Yes, indeed.

20 MR. BROWNE:  
 21 Q. Doctor, the notion of--and one of the problems  
 22 that was mentioned here, and I think you saw,  
 23 to some extent in Dr. Banerjee's report,  
 24 turnover of staff, pathologists, technologists  
 25 and oncologists. Is that difficult--putting

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1 aside the notion of, you spoke to having  
 2 metrics and that assumes, I guess, to some  
 3 extent you have a sufficient computer base in  
 4 which--and technology to do that. Would that  
 5 lead to problems--would turnovers of these  
 6 types of individuals lead to problems in  
 7 seeing trends, do you think?

8 DR. DABBS:  
 9 A. I think definitely, particularly if their  
 10 stays here, or wherever, were very short  
 11 lived. Yes, that certainly could be a  
 12 contributing factor.

13 MR. BROWNE:  
 14 Q. One last area, Doctor. You spoke, I think  
 15 towards the end of the session this morning,  
 16 about the importance of, or the relevance, I  
 17 should say, of use of ER/PR for unknown  
 18 primaries. Do you know whether it's standard  
 19 practice to treat on a basis of ER/PR result  
 20 in relation to an unknown primary?

21 DR. DABBS:  
 22 A. I think if a pathologist is confident in their  
 23 work up that they're dealing with a carcinoma  
 24 that is ER positive and/or PR positive and  
 25 it's likely everything points to a GYN

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<p>1 primary, for example, gynecologic primary, 2 then yes, I think that a clinician would take 3 that information into account and use that as 4 information based therapy.</p> <p>5 MR. BROWNE: 6 Q. Thank you. Thank you, Doctor. Thank you, 7 Commissioner.</p> <p>8 THE COMMISSIONER: 9 Q. Thank you, Mr. Browne. Ms. Newbury?</p> <p>10 DR. DAVID DABBS, EXAMINATION BY MS. JENNIFER NEWBURY 11 MS. NEWBURY: 12 Q. Good afternoon, Dr. Dabbs. My name is 13 Jennifer Newbury and I represent the Canadian 14 Cancer Society, Newfoundland and Labrador 15 Division. I just wanted to ask you a couple 16 of questions this morning, starting with the 17 issue of fixation of a specimen in alcohol, 18 whether inadvertent or intentional, and the 19 possible effect or impact of any tissue 20 reprocessing, and perhaps I'll refer first to 21 the article that you've seen at least once 22 today, P-1767. This is the article of 23 Goldstein and Clive Taylor, and I'm going to 24 show you--you're well familiar with this by 25 the sounds of it. On page, starting on page</p>	<p>1 MS. NEWBURY: 2 Q. Was this discussed at any of the meetings with 3 your consensus group?</p> <p>4 DR. DABBS: 5 A. Yes, it was.</p> <p>6 MS. NEWBURY: 7 Q. Okay, and I think you'd mentioned earlier that 8 there are no studies per se on this, no actual 9 groups of specimens taken, or are these more 10 just observations?</p> <p>11 DR. DABBS: 12 A. I think these are observations by people who 13 have done internal--a look at their internal 14 quality and comparison studies. For example, 15 when I looked at a certain tissue processor I 16 had on loan for two months, I didn't publish 17 that. I didn't think that that was something-- 18 -that was not my goal to publish. I think 19 that people had recognized, in general, that 20 alcohol was a very different--had a very 21 different mode of fixation. It's a 22 coagulation type of fixative and doesn't do 23 what formalin does, and therefore 24 immunohistochemistry, we know, becomes highly 25 sensitive with that, used as a primary</p>
<p style="text-align: right;">Page 201</p> <p>1 11, there are some questions and answers that 2 appear to be related to the article. I'm not 3 sure if you're familiar with this part of the 4 document of that.</p> <p>5 DR. DABBS: 6 A. Yes.</p> <p>7 MS. NEWBURY: 8 Q. And on page 13, in the middle column, at the 9 top, there's a reference there, an answer 10 given by Dr. Badve?</p> <p>11 DR. DABBS: 12 A. Badve, yeah.</p> <p>13 MS. NEWBURY: 14 Q. And he indicates that "standard processing 15 protocols entail the use of alcohols after the 16 tissue is fixed in formalin. Alcohol is also 17 a fixative with relatively rapid penetration. 18 So if unfixed tissues are loaded onto a 19 processor, they're more likely to undergo 20 significant alcoholic fixation which can lead 21 to altered IHC and false positive results." 22 So this is a concept, I believe, that you were 23 speaking about this morning.</p> <p>24 DR. DABBS: 25 A. That's correct.</p>	<p style="text-align: right;">Page 203</p> <p>1 fixative, and so the caution upfront that we 2 tried to stress was that if a tissue isn't 3 properly fixed in formalin when it goes into 4 the alcoholic dehydrations, that could be a 5 problem because then the tissue sees alcohol 6 as its primary fixative, if it hasn't had 7 enough formalin exposure.</p> <p>8 MS. NEWBURY: 9 Q. Okay, and that could then lead to the problem 10 of false positives, due to the over 11 sensitivity?</p> <p>12 DR. DABBS: 13 A. It could be.</p> <p>14 MS. NEWBURY: 15 Q. And you'd indicated to Mr. Simmons this 16 morning that inadequate fixation that could 17 possibly cause this would be fixation of less 18 than an hour or two?</p> <p>19 DR. DABBS: 20 A. I would say an hour or two, yes.</p> <p>21 MS. NEWBURY: 22 Q. And you indicated that the false positives 23 that might arise from that weren't even 24 consistent, so it's not like you would expect 25 with each and every specimen in that situation</p>

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<p>1 would lead to a false positive?</p> <p>2 DR. DABBS:</p> <p>3 A. Correct.</p> <p>4 MS. NEWBURY:</p> <p>5 Q. Okay. What if there were other issues with</p> <p>6 fixation, not just the time of fixation, but</p> <p>7 if the pH level, for example, of the formalin</p> <p>8 wasn't properly maintained or adjusted at the</p> <p>9 beginning?</p> <p>10 DR. DABBS:</p> <p>11 A. Yes, that in itself could be a problem, and</p> <p>12 you know, when I was in residency, I'm aware</p> <p>13 that there were laboratories that made their</p> <p>14 own formalin and buffering mechanism. Of</p> <p>15 course, if one is going to do that, it's</p> <p>16 prudent upon the laboratory to regularly check</p> <p>17 the pH of formalin to make sure that the</p> <p>18 composition hasn't changed and that everything</p> <p>19 is working as it should. Nowadays, many</p> <p>20 laboratories, including ours, buy pre-made</p> <p>21 with a predetermined pH buffered, neutral</p> <p>22 buffered formalin. So it becomes less of a</p> <p>23 problem, especially if, you know, whenever you</p> <p>24 buy formalin in packages, bottles, you tend to</p> <p>25 use it fairly rapidly. So it's not like it's</p>	<p>1 section somewhere in the middle of that</p> <p>2 specimen, in other words, one that has not</p> <p>3 been--where the surface hasn't been exposed to</p> <p>4 formalin. You're getting something which is</p> <p>5 an unknown, in terms of fixation. So you</p> <p>6 could get a poorly fixed specimen out of a</p> <p>7 centre section from thick tissue that's been</p> <p>8 sitting in a bucket and, of course, that will</p> <p>9 give you--that will be poorly fixed, and</p> <p>10 chances are, you won't get a good result with</p> <p>11 that.</p> <p>12 MS. NEWBURY:</p> <p>13 Q. Okay, and it could go either way?</p> <p>14 DR. DABBS:</p> <p>15 A. Sure.</p> <p>16 MS. NEWBURY:</p> <p>17 Q. And I'd like to refer to your presentation,</p> <p>18 Exhibit P-2621, please, and on page 14 of the</p> <p>19 exhibit. Recommendation number five there,</p> <p>20 there's a reference, and I believe you</p> <p>21 commented yesterday, during your evidence,</p> <p>22 that it would be okay to use alcohol as a</p> <p>23 fixative, but you would have to validate with</p> <p>24 appropriate alcohol fixed cytology specimens,</p> <p>25 and this isn't easy to do. So I assume that</p>
<p>Page 205</p> <p>1 going to sit around for the laboratory for a</p> <p>2 year or two, and be changed composition. So</p> <p>3 that's one of the benefits of at least</p> <p>4 obtaining formalin that's already prepackaged.</p> <p>5 MS. NEWBURY:</p> <p>6 Q. Okay, and if for some reason or another the</p> <p>7 formalin was sitting around the lab, it would</p> <p>8 be necessary to check the pH from time to</p> <p>9 time?</p> <p>10 DR. DABBS:</p> <p>11 A. Yes.</p> <p>12 MS. NEWBURY:</p> <p>13 Q. And what about a situation where fixation</p> <p>14 might be affected by the size of the specimen</p> <p>15 being too large, if it's not adequately cut</p> <p>16 when prior to being put in formalin or shortly</p> <p>17 after being put in formalin, would that be an</p> <p>18 issue as well that could cause some false</p> <p>19 positives, if exposed to alcohol?</p> <p>20 DR. DABBS:</p> <p>21 A. It could. It could also cause false negatives</p> <p>22 because, for example, if you have a reasonably</p> <p>23 large portion of tissue in a bucket and the</p> <p>24 person who's taking a section from it, say,</p> <p>25 cuts into the middle of that and takes a</p>	<p>Page 207</p> <p>1 you're saying that you can't rule out the</p> <p>2 possibility that alcohol could be used as a</p> <p>3 fixative?</p> <p>4 DR. DABBS:</p> <p>5 A. Well, our cytopathology colleagues use alcohol</p> <p>6 as a primary fixative for many of the fluids.</p> <p>7 Now if one is going to use alcohol as a</p> <p>8 primary fixative, then one should use alcohol</p> <p>9 as a primary fixative for their control</p> <p>10 tissues, okay, and ideally, they should be</p> <p>11 cytology specimens as well, so that they're</p> <p>12 fixed in the same way and processed in the</p> <p>13 same way, and that's possible to do. But</p> <p>14 again, there's a great deal of labour and</p> <p>15 expense involved in doing that, and validating</p> <p>16 that with, you know, probably 100 specimens</p> <p>17 and with a lot of different kinds of</p> <p>18 antibodies, if you're going to be using a lot</p> <p>19 of different kinds of antibodies. That is why</p> <p>20 cytology, immunohistochemistry and cytology is</p> <p>21 best performed on a formalin fixed paraffin</p> <p>22 embedded blocks, or in the instance where I</p> <p>23 mentioned, if we're going to a clinic to do a</p> <p>24 needle aspirate on a patient who is thought to</p> <p>25 have recurrent or metastatic breast cancer</p>

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<p>1 that we want to make sure that we have 2 formalin on our cart whenever we go to the 3 clinic, so that whenever we do the aspirate, 4 we basically put that material into formalin 5 to make a cell block from it, so that ER/PR 6 and HER2 can be done and used with our 7 controls that exist in the laboratory.</p> <p>8 MS. NEWBURY: 9 Q. So then this doesn't mean then that ER/PR 10 using primary fixative of alcohol is something 11 that would be recommended?</p> <p>12 DR. DABBS: 13 A. It's not desirable at all.</p> <p>14 MS. NEWBURY: 15 Q. Okay, and certainly, if you're not cognizant 16 that fixation of a specimen is occurring 17 inadvertently by alcohol due to the inadequate 18 fixation, that would be a problem in your 19 view?</p> <p>20 DR. DABBS: 21 A. Correct.</p> <p>22 MS. NEWBURY: 23 Q. Okay, and you commented to Mr. Simmons, and 24 perhaps yesterday as well, that reprocessing 25 wouldn't have any effect on the performance of</p>	<p>1 then on is going to change that. If you have 2 a specimen that was well fixed upfront and 3 needed to be reprocessed because it didn't 4 dehydrate well or something like that, when 5 you take it back, that specimen is still well 6 fixed primarily. So when you take it back and 7 dehydrate it again and embed it in paraffin, 8 nothing that you're doing there is anything 9 different than what you did the first time. 10 So there's nothing there that you're doing to 11 harm the tissue.</p> <p>12 If for some reason it got exposed to 13 extreme temperatures during that, that could 14 potentially impact it. But in general, tissue 15 reprocessing is a harmless phenomenon. It's a 16 harmless task that is meant to make the tissue 17 more readily cuttable and most of those are 18 due either to section thickness being too 19 thick in the cassette or poor dehydration.</p> <p>20 MS. NEWBURY: 21 Q. That being said though, would tissue 22 reprocessing not be desirable generally 23 speaking, for any other reasons?</p> <p>24 DR. DABBS: 25 A. Well, there's one specific reason where it</p>
<p style="text-align: right;">Page 209</p> <p>1 IHC, and this is the tissue reprocessing that 2 have been mentioned to you and you were aware 3 of that taking place?</p> <p>4 DR. DABBS: 5 A. Yes.</p> <p>6 MS. NEWBURY: 7 Q. In various laboratories. I just want to make 8 sure I understand why reprocessing of tissue 9 wouldn't have an effect on the performance of 10 IHC, and perhaps--this is my understanding 11 from what you indicated yesterday. Is this 12 due to the fact that an improperly fixed 13 specimen would already have been exposed to 14 alcohol several times through the initial 15 tissue processing, so the tissue reprocessing 16 doesn't really expose that specimen to any 17 more alcohol than the initial tissue 18 processing to begin with?</p> <p>19 DR. DABBS: 20 A. That certainly is one of the arguments that I 21 would make, in that whenever you go back, 22 basically what you have is the original tissue 23 and the exposures that it had experienced. If 24 it had experienced little formalin time and 25 done an alcohol time, nothing that you do from</p>	<p style="text-align: right;">Page 211</p> <p>1 would be undesirable and that would be, for 2 example, if on the specific block that 3 contains the tumour that the tumour is a small 4 portion of tumour and you're reprocessing that 5 and you take it back and then you have to 6 reface the block and cut it. You may be--you 7 may end up having barely enough or not enough 8 to do your testing, depending on how--you 9 know, let's say you have a three millimetre 10 tumour and you've already cut off several 11 sections and they didn't work, then you take 12 it back, you reprocess it, you put the block 13 on a microtome, you reface it and now you're 14 cutting through the last millimetre or 0.5 15 millimetres. It's possible that you may end 16 up not having enough tissue to do the testing 17 on. So reprocessing is undesirable. No 18 pathologist likes to see that in the 19 laboratory. At the very least, it will delay 20 the case probably one whole day because it 21 takes another full day to be reprocessed and a 22 new slide made.</p> <p>23 MS. NEWBURY: 24 Q. Dr. Dabbs, I wanted to ask you a couple of 25 questions now about what have been called</p>

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1 retroconverters, and those are converters from  
 2 positive results to negative results, and Dr.  
 3 Denic has given some evidence about this, and  
 4 we have some numbers. Perhaps I'll just bring  
 5 up the exhibit, just for clarity, P- 2662  
 6 please, okay, and just for the benefit of  
 7 those in the room, these are some numbers that  
 8 were brought up earlier, after the ER/PR  
 9 problem arose here, and there's a note there,  
 10 confirmed positive results, and that's  
 11 referring to ER positive results, I  
 12 understand, of 12 and there were  
 13 retroconverters of four, and those have been  
 14 explained to be ER results that converted to  
 15 zero. So there would be a total of 16  
 16 positive results that have been tested, ER  
 17 positive results tested and four of those had  
 18 converted to negative results, and perhaps to  
 19 further elaborate on that, for your benefit,  
 20 before I ask you any additional questions, I  
 21 could show you what I understand to be those,  
 22 the numbers associated with those  
 23 retroconverters, and that would be Exhibit P-  
 24 0720, please.  
 25 And this is just some data had been

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1 provided, and line 35 is what I understand to  
 2 be one of the retroconverters, and I'll just  
 3 show you a column up the top. There are the  
 4 original ER results and the original PR  
 5 results and next to that are the subsequent  
 6 results for ER and PR respectively, and line  
 7 35, the original ER was 30 and the original PR  
 8 was 40 and the subsequent ER/PR results were  
 9 zero and zero, and that was considered a  
 10 retroconverter.  
 11 DR. DABBS:  
 12 A. Now are these percent of cells, the 30 and the  
 13 40?  
 14 MS. NEWBURY:  
 15 Q. Yes, that was the percent of cells, that's my  
 16 understanding. I don't think intensity was  
 17 taken into account. Page 14, line 520,  
 18 there's actually a couple of lines for 520,  
 19 but the first one, there's a result of 40 for  
 20 ER, zero for PR, and then subsequent results  
 21 of five for ER and zero for PR.  
 22 MR. SIMMONS:  
 23 Q. That one's not on retroconverter, Ms. Newbury.  
 24 MS. NEWBURY:  
 25 Q. It's not considered a retroconverter?

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1 MR. SIMMONS:  
 2 Q. The list is at 1373.  
 3 MS. NEWBURY:  
 4 Q. Okay.  
 5 MR. SIMMONS:  
 6 Q. There's seven, narrowed down to four.  
 7 MS. NEWBURY:  
 8 Q. Perhaps we can look at that exhibit then.  
 9 There have been several lists here, so I've  
 10 had a hard time trying to figure out. I don't  
 11 believe this is the full list though, is it?  
 12 MR. SIMMONS:  
 13 Q. That's a list of seven, and the four that are  
 14 later considered retroconverters are among the  
 15 seven on this list. That's my understanding  
 16 of it.  
 17 MS. NEWBURY:  
 18 Q. Okay. Well, I'm just going to present this as  
 19 a hypothetical.  
 20 DR. DABBS:  
 21 A. Okay.  
 22 MS. NEWBURY:  
 23 Q. Okay, and I'll refer to the first two numbers  
 24 of 30, 40, 30 ER and 40 PR, and converting to  
 25 zero, zero. I'm going to go to--perhaps I can

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1 go back to Exhibit 720, please?  
 2 THE COMMISSIONER:  
 3 Q. Is the point that these illustrate the -  
 4 MS. NEWBURY:  
 5 Q. I just want to show the numbers.  
 6 THE COMMISSIONER:  
 7 Q. - do we have to go any further?  
 8 MS. NEWBURY:  
 9 Q. I just want to show the numbers and ask for  
 10 comments based on that, because the list--this  
 11 list that I have here is more comprehensive  
 12 than the subsequent list. So I'm not sure  
 13 what the -  
 14 THE COMMISSIONER:  
 15 Q. You mean you're saying more than four or are  
 16 you saying four?  
 17 MS. NEWBURY:  
 18 Q. I'm saying four.  
 19 THE COMMISSIONER:  
 20 Q. All right.  
 21 MS. NEWBURY:  
 22 Q. Based on the--I have that list that has four  
 23 of what I understood to be the  
 24 retroconverters. I don't know which is the  
 25 best list, because this one has fewer, the one

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1 that Mr. Simmons referred to, has fewer than  
 2 four, I believe.  
 3 MR. SIMMONS:  
 4 Q. No, there were seven--that list has four that  
 5 remain as retroconverters. On the seven on  
 6 that list, I can't--the redaction is there.  
 7 MS. NEWBURY:  
 8 Q. Okay.  
 9 MR. SIMMONS:  
 10 Q. (Inaudible) four.  
 11 MS. NEWBURY:  
 12 Q. I've tried to cross reference it and the  
 13 numbers don't add up to me. Anyway, perhaps  
 14 what I'll just do is give you a couple of  
 15 examples, and referring again to page 20, this  
 16 is Exhibit 0720, line 20, or sorry, line 776.  
 17 We have an ER result initially of 25 to 30 and  
 18 a PR result of 50 and next to that, we have  
 19 zero and zero are the ER/PR results  
 20 respectively, and below that, on line 778,  
 21 there is an ER result of 10 to 20 and a PR  
 22 result of 40 to 50, and then the subsequent  
 23 testing showed zero and zero. Just given  
 24 those numbers, so we'll just look at three out  
 25 of the four numbers, instead of all four, what

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1 could explain, in your view, those change in  
 2 results? What are the possibilities?  
 3 DR. DABBS:  
 4 A. So basically, we're talking about cases that  
 5 are clearly positive and become negative by  
 6 another test.  
 7 MS. NEWBURY:  
 8 Q. Yes.  
 9 DR. DABBS:  
 10 A. Well, I guess the first and foremost thing  
 11 that I would say is I would want to look at  
 12 both sets of slides and see, make sure that  
 13 what is being called positive and what is  
 14 being called negative are in fact true  
 15 positives and true negatives.  
 16 MS. NEWBURY:  
 17 Q. Okay, so interpretation issues?  
 18 DR. DABBS:  
 19 A. Interpretation would be a key item. And then  
 20 if these results hold up, then I would want to  
 21 know, the next thing I would want to know  
 22 would be what methods and what clone  
 23 antibodies are being used in each assay. I'm  
 24 assuming the second assay is being done  
 25 elsewhere, and I say that though with a word

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1 of caution because, you know, if we're going  
 2 from 30 and 40 to zero, zero, that's a big  
 3 jump, which I would not expect with any clone,  
 4 either the 1D5, 6F11 or SP1. So if something  
 5 else was used, I would need to know that. So  
 6 if one of the standard clones are used, then I  
 7 would want to know, for the second test, in my  
 8 mind becomes suspect. If in fact the first  
 9 test is a bona fide true positive, the second  
 10 test, in my mind becomes suspect. I want to  
 11 know everything about how that assay was  
 12 carried out.  
 13 MS. NEWBURY:  
 14 Q. Okay, and there has been some evidence here,  
 15 and I'm not sure now with the confusion about  
 16 what are the retroconverters, but there has  
 17 been some evidence that four retroconverters  
 18 have been reviewed by one of the physicians  
 19 and they were thought to be interpretation  
 20 issues in the sense that the staining was  
 21 background staining, rather than true staining  
 22 of the nuclei. Does that cause any less of a  
 23 concern in terms of validity of ER positive  
 24 test results to you?  
 25 DR. DABBS:

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1 A. In that regard -  
 2 MS. NEWBURY:  
 3 Q. And let's just say, if we have the numbers of  
 4 16 positive test results and four of those  
 5 being misinterpreted as positive, does that  
 6 cause any concerns?  
 7 DR. DABBS:  
 8 A. I can tell you the way I would approach that.  
 9 MS. NEWBURY:  
 10 Q. Yes.  
 11 DR. DABBS:  
 12 A. I would look at those cases specifically and  
 13 if I determined that they were not interpreted  
 14 correctly, I would want to know who the  
 15 pathologist was, and if they were four  
 16 different pathologists for four different  
 17 cases, that would be one issue. But if they  
 18 were four cases and one pathologist, that  
 19 would be a totally different realm. So then  
 20 what I would want to do probably is pull maybe  
 21 a dozen other cases that that person had  
 22 signed out and check them, and then it becomes  
 23 a personal quality assurance issue, a  
 24 professional issue with a specific  
 25 pathologist. So that's how I would go about

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1 that.

2 MS. NEWBURY:

3 Q. And what if there were four separate

4 pathologists coming up with those results?

5 DR. DABBS:

6 A. If they were four separate pathologists, then

7 what I would want to do is pull probably at

8 least a dozen cases that they had signed out

9 previous to this, these index cases, look at

10 them and see how widespread the problem was,

11 but nevertheless, at a minimum, if it turned

12 out that they had interpreted everything else

13 appropriately, they would need to be told that

14 the interpretation on these cases was

15 incorrect and they would need to generate an

16 amended report.

17 MS. NEWBURY:

18 Q. And how about if there were other known

19 concerns generally, in terms of lack of

20 optimization of any of the procedures for the

21 testing which might cause background staining

22 or cytoplasmic staining, would that cause you

23 any additional concerns, in light of possible

24 misinterpretations?

25 DR. DABBS:

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1 A. It would be. It certainly would depend highly

2 on what the sections looked like. On

3 occasion, with select antibodies, you might

4 find a cytoplasmic staining with estrogen

5 receptor. That's rare. It's a phenomenon

6 that does happen and probably is related to

7 the tumour type. There are select tumour

8 types that might do that, but other background

9 staining, that's a general term which, you

10 know, would need to be looked at critically

11 and see exactly what that was.

12 MS. NEWBURY:

13 Q. Okay. So basically, there would have to be

14 some further analysis of those particular

15 slides.

16 DR. DABBS:

17 A. Certainly.

18 MS. NEWBURY:

19 Q. Just to see what exactly is going on, what

20 else might have contributed to those positive

21 interpretations?

22 DR. DABBS:

23 A. Yes.

24 MS. NEWBURY:

25 Q. Okay. Dr. Dabbs, on this exhibit here, and I

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1 would have had this page open, there have been

2 some other results that I wonder if you can

3 comment upon. Let's start with line 767, and

4 again, the same, it's the original ER,

5 original PR, then the retesting of the ER,

6 then retesting of the PR results. Line 767

7 shows a negative ER result and a PR result of

8 40 to 50, and then upon retesting, the results

9 were zero and zero. Now these weren't

10 included in what had been called

11 retroconverters because the ER result

12 initially was negative and remained negative.

13 It was the PR result here that changed from a

14 figure of 40 to 50, and there are several

15 others, and I can just perhaps quickly refer

16 to a couple of other examples, just to give

17 you some flavour.

18 The next line is 827. There's a negative

19 result for ER, 60-70 for PR, and then zero and

20 zero, and there have been some others, and

21 I'll show you a smaller change, not as

22 significant a change, because there is a

23 variety of different types of results here.

24 So line 348, there's a negative ER result,

25 then a PR result of 20 to 30, and then on

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1 retesting, that changes to less than one for

2 ER and five for PR. Can you explain these

3 types of results?

4 DR. DABBS:

5 A. Again, part of it may be interpretation, and

6 again, part of it may be technique. If one is

7 interpreting background staining as a positive

8 staining, that becomes a significant issue,

9 and you know, looking at the results here that

10 you're showing me, they seem to be

11 significantly different between the original

12 and the retest, and so that's why I say that

13 it's either an interpretation problem or

14 technique.

15 MS. NEWBURY:

16 Q. And could the same type of factors that caused

17 these differing results from the original PR

18 test to the subsequent PR test, could those

19 types of factors be the same type of factors

20 that might influence ER results?

21 DR. DABBS:

22 A. They could be.

23 MS. NEWBURY:

24 Q. Okay. We've heard that PR tends to vary more

25 than ER.



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<p>1 DR. DABBS:</p> <p>2 A. It tends to be more heterogeneous, yes, but</p> <p>3 the same factors are in play.</p> <p>4 MS. NEWBURY:</p> <p>5 Q. Okay, and would you say that with PR results,</p> <p>6 there would be a--because of the heterogeneity</p> <p>7 of the PR, that there might be a greater</p> <p>8 swing, if you take different slices from</p> <p>9 different parts of the specimen?</p> <p>10 DR. DABBS:</p> <p>11 A. Certainly, yes.</p> <p>12 MS. NEWBURY:</p> <p>13 Q. Okay. But in light of results of this nature,</p> <p>14 what would you do if you saw this? What types</p> <p>15 of steps would you take if you saw this in</p> <p>16 your own institution?</p> <p>17 DR. DABBS:</p> <p>18 A. Well, I would want to study the slides first</p> <p>19 and make sure that the interpretations are</p> <p>20 correct. If they're incorrect, I would need</p> <p>21 to go to the pathologists who made the primary</p> <p>22 observations and point that out. I think that</p> <p>23 the issue of false positives with the</p> <p>24 background here, you know, that was pointed</p> <p>25 out, is probably the most critical aspect of</p>	<p>1 of really extreme antigen retrieval. So I</p> <p>2 have seen this on a particular case and the</p> <p>3 first time I saw it, it was pretty dramatic.</p> <p>4 It was actually on some research tissues, and</p> <p>5 it's the type of thing that when you see it,</p> <p>6 you know, you look at it and you go, well,</p> <p>7 this--it turned out that the antigen that I</p> <p>8 was looking for had no business being in the</p> <p>9 nucleus, so it was sort of an obvious tip off</p> <p>10 that there was something awry there. But for</p> <p>11 something where you're looking in the nucleus,</p> <p>12 it can become problematic, to say the least.</p> <p>13 MS. NEWBURY:</p> <p>14 Q. Okay, and how would a pathologist generally</p> <p>15 recognize this or perhaps even a technologist</p> <p>16 in the work up stage of a specimen? How would</p> <p>17 one know that over antigen retrieval is taking</p> <p>18 place or has taken place?</p> <p>19 DR. DABBS:</p> <p>20 A. Well, I think that a distinct clue would be if</p> <p>21 you're running a proper negative control in</p> <p>22 which the primary antibody is replaced with</p> <p>23 anti serum from the animal of the primary</p> <p>24 antibody you're using, because then you also</p> <p>25 are using the detection kit in there as well.</p>
<p>1 this. The other aspects are, you know, I</p> <p>2 think about the technique and I want to know</p> <p>3 what clone antibody is used and under what</p> <p>4 conditions and if the test between the first</p> <p>5 and the second are really way off and I agree</p> <p>6 with the first result, then I would be</p> <p>7 concerned about the second assay, how it was</p> <p>8 performed. So it really is a great deal of</p> <p>9 detective work.</p> <p>10 MS. NEWBURY:</p> <p>11 Q. Sure. Dr. Dabbs, you had indicated that one</p> <p>12 possible source of a false positive is over</p> <p>13 antigen retrieval with the avidin biotin or</p> <p>14 ABC method, and we've heard references here to</p> <p>15 the LSAB or labelled strept avidin biotin</p> <p>16 method. Is that in that category?</p> <p>17 DR. DABBS:</p> <p>18 A. Yes, it is. It has biotin as well, yes.</p> <p>19 MS. NEWBURY:</p> <p>20 Q. And how exactly does that antigen retrieval</p> <p>21 occur using that particular method?</p> <p>22 DR. DABBS:</p> <p>23 A. Well, there's biotin normally present to some</p> <p>24 degree in the nucleus as well, which isn't</p> <p>25 really unmasked unless you get into the realm</p>	<p>1 So if you're exposing that in the same manner</p> <p>2 with extreme antigen retrieval, you should get</p> <p>3 the same result in a negative control.</p> <p>4 MS. NEWBURY:</p> <p>5 Q. And in the event that a negative control has</p> <p>6 not been used, is there anything about the</p> <p>7 appearance of the slide that could tip you off</p> <p>8 that this has taken place?</p> <p>9 DR. DABBS:</p> <p>10 A. It would be extremely difficult to unravel</p> <p>11 that and discover that.</p> <p>12 MS. NEWBURY:</p> <p>13 Q. So then the--I take it the primary quality</p> <p>14 control method of avoiding this or ensuring</p> <p>15 that it hasn't taken place, would be the use</p> <p>16 of negative controls?</p> <p>17 DR. DABBS:</p> <p>18 A. Yes.</p> <p>19 MS. NEWBURY:</p> <p>20 Q. And, presumably, having your proper standard</p> <p>21 operating procedures to make sure that the</p> <p>22 antigen retrieval was done properly to begin</p> <p>23 with that it was established up--set up as a</p> <p>24 proper test, is that correct?</p> <p>25 DR. DABBS:</p>

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1 A. That's correct.

2 MS.NEWBURY:

3 Q. Okay, and are there any quality control

4 programs, random sampling, that you would

5 recommend to avoid these--any of these types

6 of problems of false positives, whether it's

7 through interpretation issues or through over

8 antigen retrieval?

9 DR. DABBS:

10 A. Well, I think in terms of the protocols, once

11 standardized protocols are adopted, it's going

12 to be very difficult to get into extreme

13 situations like that with antigen retrieval

14 false positives. Some detection systems are

15 now moving away from biotin altogether and are

16 going into polymers which are more sensitive

17 and cannot possibly give that sort of

18 artifact. On the other hand, interpretation-

19 wise, it's important for colleagues to show

20 each other cases. For example, if there needs

21 to be some remediation of a particular

22 pathologist, say, in interpreting ER or PR, I

23 would want to have them see the cases, fill

24 out their worksheet as to what their result

25 it, and then, you know, I would be the

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1 secondary reviewer as chief of the service to

2 show that, yes, you know, you got the next 50

3 correct and you're on your own again, you

4 know. That's basically how it would work in-

5 house.

6 MS.NEWBURY:

7 Q. Thank you, Dr. Dabbs, those are all the

8 questions I have.

9 THE COMMISSIONER:

10 Q. Mr. Crosbie.

11 DR. DAVID DABBS, EXAMINATION BY CHESLEY CROSBIE, Q.C.

12 CROSBIE, Q.C.:

13 Q. Good day, Dr. Dabbs, I introduced myself on

14 one of the breaks, Ches Crosbie. I represent

15 the members of the Breast Cancer Testing Class

16 Action. Can I bring you back to the issue of

17 the therapeutic uses of ER/PR testing, I

18 understand in certain gynecological cases, and

19 in cases of cancers of unknown primary origin,

20 unknown primary, could you say a few words as

21 to how--you seem to be of the opinion that

22 there should be some review done of those

23 cases, given that the haven't been retested

24 for ER/PR, is that correct?

25 DR. DABBS:

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1 A. Regarding the issue of using ER and PR in

2 gynecologic cancers, I know institutions vary,

3 and these requests come specifically as

4 prescriptions written by gynecologic

5 oncologists to perform hormonal receptor

6 testing on a subset of tumours. Most of the

7 time, in my experience, these have been

8 endometrial cancers or certain kinds of

9 ovarian cancers, and these requests are

10 relatively rare also in my experience. So it

11 really is on a case by case basis. In other

12 words, what I'm saying is if there are

13 clinicians at the hospital who in a fairly

14 routinely fashion say that I want to have ER

15 done on my patient with endometrial cancer,

16 then you would have to see how many of those

17 kinds of cases there are. I think you could

18 probably find that out by canvassing the

19 oncologists to see if they, in fact, request

20 those tests.

21 CROSBIE, Q.C.:

22 Q. These would be the gyne oncologists?

23 DR. DABBS:

24 A. Yes, correct. Regarding tumours or unknown

25 primary, as I mentioned before, it may be

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1 useful to have a look, but the only way that

2 one would be able to tell for certain is to

3 look at the individual cases and see what the

4 workup subsequently showed because it's not

5 about just one antibody, the ER, but there are

6 other antibodies that are part of that entire

7 puzzle of trying to discern what--the tumours

8 origin, and only in that context can one

9 determine specifically by looking at the

10 entire case and say, you know what, on this

11 one we--you know, the ER was negative, maybe

12 we should repeat it. That's--it's a

13 contextual issue for tumours of unknown

14 origin.

15 CROSBIE, Q.C.:

16 Q. So would you expect ordinarily to undertake

17 the inquiry to the extent that inquiry is

18 needed, for example, vis a vis the gyne

19 oncologist, somebody would have to canvass

20 them, would they?

21 DR. DABBS:

22 A. I think so, and perhaps the chief of the

23 service, either the gyne service, or the chief

24 of pathology, might have some number to think

25 of in terms of how frequent this is an issue,

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<p>1 going forward and looking at the cases.</p> <p>2 CROSBIE, Q.C.:</p> <p>3 Q. I'm not getting the sense the numbers would be</p> <p>4 high then in your --</p> <p>5 DR. DABBS:</p> <p>6 A. Probably not, probably not, at least --</p> <p>7 CROSBIE, Q.C.:</p> <p>8 Q. Guesstimate, yeah.</p> <p>9 CROSBIE, Q.C.:</p> <p>10 Q. Right. I think they would be low in general</p> <p>11 for both groups.</p> <p>12 CROSBIE, Q.C.:</p> <p>13 Q. Thank you. Can I just--this was touched on,</p> <p>14 and perhaps it wasn't left in any doubt, but I</p> <p>15 just want to come back to it, that's the</p> <p>16 question of the value of the negative control.</p> <p>17 If I understand this correctly, this is a</p> <p>18 piece of patient tissue which is set with your</p> <p>19 array on the same slide, but you don't add</p> <p>20 antibody to this piece of tissue, is that the</p> <p>21 idea?</p> <p>22 DR. DABBS:</p> <p>23 A. Well, typically the negative control is a</p> <p>24 separate slide that has the patient tissue on</p> <p>25 it, and applied to it is everything except the</p>	<p>1 Q. Could you--not that I want to tarry on this,</p> <p>2 but could you say a brief word about how</p> <p>3 clinical outcome validation is done? I'm</p> <p>4 guessing that this relies on feedback from the</p> <p>5 oncologists about the patient's history as</p> <p>6 time goes on.</p> <p>7 DR. DABBS:</p> <p>8 A. The clinical validation?</p> <p>9 CROSBIE, Q.C.:</p> <p>10 Q. Yes.</p> <p>11 DR. DABBS:</p> <p>12 A. Yes, well, that would be a significant</p> <p>13 undertaking, and I think that it would involve</p> <p>14 an actual institutional review board process</p> <p>15 whereby you're following a group of patients</p> <p>16 clinically. You obviously would have to have</p> <p>17 clinicians given their input onto standardized</p> <p>18 forms of what's considered to be response</p> <p>19 parameters for the drug in question, and</p> <p>20 follow them over a select period of time, and</p> <p>21 then using that information with your scores</p> <p>22 and our cutoffs, and giving that to an</p> <p>23 appropriate person who is extremely well</p> <p>24 versed in clinical statistics, to be able to</p> <p>25 make meaning out of it and using regression</p>
<p style="text-align: right;">Page 233</p> <p>1 primary antibody. The substitute for the</p> <p>2 primary antibody typically would be serum from</p> <p>3 the animal of the primary antibody type. For</p> <p>4 example, if the primary antibody type is an</p> <p>5 anti-rabbit, then you would want to use a</p> <p>6 rabbit anti-serum, just plain rabbit anti-</p> <p>7 serum in place of the primary antibody on that</p> <p>8 tissue, and then you apply all of the other</p> <p>9 steps and develop it as though you were</p> <p>10 developing the test. Everything on that slide</p> <p>11 should be clean negative.</p> <p>12 CROSBIE, Q.C.:</p> <p>13 Q. No staining?</p> <p>14 DR. DABBS:</p> <p>15 A. No staining whatsoever, correct.</p> <p>16 CROSBIE, Q.C.:</p> <p>17 Q. Would you say that it's mandatory to use a</p> <p>18 negative control?</p> <p>19 DR. DABBS:</p> <p>20 A. Yes.</p> <p>21 CROSBIE, Q.C.:</p> <p>22 Q. Would it have been so in 1997?</p> <p>23 DR. DABBS:</p> <p>24 A. Yes, it should have been.</p> <p>25 CROSBIE, Q.C.:</p>	<p style="text-align: right;">Page 235</p> <p>1 analysis, finding where the best cut points</p> <p>2 are for positive/negative for that using that</p> <p>3 assay with that particular clinical group. So</p> <p>4 it is not an easy undertaking.</p> <p>5 CROSBIE, Q.C.:</p> <p>6 Q. Sounds like a considerable organizational</p> <p>7 effort?</p> <p>8 DR. DABBS:</p> <p>9 A. It does and it costs money.</p> <p>10 CROSBIE, Q.C.:</p> <p>11 Q. Briefly, is your dedicated quality assurance</p> <p>12 person also tasked with liaising with any</p> <p>13 insurer?</p> <p>14 DR. DABBS:</p> <p>15 A. The person who does quality assurance for our</p> <p>16 laboratory does not have any external contacts</p> <p>17 with insurers. That person monitors</p> <p>18 designated parameters that we sit down at our</p> <p>19 monthly meeting and go over as an entire</p> <p>20 group. We have myself--I'm there, our</p> <p>21 laboratory administrator, and all the managers</p> <p>22 of the subsections of the laboratories, and</p> <p>23 our co-directors of surgical pathology are</p> <p>24 there. We go over all of these parameters and</p> <p>25 discuss them. The other duty of this person</p>

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1 is to do tasks basically as I assign them. So  
 2 if I want to look at a particular quality  
 3 issue, then I say I want to do a probe looking  
 4 at, you know, these parameters for this  
 5 particular group of patients, and I want it to  
 6 run for the next month. Then she'll collect  
 7 that data and sort it and present it to me as  
 8 I request. There are ongoing issues that she  
 9 does. For example, the metrics that I  
 10 mentioned, she'll send those to me on a  
 11 quarterly basis as Excel sheets, so that I  
 12 have those to review. So this is all  
 13 documented. It's part and parcel of quality  
 14 control quality assurance throughout the  
 15 laboratory.  
 16 CROSBIE, Q.C.:  
 17 Q. Thank you. Do you have any familiarity with  
 18 the Mount Sinai lab?  
 19 DR. DABBS:  
 20 A. I personally do not.  
 21 CROSBIE, Q.C.:  
 22 Q. So you know it by reputation, for example?  
 23 DR. DABBS:  
 24 A. I know it to some degree, yes.  
 25 CROSBIE, Q.C.:

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1 Q. Does it have a good reputation?  
 2 DR. DABBS:  
 3 A. Yes, it does.  
 4 CROSBIE, Q.C.:  
 5 Q. This, of course, as you may be aware, has been  
 6 called the reference lab for the lab here in  
 7 St. John's. I've been over this with a  
 8 previous witness who was the former CEO of  
 9 Eastern Health, and just to be sure we're on  
 10 common ground in understanding some of the  
 11 features of the institution in which our lab  
 12 is embedded, Mount Sinai, for example, is  
 13 affiliated with the University of Toronto and  
 14 our lab here is affiliated with Memorial  
 15 University. It has--it's in a hospital  
 16 complex with a 337 bed acute care hospital, it  
 17 has a 78 bed children's hospital, there's a  
 18 medical school, as I may have mentioned, with  
 19 52 placements each year, and there's also a  
 20 residency program in pathology and other  
 21 specialties, and in 2005, for example, there  
 22 were 204 residents in the various specialties.  
 23 There's a nursing school, a pharmacy school,  
 24 and a cancer treatment centre which is  
 25 attached to the main hospital. It's all part

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1 of what's characterized as the Health Sciences  
 2 Complex. I wonder if I could ask the  
 3 Registrar to bring up Document P-00278.  
 4 REGISTRAR:  
 5 Q. What was that number again, Mr. Crosbie?  
 6 CROSBIE, Q.C.:  
 7 Q. 278. This, as you can see, is authored by a  
 8 pathologist, Dr. Maung, January of 2007,  
 9 pathology workload review for this province.  
 10 I'd ask the Registrar to take us to page 9,  
 11 please. Perhaps a little further down the  
 12 page. I guess I can adjust that myself. Yes,  
 13 in the paragraph that starts "For St. John's  
 14 laboratory, which is", you will see, "It also  
 15 serves the province as the tertiary esoteric  
 16 referral and academic centre with  
 17 undergraduate and graduate training programs  
 18 and time allocated to research activities".  
 19 That's Dr. Maung's choice of description, I  
 20 guess, for the pathology laboratory here in  
 21 St. John's. Can we now go to Document 121,  
 22 please, and this, sir, as you can see is  
 23 "Review of Immunohistochemistry lab", and it  
 24 was prepared for the Vice-President of the  
 25 hospital, and if you could move down, the

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1 authors were Mr. Gulliver, Program Director,  
 2 and Dr. Cook, Clinical Chief, Laboratory  
 3 Medicine, October, 2005, and in essence, it's  
 4 a proposal for establishing the  
 5 immunohistochemical laboratory processes on a  
 6 sound footing." And then if we could go to  
 7 page 2 of that, please? Item 1.2 is entitled,  
 8 "Objective" and says, "The objective of this  
 9 proposal is to identify the requirements  
 10 needed to implement a complete quality  
 11 assurance program for immunohistochemistry  
 12 lab, ensuring that we provide a standardized  
 13 and reliable service equivalent to the Mount  
 14 Sinai reference lab in Toronto." Thank you  
 15 for bearing with me on all of that because  
 16 what I'm coming around to is from what you  
 17 know about our lab here in St. John's and  
 18 given the background information that I've  
 19 given you, as well, is this objective  
 20 achievable for our lab?  
 21 THE COMMISSIONER:  
 22 Q. Mr. Crosbie, perhaps we first ask the witness  
 23 whether or not he feels he's in a position to  
 24 answer that question.  
 25 CROSBIE, Q.C.:

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1 Q. Of course.

2 DR. DABBS:

3 A. So they're saying here that the objective of

4 the proposal was to identify the requirements

5 needed to implement, yeah. I think that, you

6 know, is I have to read this in the context of

7 the entire document, and I think that it's a

8 laudable goal, that is, you know, at the

9 outset of this document, but I think that's

10 about all I can say for it.

11 CROSBIE, Q.C.:

12 Q. You're not in a position to say whether you

13 feel it's achievable?

14 DR. DABBS:

15 A. Well -

16 CROSBIE, Q.C.:

17 Q. You'd have to read the document, is what

18 you're saying?

19 DR. DABBS:

20 A. Yeah. I think that whether it's achievable, I

21 would have to know everything about--let me

22 put it in context. If I was to make an

23 objective for a similar process in my

24 institution, I would have to have a read on

25 the need in the institution, the willingness

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1 of administration to go through with it, the

2 funds that are available, which I don't have

3 for, you know, the laboratory here. But I

4 think that it's clearly the proper thing to

5 do.

6 CROSBIE, Q.C.:

7 Q. I'd like to go over with you now some of the

8 points, it's about 13 that I drew from your

9 evidence to the Commission, and you can tell

10 me whether I've got this more or less right or

11 not. The first one, I wrote these out last

12 night, so the first one I have here is that in

13 your view adoption of the 30 percent cutoff in

14 1997 was ill advised and not reasonable. Is

15 that correct or incorrect?

16 DR. DABBS:

17 A. I think based on the information that I have

18 that that antibody that was published in that

19 paper was actually not in use here. If I'm

20 correct in that, then the answer to your

21 question would be correct, I would agree with

22 it.

23 CROSBIE, Q.C.:

24 Q. And it seems that in 1997 the adoption of the

25 IHC technique was probably not appropriately

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1 validated, is that correct?

2 DR. DABBS:

3 A. In 1997?

4 CROSBIE, Q.C.:

5 Q. Yes. Or, well, the document you specifically

6 looked at, I think, was from 1998, but in that

7 time period.

8 DR. DABBS:

9 A. As far as you're referring to the document by

10 Dr. Khalifa?

11 CROSBIE, Q.C.:

12 Q. I am, yes.

13 DR. DABBS:

14 A. Yes, I agree with that.

15 CROSBIE, Q.C.:

16 Q. I believe you told us that IHC is now

17 considered to be a component of general

18 pathological or pathology practice, is that

19 correct?

20 DR. DABBS:

21 A. Correct.

22 CROSBIE, Q.C.:

23 Q. It's part of your standard armamentarium?

24 DR. DABBS:

25 A. Yes.

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1 CROSBIE, Q.C.:

2 Q. And has been so since 1997 or even before

3 that?

4 DR. DABBS:

5 A. Before that, yes.

6 CROSBIE, Q.C.:

7 Q. And then you characterized one of the

8 practices of Eastern Health, in particular,

9 the absence of an SOP as a recipe for

10 disaster?

11 DR. DABBS:

12 A. Yes.

13 CROSBIE, Q.C.:

14 Q. You don't care to qualify that, you stand by

15 that statement?

16 DR. DABBS:

17 A. Well, I think that every laboratory technique

18 and test has to have a written operating

19 procedure so that people who are at least, on

20 the least going to be trained in that

21 particular testing procedure have something to

22 read and understand and go by and have as a

23 reference should it be needed for purposes of

24 optimizing testing procedure.

25 CROSBIE, Q.C.:

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1 Q. Mr. Coffey identified to you three cases which  
 2 dated from a period prior to the, what the  
 3 institution identified as the index case,  
 4 which we know as the Deane case, which in your  
 5 opinion should provoked the pathologists or at  
 6 least pathology staff to conduct an  
 7 investigation, is that correct?  
 8 DR. DABBS:  
 9 A. I believe that's correct.  
 10 CROSBIE, Q.C.:  
 11 Q. The reason I say pathologists is because in  
 12 the index case that the institution identified  
 13 here, it appeared to be driven by the  
 14 oncologist inquiring into the change in  
 15 results rather than by any pathologist. But  
 16 you would expect the pathologists themselves  
 17 to undertake an investigation if they realized  
 18 there was a dramatic change in result?  
 19 DR. DABBS:  
 20 A. Yes.  
 21 CROSBIE, Q.C.:  
 22 Q. I also understood that you were of the view  
 23 that Dr. Ejeckam's analysis, when we looked at  
 24 those memoranda of Dr. Ejeckam from 2003, his  
 25 analysis of the problem in the lab failed to

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1 recognize the extent of what you characterized  
 2 as a global problem?  
 3 DR. DABBS:  
 4 A. Are you referring to the visit that Dr.  
 5 Ejeckam or the--oh, I'm sorry. Yes, I agree,  
 6 right, I agree.  
 7 CROSBIE, Q.C.:  
 8 Q. And that you felt that, in fact, what should  
 9 have been done, Dr. Ejeckam, you may recall,  
 10 actually closed the lab for some improvements  
 11 for a period of five weeks or so. But you  
 12 felt that they should have called for help  
 13 from outside?  
 14 DR. DABBS:  
 15 A. Well, I don't know if they would have called  
 16 or if it was mandatory to do that. I think  
 17 that that was certainly a viable option that  
 18 would have been available to them, yes.  
 19 CROSBIE, Q.C.:  
 20 Q. I also took it from your evidence that IHC  
 21 testing for DCIS is an unsettled area with no  
 22 consensus as to best practice?  
 23 DR. DABBS:  
 24 A. I think that there is some variation even in  
 25 the States on this issue. You will find areas

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1 where they don't do that testing, you will  
 2 find areas where areas where they do do the  
 3 testing. And it's not that one group is wrong  
 4 and one group is right. I think that this is  
 5 the type of evolving area that only outcome  
 6 studies will give us information. I'm not  
 7 aware of anything published yet in terms of  
 8 ER/PR testing for DCIS associated with  
 9 outcomes in patients with, you know, the risk  
 10 reducing endocrine therapy and whether that  
 11 has any impact on development of new tumours  
 12 or new invasive tumours, that literature does  
 13 not yet exist.  
 14 CROSBIE, Q.C.:  
 15 Q. If this is beyond your scope of expertise,  
 16 please say so.  
 17 DR. DABBS:  
 18 A. Sure.  
 19 CROSBIE, Q.C.:  
 20 Q. But my question was going to be is the option  
 21 of testing for DCIS, hormone receptor testing,  
 22 something which clinicians ought to discuss  
 23 with the patient? And it may be that you  
 24 don't have an opinion on that.  
 25 DR. DABBS:

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1 A. Yeah. I don't have an opinion on that  
 2 particular interaction between the oncologist  
 3 and patient. But there seems to be, at least  
 4 in part, a scientific basis for wanting to do  
 5 testing along those lines in order to  
 6 determine if the patients are going to get  
 7 endocrine therapy, because the endocrine  
 8 therapy is not without risk itself.  
 9 CROSBIE, Q.C.:  
 10 Q. I took it that the lab here would have been  
 11 closed down if inspected during the subject  
 12 period, 1997 to 2005 to standards prevailing  
 13 in the United States. Is that a correct  
 14 understanding?  
 15 DR. DABBS:  
 16 A. I think that's a correct statement.  
 17 CROSBIE, Q.C.:  
 18 Q. And when asked about acceptable error rate,  
 19 your reply was that the lab, your lab is  
 20 dissatisfied with anything two percent greater  
 21 of tests which have to be repeated and then  
 22 you investigate the problem?  
 23 DR. DABBS:  
 24 A. Well, just to clarify that, the two percent  
 25 cutoff is for just repeats in

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<p>1 immunohistochemistry. This would be a result 2 of tissues that need to be reprocessed or 3 stains that come back and there's a part of 4 the tissue that is not there. Usually these 5 relate to tissue processing issues and not to 6 false negatives or false positives. That goes 7 into a whole new realm. That, whenever--you 8 know, if I were to see that, that becomes an 9 issue, a sentinel event where that needs to be 10 thoroughly investigated between myself, 11 laboratory administrator, technicians involved 12 and so forth. So that two percent really 13 relates to daily workings of the process, 14 tissue processing, labelling issues, things of 15 that nature, things that don't raise a red 16 flag and are a cause for a sentinel event. 17 This is just sort of standard operating 18 procedures. There's a known recognized repeat 19 rate, if you will, on immunostaining, there 20 may be something wrong with the immunostainer, 21 it may give an error rate, it may not dispense 22 an antibody, it all depends on, you know, a 23 bunch of those factors. But that two percent 24 does not include any serious event, if you 25 will. That's the kind of language we use in</p>	<p>1 to look at the testing, the fixation and how 2 the specimen was handled and how the specimen, 3 in fact, was interpreted. 4 CROSBIE, Q.C.: 5 Q. And I got an overall sense of validation as 6 something that should be done in house, as it 7 were? 8 DR. DABBS: 9 A. Correct. 10 CROSBIE, Q.C.: 11 Q. And I think you said that variability for this 12 particular test should be no greater than for 13 any other path lab procedure? 14 DR. DABBS: 15 A. The variability in ER testing? 16 CROSBIE, Q.C.: 17 Q. Um-hm. 18 DR. DABBS: 19 A. Correct. 20 CROSBIE, Q.C.: 21 Q. Is it mandatory for a lab to have QA when 22 undertaking this kind of testing? 23 DR. DABBS: 24 A. Yes, it is. 25 CROSBIE, Q.C.:</p>
<p style="text-align: right;">Page 249</p> <p>1 the States, there are serious events, sentinel 2 events are sort of analogous, that's a totally 3 separate issue. 4 CROSBIE, Q.C.: 5 Q. And that information about repeat rate would 6 be given you in your metrics on a quarterly 7 basis? 8 DR. DABBS: 9 A. The repeat rate is seen by us on a monthly 10 basis. 11 CROSBIE, Q.C.: 12 Q. Did you characterize the test failures here in 13 your view as being largely technique failures? 14 DR. DABBS: 15 A. To the best of my knowledge, yes. 16 CROSBIE, Q.C.: 17 Q. You stated, as well, that a negative invasive 18 lobular would provoke deep concern in your 19 institution? 20 DR. DABBS: 21 A. That's correct. And that's the type of event 22 that I would consider to be a serious or 23 sentinel event, something that needs to be 24 thoroughly investigated because of the rarity 25 of that result. It would be cause for concern</p>	<p style="text-align: right;">Page 251</p> <p>1 Q. Would that be true in 1997? 2 DR. DABBS: 3 A. Yes, it would. 4 CROSBIE, Q.C.: 5 Q. Is constant optimization mandatory? 6 DR. DABBS: 7 A. Yes, it is. 8 CROSBIE, Q.C.: 9 Q. That's all I have for you, Doctor. Thank you 10 for coming such a long distance. 11 THE COMMISSIONER: 12 Q. Thank you, Mr. Crosbie. 13 CROSBIE, Q.C.: 14 Q. I appreciate it. 15 THE COMMISSIONER: 16 Q. Do you have anything arising, Mr. Coffey? 17 COFFEY, Q.C.: 18 Q. No, Commissioner, I do not. 19 THE COMMISSIONER: 20 Q. Mr. Coffey, I have been provided with a copy 21 of a document which I assume, Mr. Browne, is 22 the one that you referred to earlier? 23 MR. BROWNE: 24 Q. Correct, yes. 25 COFFEY, Q.C.:</p>

1 Q. That's Exhibit P-2617.  
 2 THE COMMISSIONER:  
 3 Q. And you want that entered so I will have the  
 4 complete picture, do you? You say yes, Mr.  
 5 Coffey?  
 6 COFFEY, Q.C.:  
 7 Q. Oh, yes, please. Oh, I apologize,  
 8 Commissioner. I thought you were just going  
 9 to go right ahead and do it. The Layfield,  
 10 that's what you're talking about? Yes,  
 11 please, Commissioner.  
 12 THE COMMISSIONER:  
 13 Q. All right, thank you. That is now entered.  
 14 EXHIBIT ENTERED AND MARKED P-2617.  
 15 THE COMMISSIONER:  
 16 Q. Okay, that just leaves me to thank you very  
 17 much, Dr. Dabbs, for, as Mr. Crosbie would put  
 18 it, coming all this way and for what has been  
 19 for me a very interesting two days. I very  
 20 much appreciate your contribution.  
 21 DR. DABBS:  
 22 A. My privilege.  
 23 THE COMMISSIONER:  
 24 Q. Thank you. Well, we'll break and then proceed  
 25 with the next witness.

1 I'm back in August here, but there are a  
 2 couple of points that I just wanted to raise.  
 3 This is a note of Dr. Williams dated August  
 4 the 8th, 2005.  
 5 DR. LAING:  
 6 A. Um-hm.  
 7 CHAYTOR, Q.C.:  
 8 Q. And the meeting is Dr. Cook, Williams and Dr.  
 9 Gulliver--or, sorry, Mr. Gulliver. And it  
 10 says "Note 16," no date. So I take it it's  
 11 sometime shortly after that because then the  
 12 next one in the series is still in August.  
 13 DR. LAING:  
 14 A. Um-hm.  
 15 CHAYTOR, Q.C.:  
 16 Q. So sometime around August 8th, apparently. He  
 17 says, "Dr. Cook and myself talked with Dr.  
 18 Laing. Prior to 2000 ER/PR negative  
 19 postmenopausal women got Tamoxifen anyway.  
 20 This practice changed in 2002. Of women who  
 21 test positive, most are ER positive and PR  
 22 positive, less are ER positive and PR  
 23 positive, five to ten percent are ER negative,  
 24 plus PR positive. It was felt this number is  
 25 now less than five to ten percent." So I just

1 (RECESS)  
 2 THE COMMISSIONER:  
 3 Q. Please be seated. Ms. Chaytor.  
 4 CHAYTOR, Q.C.:  
 5 Q. Thank you, Commissioner. We have a number of  
 6 new exhibits this afternoon.  
 7 THE COMMISSIONER:  
 8 Q. Okay.  
 9 CHAYTOR, Q.C.:  
 10 Q. It's P-2618, 2631, 2632, 2633 and 2634,  
 11 please?  
 12 THE COMMISSIONER:  
 13 Q. Entered.  
 14 EXHIBIT ENTERED AND MARKED P-2618.  
 15 EXHIBITS ENTERED AND MARKED P-2631 THROUGH 2634,  
 16 INCLUSIVE.  
 17 CHAYTOR, Q.C.:  
 18 Q. Thank you.  
 19 DR. KARA LAING, EXAMINATION BY SANDRA CHAYTOR, Q.C.  
 20 (CONTINUED)  
 21 CHAYTOR, Q.C.:  
 22 Q. Registrar, could we have, please, P-0557?  
 23 And, Doctor, I realize last day when we met,  
 24 we were up to the disclosure of October, 2001,  
 25 but there's just--so don't be too concerned if

1 wanted to ask you your recollections around  
 2 this period of time or any other time with Dr.  
 3 Cook and Dr. Williams around the issue of  
 4 cutoffs and issues, basically, of what was  
 5 used at different periods of time for  
 6 treatment of women with anti-hormonal  
 7 treatment.  
 8 DR. LAING:  
 9 A. Sure. Well, first of all, the first bullet  
 10 I'm not sure, I have no idea what that means.  
 11 That would not have been something that I  
 12 would have said. There was a time prior to my  
 13 practice and certainly not ever when I was a  
 14 resident or in my practice a European practice  
 15 in some countries that they would just simply  
 16 would not test ER/PR receptors at all and that  
 17 post-menopausal women would have been treated  
 18 with Tamoxifen and not even considered for  
 19 chemotherapy. But this certainly wouldn't  
 20 have been, it wouldn't have been prior to  
 21 2000, this would have been even long before  
 22 that. And certainly, as I said, my only  
 23 experience as both as a resident and fellow  
 24 and in practice would be treating patients who  
 25 did have testing done. So I'm not certain



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1 where that comment--I'm not sure why he's  
 2 written that there like that.  
 3 CHAYTOR, Q.C.:  
 4 Q. So those dates would be incorrect?  
 5 DR. LAING:  
 6 A. That's right.  
 7 CHAYTOR, Q.C.:  
 8 Q. And in terms of it being long before even  
 9 2000, would it have been before 1997?  
 10 DR. LAING:  
 11 A. Oh, yes.  
 12 CHAYTOR, Q.C.:  
 13 Q. Okay.  
 14 DR. LAING:  
 15 A. Yes, yeah.  
 16 CHAYTOR, Q.C.:  
 17 Q. So not at all within--this would not have been  
 18 the practice at any point during the time  
 19 period that's under consideration?  
 20 DR. LAING:  
 21 A. No, no, no. I mean, I started as an oncology  
 22 resident in 1996 and certainly at that time  
 23 Canadian practice was standard to measure  
 24 ER/PR on breast tissue. Of the women who test  
 25 positive, most are ER positive, and I think

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1 you know, that's a correct statement. And  
 2 we've talked about the number of 75 being a  
 3 number overall. We've talked about of those  
 4 people, you know, 75 percent of those would be  
 5 positive for both and then a smaller number ER  
 6 positive, PR negative and then a much smaller  
 7 number would be ER negative, PR positive  
 8 group. And as I said, you know, this being  
 9 around ten percent, noted to be five to ten  
 10 percent here we, again, discussed the fact  
 11 that, you know, upon review and when we sat  
 12 down and actually looked at this all together  
 13 in the tumour panel, we noticed that there was  
 14 certainly a number of patients who fit into  
 15 that category of being ER negative and PR  
 16 positive.  
 17 CHAYTOR, Q.C.:  
 18 Q. Okay, and in 2005 would you have thought it  
 19 was as much as five to ten percent of tumours  
 20 being ER negative and PR positive?  
 21 DR. LAING:  
 22 A. Around that, around that number, for sure.  
 23 And -  
 24 CHAYTOR, Q.C.:  
 25 Q. And you indicate that it's now felt to be

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1 lower than that?  
 2 DR. LAING:  
 3 A. It's now felt to be lower than that. I didn't  
 4 listen to all of Dr. Dabbs' testimony, but I  
 5 did catch a little bit of it and he was even  
 6 raising this issue of the fact that now that  
 7 number is felt to be even smaller and smaller.  
 8 He used two to eight percent. I mentioned  
 9 that when we've looked back at some of the  
 10 large adjuvant hormonal trials and looked at  
 11 the number of patients who were ER negative,  
 12 PR positive on those studies it had been in  
 13 the order of, you know, three to five percent.  
 14 And in things that I've read recently in the  
 15 past year or so related to this issue some  
 16 pathologists have argued that you don't--you  
 17 shouldn't have expression of your progesterone  
 18 receptor unless you have expression of your  
 19 estrogen receptor. So I think we're seeing  
 20 that group getting to be a smaller subset of  
 21 the patients that we see.  
 22 CHAYTOR, Q.C.:  
 23 Q. Now, did you also--do you also recall that you  
 24 discussed with Dr. Cook and/or Dr. Williams  
 25 the issue of the cutoffs at different points

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1 in time and -  
 2 DR. LAING:  
 3 A. Yes.  
 4 CHAYTOR, Q.C.:  
 5 Q. Yes, okay. And did that all take place in the  
 6 same discussion, sometime in August of 2005 or  
 7 was that a separate discussion?  
 8 DR. LAING:  
 9 A. Oh, it would have been around that time. But  
 10 I could only go by, since I don't have any  
 11 notes myself from that time period, but  
 12 certainly we did discuss what the cutoffs had  
 13 been. And I had mentioned to you already  
 14 about the San Antonio meeting in late 2000 and  
 15 then a change into 2001 as to when ten percent  
 16 was being used more and more as the cutoff for  
 17 determining whether or not hormonal therapy  
 18 would be offered to patients.  
 19 CHAYTOR, Q.C.:  
 20 Q. Doctor, in talking to Dr. Williams and Dr.  
 21 Cook about using anti-hormonal treatment, did  
 22 you tell them that decisions are made not only  
 23 on the basis of a cutoff but also could be  
 24 influenced by how close the patient is to the  
 25 cutoff, for example, if you had a patient who

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1 was 15 percent, was that discussed?  
 2 DR. LAING:  
 3 A. No. I think we would have discussed that, you  
 4 know, there would be many factors that would  
 5 influence the decision as to whether or not a  
 6 patient would be offered hormonal therapy, and  
 7 certainly one of those, obviously, would be  
 8 what their report was. And you know, we did  
 9 have discussions about that people were  
 10 looking at level of expression and, in fact,  
 11 we had some early discussions, as you can see  
 12 from Dr. Williams' notes that we've looked at  
 13 already, about the importance of whether  
 14 people were ER positive and PR negative could  
 15 that potentially influence how they would  
 16 respond to treatment, not that--but not  
 17 something that we would use to make a  
 18 definitive decision about how to treat them.  
 19 And this came out of the idea that patients  
 20 that were ER positive and PR negative may  
 21 benefit better from Aromatase inhibitors. But  
 22 that was only one subset analysis of a trial  
 23 and that has not been substantiated in further  
 24 retrospective reviews of these studies.  
 25 CHAYTOR, Q.C.:

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1 Q. So would they have understood, for example, if  
 2 you had--and I believe the word that may have  
 3 been used in the progress notes that we looked  
 4 at last day, that's in reference to Ms.  
 5 Coffin, was a borderline case. So in talking  
 6 to Dr. Williams and Dr. Cook would they have  
 7 understood that in borderline cases somebody  
 8 who, you know, came in above the ten percent  
 9 but above that cutoff, that they also at the  
 10 time, based on them being only 15 percent, 16  
 11 percent, 20 percent, if it was considered a  
 12 borderline case, that would have gone into  
 13 your, influenced your decision as to whether  
 14 or not this patient should be offered  
 15 Tamoxifen, so that back in 2002, for example,  
 16 if the person was coming across as a weak  
 17 positive, you know, close to--above ten  
 18 percent cutoff, but still not much above, a  
 19 borderline case, that that person, that would  
 20 have affected or influenced your thinking as  
 21 to whether or not, along with the other  
 22 factors in the case, whether the person should  
 23 be offered anti-hormonal treatment. Did you  
 24 have that kind of a discussion with Doctors  
 25 Cook and Williams?

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1 DR. LAING:  
 2 A. Not that I remember to that degree of detail.  
 3 However, I think it's important to stress that  
 4 it's not necessarily--and, you know, you've  
 5 brought me back to that case. It wasn't the  
 6 level that ultimately plays the biggest  
 7 decision in whether or not somebody is going  
 8 to take a hormone. It's, you know, what the  
 9 risk/benefit is going to be. And the thing  
 10 with using what the level is, so to look and  
 11 say, well, you know, is it different if it's  
 12 50 percent or different if it's 95 or 100  
 13 percent is that you have to be certain that,  
 14 you know, that that level is as accurate as it  
 15 can be. And so, you know, it's something that  
 16 we think about but not something that, you  
 17 know, is as much of a factor as whether they  
 18 make the cutoff to be positive or negative.  
 19 CHAYTOR, Q.C.:  
 20 Q. Yes, and I just used that as a particular  
 21 example.  
 22 DR. LAING:  
 23 A. Sure.  
 24 CHAYTOR, Q.C.:  
 25 Q. But -

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1 DR. LAING:  
 2 A. I mean, even today in the clinic, if I'm  
 3 deciding to treat somebody who's, you know,  
 4 might come back as 15 percent ER positive and  
 5 ten percent PR, then, you know, I'm going to  
 6 offer that person hormonal therapy. If they  
 7 have an absolute contraindication, I'm not  
 8 going to give it to them. If their relative  
 9 benefit is very small, maybe only an absolute  
 10 benefit in terms of one or two percent, I'm  
 11 likely not going to give it to them. But my  
 12 thinking of that person is not going to be  
 13 hugely different than the person who's sitting  
 14 in front of me with something that's 95  
 15 percent and 95 percent, because although we  
 16 look at it in a prospective, we're looking at  
 17 it on a go forward. In many of the clinical  
 18 trials we still don't have enough data to  
 19 support that these relative levels of  
 20 expression of these predictive markers or even  
 21 expression of other predictive markers or even  
 22 expression of other predictive markers like  
 23 HER2 are enough for us to say that that means  
 24 that people should or should not have a  
 25 certain hormonal therapy or not.

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1 CHAYTOR, Q.C.:

2 Q. Yes, was one of the factors -

3 DR. LAING:

4 A. I think eventually we will.

5 CHAYTOR, Q.C.:

6 Q. It's one of the factors that goes into your

7 decision making, though, because you, in Ms.

8 Coffin's situation, the fact that she turned

9 out to be strongly positive, then she was,

10 notwithstanding any risks involved, she was

11 offered the treatment.

12 DR. LAING:

13 A. But it was a different treatment.

14 CHAYTOR, Q.C.:

15 Q. Yes. But what I'm thinking is, and that's why

16 I said anti-hormonal treatment, whatever that

17 might be.

18 DR. LAING:

19 A. Right.

20 CHAYTOR, Q.C.:

21 Q. So I'm just wondering whether or not Dr. Cook

22 and Dr. Williams understood that it's not a

23 draw a line in the sand if you're ten percent,

24 that there are other factors and depending if

25 someone were to turn out to be strongly ER

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1 positive, that may sway your decision in one

2 direction as opposed to that person being just

3 slightly above the ten percent cutoff?

4 DR. LAING:

5 A. I would have explained things to them similar

6 to what I would have explained in my opening

7 presentation. Whether they understood that or

8 not, I think you probably would have to ask

9 them.

10 CHAYTOR, Q.C.:

11 Q. Okay. And if we--I understand then in

12 September that you would have attended the

13 exit interview with Trish Wegrynowski?

14 DR. LAING:

15 A. Yes, that's correct.

16 CHAYTOR, Q.C.:

17 Q. And perhaps you could tell us what do you

18 recall from that meeting?

19 DR. LAING:

20 A. Sure. So, I had received a phone call from

21 Dr. Williams to ask if I would be able to

22 attend her exist interview, and my first

23 question was, you know, why would you like me

24 to come along. She, as you know, had been

25 there to look into the laboratory. And he

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1 mentioned that she felt that it might be

2 valuable if somebody from the clinical side

3 was present in case there were questions or,

4 you know, issues that came up. So I agreed to

5 attend the meeting.

6 CHAYTOR, Q.C.:

7 Q. So, I'm sorry, it was Ms. Wegrynowski's idea

8 that you or somebody from the clinical side -

9 DR. LAING:

10 A. I think between her and Dr. Williams they felt

11 that it would be valuable to have someone from

12 the clinical side, that's correct.

13 CHAYTOR, Q.C.:

14 Q. Okay. Sorry.

15 DR. LAING:

16 A. Okay, so I was asked to attend the meeting; I

17 went. And as you know, the various other

18 people were there from the lab and

19 pathologists and Dr. Williams. And she

20 started the meeting by asking all of us to

21 identify who we were and why we were in

22 attendance. And so I explained to her that I

23 was a medical oncologist involved with the

24 care of patients with cancer and that I had

25 been, you know, involved with this issue to

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1 date and that's why I was there. So then she

2 basically went on then to outline to all of us

3 present her findings. She went--you know, it

4 was a rather thorough presentation of the

5 various issues and things that she had found.

6 She talked about training of personnel and

7 ongoing importance of continuing medical

8 education and understanding of the lab

9 personnel as to why they were doing the test

10 and how it was utilized. She talked about

11 issues in terms of, you know, the reagents and

12 the fixation and the buffering and all the

13 sort of stuff that wasn't, you know, stuff

14 that I would be overly familiar with. And she

15 didn't have any, not that I can recall, any

16 specific questions directed to me. And that's

17 what I remember from the meeting.

18 CHAYTOR, Q.C.:

19 Q. Okay, and overall, sitting there, being the

20 clinician in the group, looking after the

21 patients who were affected, what did you take

22 away from what Ms. Wegrynowski was saying and

23 how did you feel about it?

24 DR. LAING:

25 A. What I took away was that she identified that

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1 there were a number of areas that needed  
 2 improvement in the lab, but felt that these  
 3 were areas that certainly could be addressed.  
 4 There wasn't one sort of striking thing that  
 5 she said, you know, this was because of one  
 6 thing. And I thought that she made her  
 7 comments, at least my perception at that time,  
 8 was in a very constructive way. And I never  
 9 really sort of thought about it very much  
 10 again after that. I knew that, you know, the  
 11 lab people were there and they were going to  
 12 address her recommendations and, of course,  
 13 knew that a similar thing was happening with  
 14 the pathologists with Dr. Banerjee, although,  
 15 as I said, I wasn't directly involved at all  
 16 in any of the meetings with him.

17 CHAYTOR, Q.C.:

18 Q. So it's the kind of thing that you walked away  
 19 from and, as you say, you didn't think much of  
 20 afterwards? So it wasn't the kind of thing  
 21 that raised any particular alarms or concerns,  
 22 what you were hearing her say?

23 DR. LAING:

24 A. No.

25 CHAYTOR, Q.C.:

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1 Q. Okay. Did she mention whether or not there  
 2 was an issue with not having any standard  
 3 operating procedures in place?

4 DR. LAING:

5 A. She may have, but I don't remember that  
 6 specifically.

7 CHAYTOR, Q.C.:

8 Q. Okay. And would you have understood what that  
 9 meant and the significance of that?

10 DR. LAING:

11 A. Yes, because we use standard operating  
 12 procedures in my area, as well. And, you  
 13 know, there are areas within medicine, for  
 14 example, when I think about standard operating  
 15 procedures, I think about clinical trials. I  
 16 do audits for the clinical trials group and I  
 17 know that we've been looking for the last  
 18 couple of years as regular item now is do  
 19 clinical trials groups have standard operating  
 20 procedures and we--that's part of our auditing  
 21 process.

22 CHAYTOR, Q.C.:

23 Q. And did she raise concerns about lack of  
 24 quality control measures and overall quality  
 25 assurance issues for the lab?

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1 DR. LAING:

2 A. Yes, she would have in that discussion.

3 CHAYTOR, Q.C.:

4 Q. And did that cause you any concern?

5 DR. LAING:

6 A. I think at that time, you know, I was thinking  
 7 about it in the way that, you know, somebody  
 8 had come and was making recommendations that  
 9 to me sitting there in that room people were  
 10 taking very seriously and I guess I was more  
 11 thinking about it on a go forward basis.

12 CHAYTOR, Q.C.:

13 Q. And communications issues amongst the  
 14 personnel within the laboratory medicine  
 15 program, did she raise any issues in that  
 16 respect?

17 DR. LAING:

18 A. She may have but that's not something that I  
 19 recall.

20 CHAYTOR, Q.C.:

21 Q. And what you heard in terms of lack of  
 22 standard operating procedures and issues  
 23 involving quality control and lack of a  
 24 quality assurance overall program, did it  
 25 cause you any concern as to anything else that

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1 may be happening in the lab, any other tests  
 2 that you have to rely on every day?

3 DR. LAING:

4 A. Certainly we rely on the lab, as you know, for  
 5 many, many tests that are done. She didn't--  
 6 she wasn't there to review those particular  
 7 aspects of the lab and it wasn't something  
 8 that I was thinking of at the time.

9 CHAYTOR, Q.C.:

10 Q. What did you think that--what did you  
 11 understand she had reviewed?

12 DR. LAING:

13 A. That she had reviewed the immunohistochemistry  
 14 lab.

15 CHAYTOR, Q.C.:

16 Q. So any test, not just ER/PR, but the -

17 DR. LAING:

18 A. Oh, yes, right, all the tests that were done -

19 CHAYTOR, Q.C.:

20 Q. The IHC lab overall?

21 DR. LAING:

22 A. That's correct, yes. But not the biochemical  
 23 lab or the hematology lab or any of the other  
 24 lab aspects.

25 CHAYTOR, Q.C.:

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<p>1 Q. What were you told was the purpose of her 2 review and Dr. Banerjee's review, for that 3 matter?</p> <p>4 DR. LAING:</p> <p>5 A. My understanding was that because of this 6 issue that this was taken upon as a peer 7 review, that they would have someone from the 8 outside come in and have a look at things and 9 see if they could make recommendations of how 10 things could be improved on a go forward 11 basis.</p> <p>12 CHAYTOR, Q.C.:</p> <p>13 Q. Okay. And prior to hearing Ms. Wegrynowski 14 raise the issue of quality assurance and 15 quality control, had you assumed those things 16 would have been in place in the IHC lab?</p> <p>17 DR. LAING:</p> <p>18 A. To be quite honest with you, I, you know, not 19 working in the lab and not being directly 20 responsible or, you know, I guess it would be- 21 -you the same as asking me did I think those 22 things would happen in other areas of the 23 hospital and my answer would be yes.</p> <p>24 CHAYTOR, Q.C.:</p> <p>25 Q. And you would assume, yeah.</p>	<p>1 think he had those transcribed for us, but 2 these, we understand are notes of the meeting 3 with Dr. Wegrynowski that happened on 4 September 22nd, 2005. Doctor, if you had 5 known beforehand that there were any issues of 6 quality assurance or quality control measures 7 not being in place in the IHC lab, would you 8 have done anything about it?</p> <p>9 DR. LAING:</p> <p>10 A. I'm not certain how I would have known that 11 information.</p> <p>12 CHAYTOR, Q.C.:</p> <p>13 Q. No, but if, if you had, if that had come to 14 your attention?</p> <p>15 DR. LAING:</p> <p>16 A. I probably would have spoken to the person who 17 would be in charge of that, so the clinical 18 chief of laboratory services. I think it 19 would be no different, again, if someone came 20 to me today and said there was a problem with 21 a CAT scanner or something like that, I would 22 go and speak to whoever was responsible and 23 see if I could clarify what the concern or 24 issue may be.</p> <p>25 CHAYTOR, Q.C.:</p>
<p style="text-align: right;">Page 273</p> <p>1 DR. LAING:</p> <p>2 A. Yeah.</p> <p>3 CHAYTOR, Q.C.:</p> <p>4 Q. And so I take it you were somewhat surprised 5 by that, to hear that there were issues of 6 that nature?</p> <p>7 DR. LAING:</p> <p>8 A. Somewhat, but, you know, even when I look back 9 on what she was saying and talking about all 10 these various steps of the test and those 11 sorts of things, they didn't--you know, they 12 wouldn't have had the same meaning to me as if 13 someone was perhaps talking about maybe how a 14 patient would go through the process from, you 15 know, ordering chemotherapy to that patient, 16 you know, being delivered the drug. It 17 wouldn't be something that I would be familiar 18 with in my day-to-day work.</p> <p>19 CHAYTOR, Q.C.:</p> <p>20 Q. If we could have, please, P-0596? Those are 21 notes -</p> <p>22 DR. LAING:</p> <p>23 A. Oh yes, Dr. Williams, right.</p> <p>24 CHAYTOR, Q.C.:</p> <p>25 Q. Dr. Williams, yes, and unfortunately, I don't</p>	<p style="text-align: right;">Page 275</p> <p>1 Q. Okay, and this is--in attendance, we can see 2 here, it's Dr. Cook, Dr. Laing, Ms. Predham, I 3 think it's Mr. Gulliver, and Dr. Williams, and 4 Trish Wegrynowski of Mount Sinai, and I think 5 it just says Mount Sinai technical person, but 6 we know her as Trish Wegrynowski, and 7 "statement of affairs. Frustrated and 8 overwhelmed," and we understand this from Ms. 9 Wegrynowski and Dr. Williams, this would have 10 been referring to the technical staff.</p> <p>11 DR. LAING:</p> <p>12 A. I thought that said staffing. Number one, I 13 thought it said staffing.</p> <p>14 CHAYTOR, Q.C.:</p> <p>15 Q. I see, but I've had a chance to look at it a 16 few more times.</p> <p>17 DR. LAING:</p> <p>18 A. Okay, statement of affairs, okay.</p> <p>19 CHAYTOR, Q.C.:</p> <p>20 Q. And hear other people interpret it.</p> <p>21 DR. LAING:</p> <p>22 A. All right.</p> <p>23 CHAYTOR, Q.C.:</p> <p>24 Q. So correct me if I'm wrong -</p> <p>25 DR. LAING:</p>

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<p>1 A. Okay, no, that's fine.</p> <p>2 CHAYTOR, Q.C.:</p> <p>3 Q. - someone else in the room, but I understand--</p> <p>4 is it state of affairs or staffing?</p> <p>5 MR. BROWNE:</p> <p>6 Q. Staffing.</p> <p>7 CHAYTOR, Q.C.:</p> <p>8 Q. Is it staffing? All right, you could be</p> <p>9 right, staffing. My memory is not as good.</p> <p>10 "Causes. communication issues, do not</p> <p>11 understand the theory. Need to work together</p> <p>12 as a group. Need to -</p> <p>13 DR. LAING:</p> <p>14 A. Identify who they should report to.</p> <p>15 CHAYTOR, Q.C.:</p> <p>16 Q. There you go. You can read his writing a lot</p> <p>17 better than us.</p> <p>18 DR. LAING:</p> <p>19 A. It's just being a physician, I think.</p> <p>20 CHAYTOR, Q.C.:</p> <p>21 Q. That's it. You all write the same, okay.</p> <p>22 "Suggest technical director for the</p> <p>23 immunoperoxidase laboratory," I think. Is</p> <p>24 that what it says?</p> <p>25 DR. LAING:</p>	<p>1 CHAYTOR, Q.C.:</p> <p>2 Q. - to be an MD, any of that?</p> <p>3 DR. LAING:</p> <p>4 A. No.</p> <p>5 CHAYTOR, Q.C.:</p> <p>6 Q. Okay, and do you know what this word says?</p> <p>7 MR. BROWNE:</p> <p>8 Q. Fixation.</p> <p>9 DR. LAING:</p> <p>10 A. Oh, fixation.</p> <p>11 CHAYTOR, Q.C.:</p> <p>12 Q. "Fixation, two sites."</p> <p>13 DR. LAING:</p> <p>14 A. "Must have same protocols."</p> <p>15 CHAYTOR, Q.C.:</p> <p>16 Q. "Must have same protocols. Need pathology</p> <p>17 assistants."</p> <p>18 DR. LAING:</p> <p>19 A. Right.</p> <p>20 CHAYTOR, Q.C.:</p> <p>21 Q. "We have had problems with fixation." So you</p> <p>22 do recall her discussing problems with</p> <p>23 fixation?</p> <p>24 DR. LAING:</p> <p>25 A. Um-hm.</p>
<p>Page 277</p> <p>1 A. Um-hm.</p> <p>2 CHAYTOR, Q.C.:</p> <p>3 Q. "Need triangular line of communication." So</p> <p>4 you recall were all these issues discussed, do</p> <p>5 you recall that being discussed?</p> <p>6 DR. LAING:</p> <p>7 A. I recall the--I guess what I remembered from</p> <p>8 that was that she said that she felt it was</p> <p>9 important that the staff understand why they</p> <p>10 were doing the test, not simply that they were</p> <p>11 doing this test, but you know, how it was</p> <p>12 being utilized at the other end.</p> <p>13 CHAYTOR, Q.C.:</p> <p>14 Q. Okay. So she was concerned about the</p> <p>15 knowledge level, I take it, of the</p> <p>16 technologists, in terms of the purpose for</p> <p>17 which they were doing their work?</p> <p>18 DR. LAING:</p> <p>19 A. That's the thing that I remember.</p> <p>20 CHAYTOR, Q.C.:</p> <p>21 Q. And do you recall any other detail in terms of</p> <p>22 this issue of needing a triangular line of</p> <p>23 communication, head for the immunoperoxidase -</p> <p>24 DR. LAING:</p> <p>25 A. No.</p>	<p>Page 279</p> <p>1 CHAYTOR, Q.C.:</p> <p>2 Q. And did you understand what that meant when</p> <p>3 she talked about fixation?</p> <p>4 DR. LAING:</p> <p>5 A. My understanding was it was, you know, from</p> <p>6 the time that the tissue was taken from the</p> <p>7 patient and put in the formalin and delivered</p> <p>8 to the lab.</p> <p>9 CHAYTOR, Q.C.:</p> <p>10 Q. Okay, and I think this is controls.</p> <p>11 DR. LAING:</p> <p>12 A. Controls.</p> <p>13 CHAYTOR, Q.C.:</p> <p>14 Q. Do you recall a discussion about controls and</p> <p>15 what may have been lacking or any</p> <p>16 recommendations she had regarding controls?</p> <p>17 DR. LAING:</p> <p>18 A. Not specific details, no.</p> <p>19 CHAYTOR, Q.C.:</p> <p>20 Q. "Must be running positive and negative</p> <p>21 controls. Validation must be done, and record</p> <p>22 keeping"</p> <p>23 DR. LAING:</p> <p>24 A. Yeah, she was -</p> <p>25 CHAYTOR, Q.C.:</p>

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<p>1 Q. Talked about the buffers, the antibodies, 2 which you've mentioned. 3 DR. LAING: 4 A. Yes, I remember her talking about that, yeah. 5 CHAYTOR, Q.C.: 6 Q. Okay, and "need to write their own manuals. 7 Reagents must be validated," and then it goes 8 on. I don't know if you've had a chance to 9 look at this in any detail in preparation for 10 coming here, but - 11 DR. LAING: 12 A. I didn't look at it in great detail, but I did 13 see it prior to coming here, and of course. 14 CHAYTOR, Q.C.: 15 Q. Okay, and I take it then this is consistent 16 with what you remember her talking about, and 17 the issue of competency testing, give 18 scenarios to the techs. So having something in 19 the way of competency and testing for the 20 techs. And at this point in time, it appears 21 you're still doing HER2/neu testing, and do 22 you recall what was said about that? "Move 23 off the benches quickly as is possible." 24 DR. LAING: 25 A. No.</p>	<p>1 CHAYTOR, Q.C.: 2 Q. Were you provided a copy or did you see a copy 3 of her report when it was presented? 4 DR. LAING: 5 A. No. 6 CHAYTOR, Q.C.: 7 Q. And did you also sit in on Dr. Banerjee's 8 interview? 9 DR. LAING: 10 A. No. 11 CHAYTOR, Q.C.: 12 Q. And did you see, at any point in time, or were 13 you provided any information regarding his 14 report or the outcome of his review? 15 DR. LAING: 16 A. No, only in preparation for this testimony, 17 and just the piece that we looked at last week 18 about the 92 percent. 19 CHAYTOR, Q.C.: 20 Q. That's right, I asked you about that. 21 DR. LAING: 22 A. Yeah. 23 CHAYTOR, Q.C.: 24 Q. Doctor, we know Ms. Wegrynowski came back then 25 in the spring of 2006. Did you meet with her</p>
<p style="text-align: right;">Page 281</p> <p>1 CHAYTOR, Q.C.: 2 Q. Okay. 3 DR. LAING: 4 A. I don't know what that means. 5 CHAYTOR, Q.C.: 6 Q. Okay, and overall then, it ends with "ensure 7 validation processes in place." How long do 8 you recall--how long did this meeting last 9 with Ms. Wegrynowski? 10 DR. LAING: 11 A. I'm not 100 percent certain, but I would say 12 that it was probably in the order of about 45 13 minutes. It certainly wasn't, you know, kind 14 of a 10-minute briefing. It was a fairly 15 lengthy meeting, from what I recall. 16 CHAYTOR, Q.C.: 17 Q. And was there any discussion then of the group 18 of you afterwards, after Ms. Wegrynowski left? 19 Was there any discussion amongst the 20 individuals from Eastern Health in attendance? 21 DR. LAING: 22 A. Not that I recall. I'm sure that the lab 23 people probably discussed it further, but when 24 she was finished, the meeting was over, I 25 would have left.</p>	<p style="text-align: right;">Page 283</p> <p>1 at that time? 2 DR. LAING: 3 A. No. 4 CHAYTOR, Q.C.: 5 Q. So you weren't asked to sit in on the follow 6 up interview? 7 DR. LAING: 8 A. No, I was not. 9 CHAYTOR, Q.C.: 10 Q. And do you know if any clinician did, anybody 11 from oncology? 12 DR. LAING: 13 A. No, I don't--not that I know of at all, no. 14 CHAYTOR, Q.C.: 15 Q. Okay. Doctor, just one other point to go back 16 to on the decision about disclosure and then 17 perhaps we can carry on a little bit in 18 chronology, in the order of the chronology 19 here. When the issue of whether to tell the 20 patients upfront or prior to the retesting or 21 around the time the retesting was happening 22 and you've told us in some detail about your 23 input into that last time. At any point in 24 time in the discussions, did you hear anyone 25 refer to any issues regarding insurance</p>

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1 company's opinion on it, HIROC's opinion, any  
2 issues with insurance coverage?

3 DR. LAING:  
4 A. No.

5 CHAYTOR, Q.C.:  
6 Q. So you've never--you never heard that  
7 discussed within your ear shot?

8 DR. LAING:  
9 A. No.

10 CHAYTOR, Q.C.:  
11 Q. Okay, and have you since learned anything  
12 along those lines about the issue?

13 DR. LAING:  
14 A. Not in any great de--no, not that I can think  
15 back to, no.

16 CHAYTOR, Q.C.:  
17 Q. Okay, in any detail whatsoever, has it ever  
18 been suggested to you, whether or not the  
19 insurer had any input or any view on the  
20 issue?

21 DR. LAING:  
22 A. Not--there was some discussion later on, as  
23 to, I believe Dan Boone was at one of the  
24 meetings at some point, and I was asked did I  
25 recall him making any comment about it, and I

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1 didn't.

2 CHAYTOR, Q.C.:  
3 Q. Okay. So you may have been in attendance at  
4 meetings in which it was discussed, but you  
5 wouldn't remember?

6 DR. LAING:  
7 A. I don't remember discussing it, no.

8 CHAYTOR, Q.C.:  
9 Q. All right, and no one ever brought to your  
10 attention any issue about any concern as to  
11 any effect disclosure might have on insurance  
12 coverage?

13 DR. LAING:  
14 A. No, not that I--no.

15 CHAYTOR, Q.C.:  
16 Q. Okay. If we could have, please, P-2589? And  
17 this is an e-mail from Heather Predham to  
18 yourself and others, including Dr. Williams  
19 and Ms. Pilgrim, and it appears that it's a  
20 draft of a letter and it's now October 4th,  
21 2005. So a couple of days after The  
22 Independent story has run.

23 DR. LAING:  
24 A. Right.

25 CHAYTOR, Q.C.:

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1 Q. And it's a draft letter to physicians. Do you  
2 recall having had any input into this draft  
3 letter or any letter potentially to go to  
4 physicians?

5 DR. LAING:  
6 A. Dr. Gardiner had drafted a letter to go to  
7 physicians and I had been sent an e-mail  
8 asking if I could put in sort of what the  
9 recommendations was, which is this paragraph,  
10 "it is recommended that patients who are now  
11 known to be ER/PR positive should be offered  
12 Tamoxifen for five years, if it is  
13 contraindicated," dah, dah, dah, "then  
14 aromatase inhibitor could be considered if  
15 they were post-menopausal."

16 CHAYTOR, Q.C.:  
17 Q. So you drafted that paragraph?

18 DR. LAING:  
19 A. Yes, because that would be--I think, I'm not  
20 sure if this was the--what it had finally, but  
21 that was what our recommendation was going to  
22 be at that time, was that people that were  
23 hormone receptor positive would be offered  
24 Tamoxifen or if that was contraindicated or  
25 not tolerated, then an AI, and that was the

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1 decision that we had made as to how we would  
2 treat these patients.

3 CHAYTOR, Q.C.:  
4 Q. Which physicians was this letter intended to  
5 go to?

6 DR. LAING:  
7 A. It was intended to go to--my understanding was  
8 that it was going to go out to physicians  
9 within the province, so it would include  
10 family physicians, surgeons, people that would  
11 potentially be following up on breast cancer  
12 patients.

13 CHAYTOR, Q.C.:  
14 Q. And what was the purpose in sending such a  
15 letter at the beginning of October, 2005?

16 DR. LAING:  
17 A. That at this point, this would have been as we  
18 know that this was something that broke in the  
19 news just a couple of days before this. So  
20 there had been some discussion with Dr.  
21 Gardiner and Dr. Williams as to whether or not  
22 they would send some information to physicians  
23 that may be dealing with these patients. But  
24 subsequent to this, we made a decision that we  
25 would do the tumour panel, that we would do a



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<p>1 tumour board specific to this issue, which we</p> <p>2 would then not only look at just sort of</p> <p>3 generally recommending this to all patients,</p> <p>4 but we would look at the patient's prognosis</p> <p>5 at this point in time to make a recommendation</p> <p>6 that was a little bit more specific to the</p> <p>7 information that we had at hand about</p> <p>8 individual patients.</p> <p>9 CHAYTOR, Q.C.:</p> <p>10 Q. So do you know whether or not this type of</p> <p>11 letter ever went out to the physicians?</p> <p>12 DR. LAING:</p> <p>13 A. I don't know, in fact. I'm not sure. It was</p> <p>14 going to come from Dr. Gardiner, but then we</p> <p>15 moved on and I don't recall having any further</p> <p>16 discussions about that letter and turned my</p> <p>17 attentions to the tumour panel.</p> <p>18 CHAYTOR, Q.C.:</p> <p>19 Q. Okay, and if we could have, please, 2590? And</p> <p>20 this is an e-mail again from Ms. Predham and</p> <p>21 it's sent to you and Ms. Pilgrim, Dr. Williams</p> <p>22 and Ms. Bonnell. It's October 18th, 2005, and</p> <p>23 the re: is a patient letter, and attached here</p> <p>24 is a draft to "Dear Patient."</p> <p>25 DR. LAING:</p>	<p>1 discussions about whether a letter would still</p> <p>2 be sent or not, and from then on, most of--as</p> <p>3 I said, most of what I was focused upon was</p> <p>4 the tumour panel.</p> <p>5 CHAYTOR, Q.C.:</p> <p>6 Q. So if this letter didn't go out at that time,</p> <p>7 do you recall taking part in any discussion as</p> <p>8 to whether or not a letter should be sent or</p> <p>9 the decision ultimately not to send such a</p> <p>10 letter?</p> <p>11 DR. LAING:</p> <p>12 A. No.</p> <p>13 CHAYTOR, Q.C.:</p> <p>14 Q. Okay, so while you were sent a draft of what</p> <p>15 the letter could potentially say and you're</p> <p>16 saying you didn't provide any input into the</p> <p>17 actual content of the letter, nor did you</p> <p>18 provide any input into as to whether or not</p> <p>19 you should be telling the patients anything at</p> <p>20 this point in time?</p> <p>21 DR. LAING:</p> <p>22 A. Well, at that point, we had--we were starting</p> <p>23 the tumour panel and, you know, patients would</p> <p>24 be then contacted by the physician and then if</p> <p>25 the results didn't change, initially they were</p>
<p>1 A. Um-hm.</p> <p>2 CHAYTOR, Q.C.:</p> <p>3 Q. October 17th, 2005. "We are contacting</p> <p>4 patients that have been diagnosed with breast</p> <p>5 cancer between 1997 and 2004. Our records</p> <p>6 show that the initial pathology results from</p> <p>7 your breast cancer indicated that your tumour</p> <p>8 was negative for estrogen receptors," and it</p> <p>9 goes on from there. Did you have--do you</p> <p>10 recall receiving this e-mail, and did you have</p> <p>11 any input into the drafting of the letter to</p> <p>12 the patients?</p> <p>13 DR. LAING:</p> <p>14 A. I recall receiving the e-mail, but I didn't,</p> <p>15 to this date, I didn't have any input into the</p> <p>16 drafting of that letter.</p> <p>17 CHAYTOR, Q.C.:</p> <p>18 Q. And do you know whether or not such a letter</p> <p>19 ever went out to the patients?</p> <p>20 DR. LAING:</p> <p>21 A. At that time, you know, we had clearly had</p> <p>22 lots and lots of discussion as we went through</p> <p>23 about a letter prior to when this became</p> <p>24 public knowledge, and really afterwards, I</p> <p>25 wasn't involved a lot with any further</p>	<p>1 being contacted by people from the Quality</p> <p>2 office.</p> <p>3 CHAYTOR, Q.C.:</p> <p>4 Q. And however, I understand it was still early,</p> <p>5 in terms of even getting results back from</p> <p>6 Mount Sinai?</p> <p>7 DR. LAING:</p> <p>8 A. It was, yeah.</p> <p>9 CHAYTOR, Q.C.:</p> <p>10 Q. And you would have only had your first tumour</p> <p>11 board panel four days before this, October</p> <p>12 13th.</p> <p>13 DR. LAING:</p> <p>14 A. Okay.</p> <p>15 CHAYTOR, Q.C.:</p> <p>16 Q. So I'm just wondering whether you thought it</p> <p>17 would be a good idea to get something out to</p> <p>18 the patients and, you know, let them know that</p> <p>19 they are one of the people that are being</p> <p>20 reviewed because the matter is now a matter of</p> <p>21 public discussion. So let them know they are</p> <p>22 one of the people being reviewed and what they</p> <p>23 can expect in terms of any follow up?</p> <p>24 DR. LAING:</p> <p>25 A. Sure, but as I said, I just was not part of</p>

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1 any of those subsequent discussions about the  
2 letter.

3 CHAYTOR, Q.C.:

4 Q. So if you had been included in the discussion,  
5 you would have thought the letter was a good  
6 idea to go to the patients?

7 DR. LAING:

8 A. You know, at this point, one could--I mean,  
9 looking back, if you're asking me to do that,  
10 you know, would a letter have been the best  
11 way? Would a phone call have been a better  
12 way? I can't help but think of subsequent  
13 letters that were sent to patients and often  
14 they raised more questions than they gave  
15 answers to, but so, you know, I guess looking  
16 back, perhaps some sort of contact, whether a  
17 letter or a phone call, may have been  
18 beneficial to patients, in retrospect, but as  
19 I said, really at this point, we were, from  
20 the point of view of the physicians in the  
21 Cancer Care Program, concentrating our efforts  
22 on the tumour panel.

23 CHAYTOR, Q.C.:

24 Q. Yes, and I'm just wondering though, in terms  
25 of because, of course, you were--you did have

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1 a significant role to play and -

2 DR. LAING:

3 A. Prior.

4 CHAYTOR, Q.C.:

5 Q. - in terms of the disclosure to patients, and  
6 your opinion on that was sought, and it  
7 appears, you know, given some weight, in terms  
8 of how to disclose and when to disclose to the  
9 patients. So just wondering how much  
10 involvement then you had at this stage then,  
11 after it has broken in the media.

12 DR. LAING:

13 A. Not a lot on this issue, no.

14 CHAYTOR, Q.C.:

15 Q. Not a lot at all?

16 DR. LAING:

17 A. No.

18 CHAYTOR, Q.C.:

19 Q. In terms of what should now be told to the  
20 patients and what manner in which they should  
21 be told?

22 DR. LAING:

23 A. Yeah.

24 CHAYTOR, Q.C.:

25 Q. You weren't contacted and your opinion wasn't

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1 sought?

2 DR. LAING:

3 A. No, and of course, you have to realize that at  
4 this point, we are having a lot of contact  
5 with the patients as clinicians. So by this  
6 time, we're getting phone calls to the Cancer  
7 Centre. Every day that I'm in the clinic, I'm  
8 talking with patients about this issue, and  
9 dealing with it, you know, at that level,  
10 getting calls from my own patients and -

11 CHAYTOR, Q.C.:

12 Q. Yes, for those coming through the door or for  
13 those who were already have--are still  
14 patients of the clinic?

15 DR. LAING:

16 A. Or even people calling.

17 CHAYTOR, Q.C.:

18 Q. Yes.

19 DR. LAING:

20 A. Yeah, and people calling. So -

21 CHAYTOR, Q.C.:

22 Q. So your idea as to, you know, perhaps making--  
23 sending the letter or not sending the letter,  
24 your opinion wasn't solicited at this point in  
25 time. Okay. And we know that telephone calls

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1 were made later on then in the month, and  
2 again, there was an attempt to try and reach  
3 patients by telephone. Were you involved in  
4 that decision?

5 DR. LAING:

6 A. No, no, I wasn't involved in calling those  
7 patients or, you know, we sort of went on and  
8 were still dealing with what was coming in the  
9 clinic and the queries that were coming that  
10 way, the patients that were coming to the  
11 clinic, and doing the tumour panel.

12 THE COMMISSIONER:

13 Q. Just to make sure I'm clear on this point, Dr.  
14 Laing. In this e-mail from Heather Predham to  
15 a number of people, including you, Ms. Predham  
16 raises certain points in the body of the  
17 letter and then says "let me know what changes  
18 you made." So do I take it you did not  
19 respond?

20 DR. LAING:

21 A. Not that I have any recollection of. No, not  
22 at all.

23 THE COMMISSIONER:

24 Q. Okay, thank you.

25 CHAYTOR, Q.C.:

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1 Q. And Ms. Predham writes in the final paragraph  
 2 of her letter, "I'm going to send this on to  
 3 Dan Boone as well. I'm not sure how HIROC  
 4 will feel about notifying people at this point  
 5 in time and whether the media attention will  
 6 make any difference." Do you recall any  
 7 discussion around that?  
 8 DR. LAING:  
 9 A. No.  
 10 CHAYTOR, Q.C.:  
 11 Q. And do you recall when you read that wondering  
 12 what that could be referring to?  
 13 DR. LAING:  
 14 A. No.  
 15 CHAYTOR, Q.C.:  
 16 Q. So Doctor, at this point in time, by the  
 17 middle of October, you're seeing patients.  
 18 They're showing up in the clinic and they've  
 19 heard about the issue.  
 20 DR. LAING:  
 21 A. Yes.  
 22 CHAYTOR, Q.C.:  
 23 Q. And they're asking you questions about it.  
 24 DR. LAING:  
 25 A. Yes.

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1 CHAYTOR, Q.C.:  
 2 Q. And the Cancer Clinic is also receiving phone  
 3 calls, and you're receiving some phone calls  
 4 directly yourself on this issue. But the  
 5 administration or the people handling the  
 6 issue didn't ask your opinion as to what  
 7 should--whether or not this letter should in  
 8 fact go, whether or not phone calls should  
 9 take place?  
 10 DR. LAING:  
 11 A. No, that wasn't something that I can recall  
 12 being asked to come and sit in a meeting and  
 13 formally discuss, no.  
 14 CHAYTOR, Q.C.:  
 15 Q. They're sending along the letter to you, so  
 16 they're obviously looking for your input, in  
 17 terms of what would be said to the patients in  
 18 the letter, should it go. But whether the  
 19 letter goes or whether phone calls are made,  
 20 you're not asked your advice on that?  
 21 DR. LAING:  
 22 A. No.  
 23 CHAYTOR, Q.C.:  
 24 Q. And in terms of the staff at the Cancer Clinic  
 25 being able to answer the questions that may be

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1 posed to them, the frontline staff, the people  
 2 who are greeting the patients as they first  
 3 come in, were they given any information as to  
 4 what could be told to the patients?  
 5 DR. LAING:  
 6 A. Well, most of the times when we would get  
 7 phone calls or queries, they were actually  
 8 directed to us. You know, if patients called  
 9 looking for test results or they have  
 10 questions, most of the time that information  
 11 would be forwarded directly to us as a memo,  
 12 or it would be sent through to one of the  
 13 nurses working with us, but most often those  
 14 queries even to date come directly to the  
 15 physician.  
 16 CHAYTOR, Q.C.:  
 17 Q. I'm just wondering back then, though, what the  
 18 staff were told. You know, undoubtedly  
 19 they're going to get questions and what were  
 20 they told, and were they told in any--were  
 21 they given a memo, were they told anything  
 22 directly to be consistent as to here's what  
 23 patients need to know, here's who to put them  
 24 in contact with?  
 25 DR. LAING:

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1 A. Well, at some point, and I'm not exactly sure  
 2 which process, but Nancy Parsons was given as  
 3 the contact person for people to inquire as to  
 4 whether or not they had to be retested because  
 5 that was where the master list, if you will,  
 6 of patients who had been sent for retesting  
 7 was. So certainly if patients wanted to call  
 8 and ask us questions, you know, what's going  
 9 on, is this about me, then we could look and  
 10 say, well, you know, no, I know that your  
 11 hormone receptor positive, I know how I've  
 12 treated you, and if it was my patient, I could  
 13 let them know. If it was someone who was  
 14 asking if they had been retested, then  
 15 eventually we would direct that they would  
 16 call Nancy Parsons phone number to see if they  
 17 were being retested or not.  
 18 CHAYTOR, Q.C.:  
 19 Q. And how was that--how was that information  
 20 given to the staff at the Cancer Clinic?  
 21 DR. LAING:  
 22 A. I'm not certain if it would have been a memo  
 23 or if we would have told them.  
 24 CHAYTOR, Q.C.:  
 25 Q. That wouldn't have been your responsibility, I

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<p>1 take it? Who would be responsible for doing</p> <p>2 that?</p> <p>3 DR. LAING:</p> <p>4 A. I'm not sure if it was Dr. Gardiner at the</p> <p>5 time or--I can't recall.</p> <p>6 CHAYTOR, Q.C.:</p> <p>7 Q. And as you continued to see the patients and</p> <p>8 they asked you questions about it, and you</p> <p>9 told them there was a retesting happening, I</p> <p>10 take it the patients would inquire as to</p> <p>11 whether or not they were part of it, and in</p> <p>12 those cases you would check their chart.</p> <p>13 Would you do that for all patients, or would</p> <p>14 it be if they inquired? So every patient</p> <p>15 coming through, would you check the chart to</p> <p>16 see if they, in fact, qualified for the</p> <p>17 retesting?</p> <p>18 DR. LAING:</p> <p>19 A. Oh, yes, we were--at this point we would be</p> <p>20 looking at their--you know, we would be</p> <p>21 looking at their pathology and seeing where</p> <p>22 they were because even at this point you'll</p> <p>23 recall that, although, the slides had been</p> <p>24 sent to Mount Sinai --</p> <p>25 CHAYTOR, Q.C.:</p>	<p>1 DR. LAING:</p> <p>2 A. I think that that would probably be the main</p> <p>3 one.</p> <p>4 CHAYTOR, Q.C.:</p> <p>5 Q. That's the only --</p> <p>6 DR. LAING:</p> <p>7 A. I'm trying to think of some other--I don't</p> <p>8 recall at that time having identified other</p> <p>9 people that were lobular histology. I had</p> <p>10 those few that we talked about before, but I</p> <p>11 think the metastatic disease is the only</p> <p>12 reason that I can think of right now that we</p> <p>13 would have asked for that to happen sooner</p> <p>14 than just in the queue with everybody else to</p> <p>15 be retested.</p> <p>16 CHAYTOR, Q.C.:</p> <p>17 Q. Okay. So the metastatic disease patients were</p> <p>18 given priority?</p> <p>19 DR. LAING:</p> <p>20 A. If we had someone who, for example, was being</p> <p>21 treated with chemotherapy for metastatic</p> <p>22 disease and we were thinking, okay, you've had</p> <p>23 however many cycles of such and such a</p> <p>24 treatment, and we were thinking about what to</p> <p>25 do next--certainly if we were at the treatment</p>
<p>1 Q. The blocks.</p> <p>2 DR. LAING:</p> <p>3 A. The blocks had been sent to Mount Sinai, it</p> <p>4 was still--at that point if we had seen</p> <p>5 someone for any particular reason that we</p> <p>6 wanted to have the retesting results then, be</p> <p>7 it, you know, that they had metastatic disease</p> <p>8 or there was something about that patient,</p> <p>9 then we could certainly ask for retesting to</p> <p>10 happen as well.</p> <p>11 CHAYTOR, Q.C.:</p> <p>12 Q. And those were the ones sent as a consult, I</p> <p>13 understand?</p> <p>14 DR. LAING:</p> <p>15 A. That's correct.</p> <p>16 CHAYTOR, Q.C.:</p> <p>17 Q. And what criteria--other than the people with</p> <p>18 metastatic disease, I understand those you</p> <p>19 would pull and you sent as consults --</p> <p>20 DR. LAING:</p> <p>21 A. Yeah.</p> <p>22 CHAYTOR, Q.C.:</p> <p>23 Q. What other criteria did you use for</p> <p>24 determining who got sent as a consult as</p> <p>25 opposed to who stayed in the batch?</p>	<p>1 decision point for the patients with</p> <p>2 metastatic disease, then, yes, we would have</p> <p>3 sort of said, well, can we get this one done</p> <p>4 because we may--you know, this may be an</p> <p>5 option for us to offer this patient hormonal</p> <p>6 therapy at this point, again depending on</p> <p>7 where the disease was, you know.</p> <p>8 CHAYTOR, Q.C.:</p> <p>9 Q. And was that something then--and because</p> <p>10 that's like doing it on a priority basis</p> <p>11 because this person is running out of options,</p> <p>12 I take it?</p> <p>13 DR. LAING:</p> <p>14 A. That's right, and that was right from--you</p> <p>15 know, right from the index case, you know,</p> <p>16 some of the first few that we did retesting on</p> <p>17 were exactly that cohort of patients.</p> <p>18 CHAYTOR, Q.C.:</p> <p>19 Q. And was that communicated to the other</p> <p>20 oncologists so they would know --</p> <p>21 DR. LAING:</p> <p>22 A. Yes.</p> <p>23 CHAYTOR, Q.C.:</p> <p>24 Q. To pull the patients that most urgently needed</p> <p>25 to be retested?</p>

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<p>1 DR. LAING:</p> <p>2 A. We would have--that would have been something</p> <p>3 that everybody would have--all the oncologists</p> <p>4 would have known that was available to them.</p> <p>5 CHAYTOR, Q.C.:</p> <p>6 Q. And did you send them an e-mail, a memo, how</p> <p>7 did they know to do that?</p> <p>8 DR. LAING:</p> <p>9 A. We would have communicated it at staff</p> <p>10 meetings.</p> <p>11 CHAYTOR, Q.C.:</p> <p>12 Q. At staff meetings, okay.</p> <p>13 DR. LAING:</p> <p>14 A. And, of course, because we're such a small</p> <p>15 group, you know, we would always be discussing</p> <p>16 things with each other, but they definitely--</p> <p>17 I can tell you they definitely would have</p> <p>18 known that they could do that.</p> <p>19 CHAYTOR, Q.C.:</p> <p>20 Q. And pulling the charts or having the chart of</p> <p>21 a patient who is coming before you --</p> <p>22 DR. LAING:</p> <p>23 A. Uh-hm.</p> <p>24 CHAYTOR, Q.C.:</p> <p>25 Q. So every patient who would come in, you would</p>	<p>1 DR. LAING:</p> <p>2 A. Yes.</p> <p>3 CHAYTOR, Q.C.:</p> <p>4 Q. So in terms of--so you pulled--their chart is</p> <p>5 pulled and you check and see that the person</p> <p>6 is ER negative, and do I understand you to say</p> <p>7 only if they asked am I part of the retest,</p> <p>8 you would tell them you're likely part of the</p> <p>9 retest or would you offer to them, look, I see</p> <p>10 that you're ER negative --</p> <p>11 DR. LAING:</p> <p>12 A. Oh, no, we'd offer that to them.</p> <p>13 CHAYTOR, Q.C.:</p> <p>14 Q. So you would talk to them?</p> <p>15 DR. LAING:</p> <p>16 A. Oh, yes.</p> <p>17 CHAYTOR, Q.C.:</p> <p>18 Q. So anyone that you had a chart before you and</p> <p>19 a person standing there with you, you would</p> <p>20 look and see, oh, you're ER negative, confirm</p> <p>21 that they hadn't been on anti-hormone therapy</p> <p>22 before that and say to them that you are part</p> <p>23 of the retest?</p> <p>24 DR. LAING:</p> <p>25 A. Yeah, when we see a patient in the clinic, we</p>
<p>Page 305</p> <p>1 check her--for the most part, her or his</p> <p>2 chart, and make sure--and determine whether or</p> <p>3 not they should be in the retest group or not?</p> <p>4 DR. LAING:</p> <p>5 A. Yes. So we would be--you know, so someone was</p> <p>6 coming in the clinic and they had breast</p> <p>7 cancer, you'd be sort of looking to see, you</p> <p>8 know, is this someone who's likely going to be</p> <p>9 in that retesting because of where they were.</p> <p>10 If they had asked the question, I'd say, yes,</p> <p>11 you will be retested and once we know that, we</p> <p>12 will give you the results. Patients who are</p> <p>13 on well follow-up are often seen about every</p> <p>14 six months by the medical oncologist. So, of</p> <p>15 course, there would have been a number of</p> <p>16 people who just simply would not have fallen</p> <p>17 into the time period to have a visit during</p> <p>18 that period of time. The people that we would</p> <p>19 have been seeing more frequently would have</p> <p>20 been the people who had metastatic disease,</p> <p>21 and, of course, the people who were having</p> <p>22 their adjuvant therapy currently.</p> <p>23 CHAYTOR, Q.C.:</p> <p>24 Q. Or the people who fell within--their six month</p> <p>25 visit fell within that Fall?</p>	<p>Page 307</p> <p>1 always have their chart.</p> <p>2 CHAYTOR, Q.C.:</p> <p>3 Q. Yes.</p> <p>4 DR. LAING:</p> <p>5 A. Even if somebody drops in, we, say, pick up</p> <p>6 the chart and then you go see the patient</p> <p>7 because, of course, that's where you have the</p> <p>8 information, and in the chart at the top of</p> <p>9 each progress note, we would have a summary of</p> <p>10 how they would be treated.</p> <p>11 CHAYTOR, Q.C.:</p> <p>12 Q. Yes.</p> <p>13 DR. LAING:</p> <p>14 A. So it would --</p> <p>15 CHAYTOR, Q.C.:</p> <p>16 Q. So it would be very easy to check because it's</p> <p>17 right up --</p> <p>18 DR. LAING:</p> <p>19 A. And if it wasn't clearly written there, then,</p> <p>20 you know, you could go to the pathology</p> <p>21 section and see if it was there, and, you</p> <p>22 know, see if this was someone who would be</p> <p>23 involved in the retest, and explain to them</p> <p>24 that when the results came back, we would look</p> <p>25 at that and discuss it and decide.</p>

1 CHAYTOR, Q.C.:

2 Q. So anyone who came to see you during that time

3 period who was ER negative and had not been

4 treated, you would have indicated to them that

5 the retest is happening, they will be

6 retested, and that we'll be back in touch with

7 them?

8 DR. LAING:

9 A. Right, and even for some of those patients,

10 you know, we wouldn't say that you are--this

11 means that we are going to give you. We would

12 say, well, we're going to look at that result

13 and then see.

14 CHAYTOR, Q.C.:

15 Q. We'll be back to you.

16 DR. LAING:

17 A. Yeah.

18 CHAYTOR, Q.C.:

19 Q. So any patients that came to you would have

20 been told that. How about the other

21 oncologists, were they also told to do the

22 same thing?

23 DR. LAING:

24 A. So they would have been--you know, they would

25 have been doing the same thing. We would have

1 had patients--you have to realize that we were

2 getting phone calls not only from the breast

3 cancer patients, but from many, many cancer

4 patients. You know, you hear something in the

5 news, you're not certain--all you hear is the

6 word cancer; you've been a cancer patient,

7 you're concerned, so we had phone calls from

8 people with different malignancies, we had--

9 you know, we had a lot of people coming into

10 the clinic and saying, well, if this--okay,

11 this is about breast cancer, then why is it--

12 is it about my cancer too, and just trying to

13 explain how this test was used as a predictive

14 marker. We certainly had people who had breast

15 cancer saying, well, do I still have cancer;

16 we'd say, yes, you know, this doesn't change

17 the diagnosis, and--so there was a lot of

18 questions from patients.

19 CHAYTOR, Q.C.:

20 Q. And seemed to be a lot of confusion--from the

21 kinds of questions that you're saying, there

22 seemed to be a lot of confusion amongst the

23 patients?

24 DR. LAING:

25 A. Yeah. You know, when--at this point, we're in

1 October, 2005. We're dealing with this, this

2 is all happening, and many things going on.

3 I'm sure we'll talk over the next day about

4 other times when letters came out, but, you

5 know, each time this issue came and became a

6 public issue again, be it at the times that we

7 know about when we did the press release in

8 2006, be it, you know, May of 2007, be it the

9 start of your work here just this last Spring,

10 often every time this has come out, we would

11 still get phone calls from patients to say can

12 you tell me again now what this was about, and

13 am I okay, and what does this mean.

14 CHAYTOR, Q.C.:

15 Q. Yes.

16 DR. LAING:

17 A. So it is somewhat of a complex issue and --

18 CHAYTOR, Q.C.:

19 Q. So, Doctor, my question about the other

20 oncologists then, if the other oncologists are

21 meeting with patients throughout that Fall

22 while the retesting is going on, were they

23 also told to do the same thing, what your

24 practice was?

25 DR. LAING:

1 A. Sure.

2 CHAYTOR, Q.C.:

3 Q. To check their chart, find out whether or not

4 they are part of the group, speak to them

5 about it, tell them someone will be in touch

6 with them?

7 DR. LAING:

8 A. Yeah, this was something that all the

9 oncologists--not only the medical oncologists,

10 but the radiation oncologists who were seeing

11 the patients, you know, people that were

12 coming through the door would ask questions.

13 CHAYTOR, Q.C.:

14 Q. So everybody was told that's the practise,

15 that's what we should do. What about then in

16 terms of--you've identified through the chart

17 that this is a person who likely should be

18 part, in your opinion, should be part of the

19 retest. Would you then do anything to make

20 sure she, in fact, had been captured, for

21 example, just put a Post-It note on her file

22 for your assistant and say make sure this

23 person is on the list? Would you do anything

24 like that?

25 DR. LAING:

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<p>1 A. No, I don't think at the time that we did. 2 You know, I don't remember calling Nancy 3 Parsons myself and saying can you make sure 4 that this person is being retested. You know, 5 I think that we just assumed that they were in 6 that retest. We had made contact with them. 7 Certainly if they hadn't heard anything as 8 time went on, you know, many, many of these 9 patients called us back and said have you 10 heard anything yet, have you heard anything 11 yet. So, you know, there was for many 12 patients fairly regular contact between us and 13 them during this process as they waited for 14 their results. 15 CHAYTOR, Q.C.: 16 Q. And I take it at this point in time then, 17 Doctor, as you're seeing those patients 18 throughout the Fall, October, November, into 19 December, did you have any concerns yourself 20 that the list may not be thorough, the list 21 from which the retest was happening? Did you 22 have any concerns that there are people who 23 aren't on the list that perhaps should be on 24 the list? 25 DR. LAING:</p>	<p>1 and under business arising it says, "ER/PR 2 testing. Dr. Laing provided a brief update on 3 the ER/PR testing. Results for the ER/PR 4 testing are coming back and patients are being 5 notified. Dr. Laing and Dr. Ganguly will be 6 attending a tumour board rounds meeting this 7 afternoon to review cases and discuss 8 appropriate actions. It was noted that this is 9 not a cancer clinic issue, but a lab issue, 10 however, which affects our patients. Any 11 calls that staff review", I think should be 12 receive, "regarding ER/PR testing and 13 reporting should be directed to Nancy Parsons 14 at quality initiatives". So it appears at 15 this point in time Nancy is indicated to be 16 the contact? 17 DR. LAING: 18 A. Yes. 19 CHAYTOR, Q.C.: 20 Q. Appropriate contact person? 21 DR. LAING: 22 A. Yeah. 23 CHAYTOR, Q.C.: 24 Q. And it says you're going to be attending 25 tumour board rounds meeting, and I take it</p>
<p>1 A. Not that I can recall in those early days, no. 2 CHAYTOR, Q.C.: 3 Q. If we could have, please, P-0432. Let's try 4 431. I think we just jumped ahead of my whole 5 -- 6 DR. LAING: 7 A. January, 2007. 8 CHAYTOR, Q.C.: 9 Q. I think I have the wrong date. That one looks 10 like it's '07 too. I'm not going to ask you 11 to try and read that because I don't even 12 think that's a doctor's writing. Let's try 13 639, please. We'll come back to those. 14 That's better. That's the--this is a meeting 15 of October 13th, 2005, and it's an agenda, a 16 meeting of senior management. 17 DR. LAING: 18 A. Of senior management. 19 CHAYTOR, Q.C.: 20 Q. Of the NCTRF at the time, and this indicates 21 that there's--on business arising, "ER/PR 22 testing", and the minutes then are attached 23 and Dr. Gardiner is present, Dr. Ganguly, 24 yourself, Ms. Pilgrim, Ms. Power, and Ms. 25 Michelle Gregory, as the recording secretary,</p>	<p>1 October 13th would be the first day that the 2 tumour board panel actually met? 3 DR. LAING: 4 A. Is this the same day as that? This is a 5 Thursday? 6 CHAYTOR, Q.C.: 7 Q. That's right. 8 DR. LAING: 9 A. Yeah. 10 CHAYTOR, Q.C.: 11 Q. So it's the physician review panel. 12 DR. LAING: 13 A. Yes. 14 CHAYTOR, Q.C.: 15 Q. And sometimes that gets confusing because it 16 is referred to as the tumour board as well. 17 DR. LAING: 18 A. Well, we try and--yeah, I mean, it was a 19 tumour board, but we called it the panel to 20 try and think about it as being separate, 21 although the premise of it was the same. 22 CHAYTOR, Q.C.: 23 Q. Doctor, what did this mean, "It was noted that 24 this is not a cancer clinic issue, but a lab 25 issue"? What did that mean?</p>

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1 DR. LAING:  
 2 A. I think that just simply referred to the fact  
 3 that, you know, that this was a report that  
 4 came from the lab and that the retest and, you  
 5 know, the list of patients who were being  
 6 retested and all that was something that the  
 7 lab people had and that was why, I think, a  
 8 decision was made to forward inquiries to  
 9 Nancy Parsons so that patients would be able  
 10 to know directly from her whether or not they  
 11 were being retested. This was--you know, this  
 12 was minutes that were meant to reflect the  
 13 discussion. You know, certainly this was  
 14 always felt by the physicians at the cancer  
 15 clinic to be an issue for us because,  
 16 obviously, these were our patients and these  
 17 were people that we were seeing. So, you know,  
 18 it's--when I look at it written that way, you  
 19 know, it certainly was an issue that was very  
 20 important to us at the cancer clinic and one  
 21 that we took very seriously.  
 22 CHAYTOR, Q.C.:  
 23 Q. And if we could have, please, P-0308, and I  
 24 will take you to the tumour board panel, but I  
 25 think we'll start that tomorrow because we're

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1 running short on time. So I'll just take you  
 2 to a couple of other points. This is an e-  
 3 mail Heather Predham wrote October 18th, 2005.  
 4 Again it's to yourself, Ms. Pilgrim, Dr.  
 5 Williams, and Susan Bonnell.  
 6 DR. LAING:  
 7 A. Is this the same one that we looked at  
 8 earlier?  
 9 CHAYTOR, Q.C.:  
 10 Q. This is the same one, I think, that we did  
 11 look at.  
 12 DR. LAING:  
 13 A. Yeah.  
 14 CHAYTOR, Q.C.:  
 15 Q. It is--oh, yes, it's without the copy, that's  
 16 right, and I just wanted to--I didn't bring to  
 17 your attention at the time, it is the same  
 18 exhibit without the attachment, that's right.  
 19 DR. LAING:  
 20 A. Okay.  
 21 CHAYTOR, Q.C.:  
 22 Q. She indicates, "Before we send it out, we have  
 23 to consider the following; the patients from  
 24 St. Pierre, patients in nursing homes and  
 25 personal care homes, will we send this letter

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1 out by registered mail through one central  
 2 area, and I guess we also have to remember  
 3 that we will get a negative reaction from the  
 4 letters, everything from timing, upsetting  
 5 people with no information, and, of course, we  
 6 will send some unintentionally to people who  
 7 have died. I guess we should compare the  
 8 mailing list to the obituaries to ensure that  
 9 we don't send letters to the recently  
 10 deceased. Finally, I think we should be aware  
 11 we will not be able to notify everyone.  
 12 Several on the list have moved and we have no  
 13 other contact information".  
 14 DR. LAING:  
 15 A. Uh-hm.  
 16 CHAYTOR, Q.C.:  
 17 Q. That's what I was just wondering, in terms of  
 18 seeing people that were coming through and  
 19 having these caveats spoken of by Ms. Pilgrim  
 20 on the 18th, did it cause you any concern that  
 21 --I'm sorry, Ms. Predham--did it cause you any  
 22 concern that she--that they may be having  
 23 difficulty trying to organize information or  
 24 identify who the patients are and how they  
 25 should be contacted?

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1 DR. LAING:  
 2 A. You know, that whole sort of issue about  
 3 finding patients and identifying patients,  
 4 and, you know, we know as time went on, and we  
 5 know even to this day that there were people  
 6 that were not found by various different  
 7 means, and--but at that time, I think if  
 8 anything, we had such a volume of people that  
 9 we were seeing and dealing with, you know,  
 10 back in those early days, that wasn't  
 11 something that I can recall thinking about. I  
 12 know that as time went on, there were some  
 13 patients that--I remember talking about who  
 14 had been my own patients, and we really didn't  
 15 have a way that we could get in contact with  
 16 them again and various different things had  
 17 been tried, but that would have been just a  
 18 very few people that I can remember at that  
 19 time.  
 20 CHAYTOR, Q.C.:  
 21 Q. And, Doctor --  
 22 DR. LAING:  
 23 A. The whole issue about the deceased patients  
 24 was one that we had talked about because even  
 25 --as I said, even we wouldn't necessarily know



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1 that patients had died. I recall that when we  
 2 would ask for the list for tumour board  
 3 rounds, that after a while we realized that if  
 4 patients were deceased, that their charts  
 5 would be stored off site, and, you know, we  
 6 could then recognize if a chart wasn't there,  
 7 we'd think, oh, that might be someone who has  
 8 died and subsequently their cancer clinic  
 9 chart was stored off site, but to be able to  
 10 go in right away, either to our OPUS system or  
 11 whatever and readily identify a list of  
 12 patients who were deceased at the time wasn't  
 13 something that was easy to do, and, in fact,  
 14 we did panel some patients who subsequently  
 15 before the letter was sent out, we discovered  
 16 that they were, in fact, through some queries  
 17 had found that they were people who had  
 18 actually died.

19 CHAYTOR, Q.C.:

20 Q. After you had already --

21 DR. LAING:

22 A. Yeah, discussed it. So we may not even have  
 23 known when we talked about people that they  
 24 had died.

25 CHAYTOR, Q.C.:

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1 Q. Doctor, what happened in that situation, what  
 2 happened with the information or the  
 3 recommendation that came out of--for that  
 4 deceased patient or the--I think it happened a  
 5 couple of times.

6 DR. LAING:

7 A. We didn't--if we knew before the letter was  
 8 sent, then we didn't send the letter. And we  
 9 put those patients into the side pile, if you  
 10 will, for dealing with the patients who had  
 11 been deceased after we had finished dealing  
 12 with the patients that were alive.

13 CHAYTOR, Q.C.:

14 Q. And do you know ultimately what happened with  
 15 the information, the opinion of the panel with  
 16 respect to those people?

17 DR. LAING:

18 A. I'm not certain, no.

19 CHAYTOR, Q.C.:

20 Q. When people would call you in this time period  
 21 in October and you were receiving calls from  
 22 the patients, what did you do with that  
 23 information? So, if somebody called you and  
 24 had an inquiry, what did you do with the fact  
 25 that you had received contact from a

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1 particular person?

2 DR. LAING:

3 A. Sometimes, I would have put a note in the  
 4 chart, but not always. And if I had told the  
 5 patient that, you know, when the results came  
 6 available, that we would be in contact with  
 7 them, then I would have just waited until they  
 8 came through to me through the panel or  
 9 through the process of the new results being  
 10 sent out to us as the attending physicians.

11 CHAYTOR, Q.C.:

12 Q. So, in terms of passing on to the quality  
 13 initiatives department, Heather Predham or  
 14 anyone else, would you pass that information  
 15 on?

16 DR. LAING:

17 A. That someone had called?

18 CHAYTOR, Q.C.:

19 Q. Yes, that you had received contact.

20 DR. LAING:

21 A. I know that as time went on we certainly did  
 22 share that information, but I can't tell you  
 23 exactly when it was that we would have started  
 24 to do that.

25 CHAYTOR, Q.C.:

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1 Q. So, why did you start the practice? Was it  
 2 suggested to you that that would be something  
 3 you should or how is that you came to do that?

4 DR. LAING:

5 A. I think it was because we, you know, as the  
 6 tumour panel started, Heather was part of that  
 7 and so, we would have spent a lot of time, you  
 8 know, sitting in a room and going over the  
 9 list of patients. And you know, if we knew  
 10 that someone had notified us or vice versa, if  
 11 they had gotten a query from a patient and  
 12 they didn't feel they were able to answer the  
 13 question, then they would have sent us an e-  
 14 mail or a note that the patient, or a phone  
 15 call that the patient had called. But I don't  
 16 recall in the early days, that we had a direct  
 17 sort of, communication back and forth between  
 18 people. And I think at the end of the day  
 19 that we should have had a keeper of a list and  
 20 that that person should have, you know--I  
 21 think that what was happening is that a bunch  
 22 of very, very well intentioned people were  
 23 dealing with their little pieces of this and  
 24 then I think that when I look back, that if  
 25 there had been one person who was co-

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1 ordinating that and was a central, you know,  
2 place -  
3 CHAYTOR, Q.C.:  
4 Q. Central registry for all the information.  
5 DR. LAING:  
6 A. - for registry for all the patients' contact,  
7 I think that would have been much, much  
8 better. But we were dealing with the issue,  
9 with what we had and -  
10 CHAYTOR, Q.C.:  
11 Q. So, nobody had that role? To your knowledge,  
12 nobody had that role?  
13 DR. LAING:  
14 A. No.  
15 CHAYTOR, Q.C.:  
16 Q. So, if we look at the names of the people in  
17 this e-mail, by the middle of October, why are  
18 you still being included in any decision  
19 making around patient contact?  
20 DR. LAING:  
21 A. I guess because I had given opinions and this  
22 is something that I had discussions in right  
23 back from August, July and August, but -  
24 CHAYTOR, Q.C.:  
25 Q. And did you consider yourself still to be part

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1 of the committee that was managing the issue?  
2 DR. LAING:  
3 A. I didn't consider myself to be a big part of  
4 that because I'd felt I had moved on to  
5 chairing the tumour panel and to the roles and  
6 responsibilities associated with that.  
7 CHAYTOR, Q.C.:  
8 Q. And so that's where you saw your piece to be in  
9 the whole thing by this point in time.  
10 DR. LAING:  
11 A. Yes.  
12 CHAYTOR, Q.C.:  
13 Q. And Ms. Pilgrim, what did you understand her  
14 role to be?  
15 DR. LAING:  
16 A. Well, she was taking over as the--this is  
17 2005, we're still in our transition into  
18 Eastern Health and cancer care was her  
19 responsibility. So, she was involved at that  
20 time as a senior person to help co-ordinate  
21 this.  
22 CHAYTOR, Q.C.:  
23 Q. And Dr. Williams, what was his role?  
24 DR. LAING:  
25 A. Well, I mean, as you know, he had been

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1 involved with this issue for quite some time  
2 and continued to be one of leads. And you  
3 know, really it was him who, through Allan  
4 Kwan, had come up with the idea of having the  
5 tumour panel, be a tumour board for this issue  
6 and he was the one who had asked me to chair  
7 it. And so he was still very much a lead  
8 person involved in this for sure.  
9 CHAYTOR, Q.C.:  
10 Q. Okay. And in the fall then of 2005, are you  
11 involved in any further meetings with  
12 government on the issue?  
13 DR. LAING:  
14 A. In the fall of 2005? No.  
15 CHAYTOR, Q.C.:  
16 Q. Okay. Were you involved in meetings with  
17 government on other issues, for example, the  
18 Herceptin issue?  
19 DR. LAING:  
20 A. Yes.  
21 CHAYTOR, Q.C.:  
22 Q. Do you recall attending meetings regarding  
23 that?  
24 DR. LAING:  
25 A. Yes. So, at that same time, you know, as you

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1 can imagine, the day-to-day running of a  
2 cancer care program continues, we're in this  
3 transition period, we have a lot of issues  
4 related to drug coverage. We had made a  
5 presentation and had written, looking for  
6 funding for Herceptin for the Trastuzumab.  
7 And one of the things that that really struck  
8 home for us--because that meeting was in June  
9 of 2005, the American Society of Clinical  
10 Oncology meeting that showed such a tremendous  
11 benefit to this treatment. Some provinces  
12 were, sort of, lined up and ready to go and  
13 had funding secured by that summer and we were  
14 one of the last provinces to secure funding.  
15 And we felt that we would really like to, on a  
16 go forward basis, be able to say, look these  
17 are the things that are coming down the line  
18 and, in fact, that's what we did with Avastin  
19 and Folfex. So, yes, you know, we continued  
20 to--we had a presentation with government and  
21 subsequently, I did meet again with Minister  
22 Ottenheimer just prior to the press release  
23 that announced, around this time, I believe it  
24 was, some time in October of 2005, that indeed  
25 the government did fund and continue to fund

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1 this very important treatment for our  
 2 patients.  
 3 CHAYTOR, Q.C.:  
 4 Q. And in those meetings, do you recall any  
 5 issues of ER/PR coming up? Do you recall the  
 6 minister or anybody on his staff or anyone in  
 7 the Department of Health asking you anything  
 8 about the ER/PR issue?  
 9 DR. LAING:  
 10 A. When we had had the meeting and made the case  
 11 for the Herceptin, just prior to announcing  
 12 the funding, Minister Ottenheimer asked if I  
 13 would come by and have a look at the media  
 14 briefing or the press release or whatever you  
 15 would call it that he had prepared with his  
 16 assistant. And I can't remember her name,  
 17 maybe it was Tanis or -  
 18 CHAYTOR, Q.C.:  
 19 Q. Tansy Mundon?  
 20 DR. LAING:  
 21 A. Tansy, that's right. And so I had gone by the  
 22 Department of Health and had looked at that  
 23 with the Minister and really, he was very  
 24 pleased that--it was a big deal to get funding  
 25 in the tune of a million dollars for a drug at

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1 not budget time. So, we were very pleased  
 2 with their decision to give us the funding to  
 3 get things going right away. And at that  
 4 time, one of his assistants, I believe it was  
 5 Mr. Hynes was there, and I would have said,  
 6 yes, we have started the panel, the results  
 7 are coming back and that would have been a  
 8 very brief discussion only that we would have  
 9 had about that at the time, that I can recall.  
 10 CHAYTOR, Q.C.:  
 11 Q. Okay. So, you recall Mr. Hynes asking you  
 12 about it?  
 13 DR. LAING:  
 14 A. I think they both did. He happened to be  
 15 there as well. And me saying that, you know,  
 16 we've decided to do this tumour panel and  
 17 results are coming back and we're reviewing it  
 18 and making recommendations.  
 19 CHAYTOR, Q.C.:  
 20 Q. Do you recall him asking whether or not there  
 21 are people who could have been impacted by  
 22 this delay in having had the treatment and in  
 23 particular, whether or not anyone who was  
 24 deceased could have been impacted by not  
 25 having had the treatment?

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1 DR. LAING:  
 2 A. Yeah. Do I recall having that conversation  
 3 with him specifically, no, but I've been asked  
 4 about this subsequently, and I certainly would  
 5 have said to him, you know, this is a  
 6 treatment that in the adjuvant setting is  
 7 given to try and reduce the risk of the cancer  
 8 coming back and reduce the risk of mortality.  
 9 So yes, there would have been people that, you  
 10 know, had been said to be negative who would  
 11 not have received these therapies, and it is  
 12 potential that those patients may have had a  
 13 relapse that could have been avoided by having  
 14 had Tamoxifen, and I certainly would have said  
 15 that type of thing to him and to many other  
 16 people subsequent, or people who would ask me  
 17 today the same question.  
 18 I don't recall having a specific--you  
 19 know, subsequently, we did have discussions  
 20 around the deceased patients, but that's not  
 21 something that I remember, you know, strongly  
 22 from that interaction. I remember it as being  
 23 a very pleasant visit and mostly because of  
 24 the significance of the funding for the  
 25 Herceptin.

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1 CHAYTOR, Q.C.:  
 2 Q. Okay, and -  
 3 THE COMMISSIONER:  
 4 Q. Ms. Chaytor, it's past the 5:00 time, so  
 5 wherever it's a convenient spot. If you're in  
 6 the middle of something, complete it, but.  
 7 CHAYTOR, Q.C.:  
 8 Q. Sure, yes. That's fine. Just before I leave  
 9 that then, on the Herceptin proposal or the  
 10 meetings around the Herceptin and what you saw  
 11 in terms of the media proposal on it, were you  
 12 ever aware of any linkage being made in terms  
 13 of the decision to fund the Herceptin and that  
 14 having anything to do with offsetting any  
 15 negativity messaging about the ER/PR issue?  
 16 DR. LAING:  
 17 A. Oh no, absolutely not. I mean, this was  
 18 because of, at that time, three large  
 19 international phase three trials that showed a  
 20 tremendous benefit in terms of decreased  
 21 disease free survival and improved--or  
 22 improved, sorry, disease free and overall  
 23 survival. I think it's a mere coincidence  
 24 that it happened at the same time, and I never  
 25 ever felt at all that the two were linked in

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1 any way.

2 CHAYTOR, Q.C.:

3 Q. And any document suggesting anything in terms

4 of -

5 DR. LAING:

6 A. Absolutely not.

7 CHAYTOR, Q.C.:

8 Q. - negativity in the messaging?

9 DR. LAING:

10 A. No.

11 CHAYTOR, Q.C.:

12 Q. And offsetting that, you've never seen

13 anything along those lines?

14 DR. LAING:

15 A. No, no.

16 CHAYTOR, Q.C.:

17 Q. And perhaps if we could just bring up then, P-

18 1533, page 19? And then that'll be it, I

19 promise, for today. The story, and it's

20 referring to "the ER/PR story has received

21 national media attention," and it goes on and

22 quotes a recent CBC story, what it was titled,

23 warning that "medical technology expert warned

24 that a lab problem that occurred in

25 Newfoundland and Labrador could be repeated

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1 across the country. Given the negative

2 coverage of this story and the resulting lack

3 of confidence among breast cancer patients and

4 the reliability of testing procedures in the

5 province, it is important that government

6 respond with positive messages about the

7 introduction of Herceptin to the provincial

8 systemic therapy, chemotherapy program." So

9 anything of that nature, that wasn't brought

10 to your attention in what you saw, in terms of

11 media releases or whatever?

12 DR. LAING:

13 A. No. No, and again, I stress the timing was

14 because it was the same timing in the rest of

15 the country, and in fact, in the world. You

16 know, this was when--the summer and fall of

17 2005 is when everybody was coming out with

18 their recommendations. It was in fact when we

19 as a group in Atlantic Canada wrote our very

20 first Atlantic Canada guideline with the

21 oncologists in the rest of Atlantic Canada

22 addressing adjuvant Herceptin and those

23 issues.

24 CHAYTOR, Q.C.:

25 Q. Okay. Thank you, Doctor. Thank you,

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1 Commissioner.

2 DR. LAING:

3 A. Okay.

4 THE COMMISSIONER:

5 Q. All right then, we'll meet at 9:30 in the

6 morning. Thank you.

7 Upon conclusion.

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1

2 CERTIFICATE

3

4

5 I, Judy Moss, hereby certify that the foregoing is

6 a true and correct transcript in the matter of the

7 Commission of Inquiry on Hormone Receptor Testing,

8 heard on the 16th day of September, A.D., 2008

9 before the Honourable Justice Margaret A. Cameron,

10 Commissioner, at the Commission of Inquiry, St.

11 John's, Newfoundland and Labrador and was

12 transcribed by me to the best of my ability by

13 means of a sound apparatus.

14

15 Dated at St. John's, Newfoundland and Labrador

16 this 16th day of September, A.D., 2008

17

18

19

20 Judy Moss

**Inquiry on Hormone Receptor Testing**

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