COMMISSION OF INQUIRY
ON HORMONE RECEPTOR TESTING

BEFORE THE HONOURABLE JUSTICE CAMERON - COMMISSIONER

October 9, 2008

Appearances:

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

Rolf Pritchard, Jackie Brazil, Q.C. . Her Majesty in Right of NL

Peter Browne, Q.C./Jane Hennebury . . . Doctors Kara Laing et al

Daniel Simmons . . . . . Eastern Regional Integrated
. . . . . Health Authority

Chesley Crosbie, Q.C.. . . . . Members of the Breast Cancer
. . . . . Testing Class Action

Mark Pike, Q.C. . . . . NL Medical Association
Jennifer Newbury . . . . . Canadian Cancer Society (NL Division)
Blair Pritchett. . . . . Central, Western and Labrador-Grenfell
Regional Integrated Health Authorities

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THE COMMISSIONER:
Q. Mr. Coffey.
COFFEY, Q.C.:
Q. Commissioner, the next witness is Dr. Emina Torlakovic.
DR. EMINA TORLAKOVIC, SWORN, EXAMINATION BY BERNARD COFFEY, Q.C.
REGISTRAR:
Q. Would you please state and spell your complete name for the Commission?
DR. TORLAKOVIC:
A. Emina Torlakovic, E-M-I-N-A, T, as in Tom, O-R-L-A-K-O-V-I-C.
REGISTRAR:
Q. Thank you.
COFFEY, Q.C.:
Q. Thank you, Doctor. Commissioner, there are three new exhibits, please, they are Exhibits 3360, 3361 and 3362.
THE COMMISSIONER:
Q. Entered.
EXHIBITS ENTERED AND MARKED P-3360 THROUGH P-3362, INCLUSIVE.
COFFEY, Q.C.:
Q. Thank you. Registrar, when you're ready,

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please, Exhibit P-3360? Doctor, is this your curriculum vitae?

DR. TORLAKOVIC:

A. Yes, it is.

COFFEY, Q.C.:

Q. And, Doctor, as well, I understand that you have prepared a PowerPoint presentation to assist, well, in effect, assist me in leading you through your testimony here today. So I'm going to ask, please, Registrar, if you could bring up Exhibit P-3361?

REGISTRAR:

Q. Actually, Mr. Coffey, I'm going to bring up the PowerPoint presentation itself.

COFFEY, Q.C.:

Q. Okay, yeah, thank you. I appreciate that. And that's the presentation, Doctor, itself?

DR. TORLAKOVIC:

A. Yes, it is.

COFFEY, Q.C.:

Q. Okay. And if we could go to the page, the second page, please, Registrar? Doctor, I take it that this is really an outline here on this page of your academic and your professional background?

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DR. TORLAKOVIC:

A. Yes, it's a summary. It basically shows my training, education and training in the special skill of pathology and my credentials.

COFFEY, Q.C.:

Q. Take us through, please then, your academic and your professional background, go ahead?

DR. TORLAKOVIC:

A. I have attended and graduated medical school in Croatia, actually, that was former Yugoslavia at the time, in Zagreb Medical School and I graduated in 1986. And so afterwards I moved to United States to continue my education. I have spent two years in New York City at Columbia University affiliated hospital, St. Luke's/Roosevelt, actually, it's two hospitals together, where I have spent one year in anatomic pathology and one year in clinical pathology; after which we moved to University of Minnisota where I continued my education in pathology as a resident for next two years also doing anatomic and clinical pathology; and after which, I mean, the reason for moving there was my interest in the program that they had

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because they had excellent fellowship programs in surgical pathology and hematopathology, somewhat the best in the country. And I have continued after my residency there fellowship in hematopathology and two years of fellowship in surgical pathology where I did a lot of training in molecular biology and in addition to that cytology. And after which I actually moved to Oslo, to Norway, where I was recruited as a pathologist with adequate background to help establish a modern immunohistochemistry laboratory for their national cancer institute equivalent, which was Norwegian Radium Hospital at the time, and that was the name, the Det Norske Radium Hospital. So when I moved in 1997, I have spent there seven years working, my main task, my main job was to work in immunohistochemistry laboratory where I also started some national and international project in quality control and so on. So I think that, I don't know if it's the time to mention these details or not, but I would like to mention it because I think it's pertinent to this testimony overall. So after I moved

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to Norway and started to work in that particular lab that I had a large number of cancer patients, so that immunohistochemistry is a critical tool for the pathologist to properly classify the diseases and also to identify prognostic and predictive markers for these cancers. I noticed that as a consultation specimens that you were getting from local hospitals that there was great variability -

COFFEY, Q.C.:

Q. Doctor -

DR. TORLAKOVIC:

A. - in their outcomes.

COFFEY, Q.C.:

Q. If I could?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. I just ask you just to slow down? You speak even--here in Newfoundland we speak very quickly and you speak as fast or even faster, okay.

DR. TORLAKOVIC:

A. All right.

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COFFEY, Q.C.:
Q. So if you could just because I'm following you and I appreciate -
DR. TORLAKOVIC:
A. A little bit slower.
COFFEY, Q.C.:
Q. If you would, please?
DR. TORLAKOVIC:
A. Okay, fine.
COFFEY, Q.C.:
Q. Thanks.
DR. TORLAKOVIC:
A. I will.
COFFEY, Q.C.:
Q. So you were saying, Doctor, you had noticed in the course of your practice there that you were seeing samples from regional hospitals in the area who were coming in?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Could you--okay, I'm sorry, Doctor, go ahead?
DR. TORLAKOVIC:
A. With very variable results. And I just wanted why is this happening and why there is no

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program that would help laboratories achieve better results. So therefore I started an initial--I attempted to start the national Norwegian program that would help improve quality. Norway as most--I shouldn't say most, because I actually don't know the number, but I know that many countries in the Europe have laboratories that do not need to be accredited and there is no need for certification of specialized, many specialized tests and therefore immunohistochemistry was not regulated as laboratory technique at all.
COFFEY, Q.C.:
Q. And, Doctor, what year would this have been? What years would this be, around 19?
DR. TORLAKOVIC:
A. This was 1997, '98.
COFFEY, Q.C.:
Q. Okay. Go ahead, Doctor, I'm sorry.
DR. TORLAKOVIC:
A. And so at that time my initial pilot study, some of the results I'm going to show later in this presentation, showed that there was very high difference between the laboratories.

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Some achieved excellent results and some achieved very poor results, but all of the participants believed that their results were actually good. So there was a component that I noticed, an educational component that was missing in the insight to what results are supposed to look like, what are the expected outcomes. It's very difficult to improve on any technique or any results if the achieved goal is not fully understood or known. And Norway was actually too small of a country to have a strong program, because there are just a small number of laboratories that are present. And at the same time there was an initiative from a company that is making--that is producing reagents for immunohistochemistry, the branch of them, it's DAKO Nordic was that they thought they wanted to do something that would be of interest to improve the qualities. Many of the reagent producing companies try to do and even more so today they pay attention to quality issues a lot. And so when they become aware, as they are continuously aware, I think that this is the area that needs more standardization and

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improvement, they do try to collaborate with professionals in the certain areas. And this was the case they have actually provided funds for representatives from Scandinavian countries to get together and to discuss this issue. And this was just in the very beginning of that initiative that actually ended up creating a Scandinavian quality control program that is called NordiQC. I was the Norwegian representative and was there from the first types of its inception until I left Europe and moved to Canada, which was in December, 2003.

I think it's important I shall emphasize here for the benefit of NordiQC and many other programs that are supported occasionally with funds from the industry that NordiQC was, even though it was, even though the company paid for the travel cost and hotel accommodation costs, there was, it was all the time from the very beginning a profession dissociation from the company, from the reagents they supply or any preference to their products. It is true that at the time our lab was using products from DAKO company, but we have chosen to do so

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before this initiative because we thought that the products that they were using were good for us. It doesn't mean that there aren't other companies that are producing excellent if not better products, makes no difference at all, but at the moment we were using--and I do want to emphasize again that this organization is totally independent and currently is actually supported by several different companies also that are posted on their home website clearly as supporters.

So the point about NordiQC is that just that together these four countries now. So it was Denmark, Norway, Sweden and Finland, they were big enough with large enough, large number of laboratories that this program actually could make sense and also provided enough of highly qualified specialists to be able to do what we call in quality assurance program assessments.

Assessments are a critical part of a quality assurance programs because experts are evaluating the results of laboratories and making a judgment of how good the results are and also at the same time they could and often

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make the conclusions and recommendations what can be changed that the results should be improved. This is not a part of practice of every external quality assurance program, but when that part is missing, then the feedback that laboratory is getting is of very limited value. So I personally believe that NordiQC has become what it has become as external quality assurance program so important and useful to laboratories in Scandinavia because it does provide this feedback and helped laboratories to change and improve these results.

I do want to mention that there are other organizations that with even longer history, of course, and probably the most famous one is UK NEQAS that was originally created to support external quality assurance and have accreditation of laboratories in United Kingdom. In '80, '84 I believe they started their module on immunocytochemistry, they call it, but it's basically immunohistochemistry. And since then large number of laboratories from outside of UK, that means European and globally have decided to participate in their

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program and use their expertise to improve what they do. However, it is interesting that their own results show that from run to run results do improve for UK laboratories which accreditation depends on the results they produce in this program. But they did not improve according or not to that degree in those other laboratories that are international laboratories that are participating because most of this--well, not to say most, I don't know the number, but I know that in many of these laboratories this is not follow--this is not a requirement for accreditation and therefore there is not follow up with the requirement for accreditation, the success is much less. They continue to repeat the same sub-optimal practice from one run to another.

And that's why am I mentioning this at all, I'm mentioning because I want to point out that external laboratory assurance programs are not sufficient if they're not linked to appropriate accreditation. But on the other hand, I also want to credit NordiQC which still today functions with most of the

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labs, this is not a requirement for accreditation, their participation, but they have seen great improvements from one run to another assuring that direct feedback and close communication with laboratories and emphasis on education and posting the results on the internet really available that all of that in itself, even without requirements for accreditation can change the practice how laboratories function.

COFFEY, Q.C.:

Q. Okay, so, Doctor, what I'd like to do is, if I could, ask, please, if perhaps we could go to the next--let me see there. The next slide, I'll take you through this, your own personal background first so the Commissioner gets--and I appreciate you've given us an overview. The Commissioner get some actual sense of what you have been involved in in a more detailed way. You've pointed out to the Commissioner already that the beginning of 1997, you'll see here on the screen, you were the director of the immunohistochemistry from '97 through 2003 at the department of pathology, the Norwegian Radium Hospital in Oslo, Norway. Doctor, at

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the time director of immunohistochemistry, what did that actually mean during those six years, in a practical way, what did that involve?

DR. TORLAKOVIC:

A. For my own practice it involved actually not only administratively overseeing what laboratory is doing, but actually because we were trying to develop the centre for excellence in immunohistochemistry, at the time, actually, when new techniques have been just introduced to diagnostic immunohistochemistry, meaning normal antibodies were just put--were made available for paraffin embedded tissues, meaning that highly sensitive methods were just starting to be available commercially, like polymer based methods, and suddenly we were faced that we are looking at the results of immunohistochemistry that has totally different outlook than it had just a few years ago. So this meant for me, as a laboratory director, that I had to learn everything about what we were producing. That means suddenly we have seen, for example, there is this new

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antibody CD14; CD14 was traditionally used with flowcytometry only and now I'm faced with looking at tissue sections and there is no literature published on that, how it should look like, not pathology literature. So I had to go resources like basic science literature and try to find all kinds of different resources in the--whatever source I could get my hands on to try to figure out whether the results we are getting are truthful, whether they're okay, whether they're acceptable, is this antibody cross-reactive or not or is it--so whether that is something we can use for patient care.

COFFEY, Q.C.:

Q. This was back in '97, '98, that time?

DR. TORLAKOVIC:

A. Yes, yes.

COFFEY, Q.C.:

Q. Doctor, and -

DR. TORLAKOVIC:

A. But I want to say on more thing, also, that that was like in addition, that was not routine, that is not part of the job that is routinely thought up as being for director of

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immunohistochemistry. Much more routine thing is to make sure that laboratory is using adequate positive controls, adequate negative controls, that I also evaluated every slide that came out, from the--every run in that laboratory to be sure that what we are seeing in the controls and in the tissues make sense and so on. But this was little bit more, I think, that would belong to a usual description to that, but -

COFFEY, Q.C.:

Q. To actually get into like for the CD14, for example, to actually have to research it all yourself?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Okay. Doctor, I want to backup a bit because, well, first of all, before you took the position in Oslo.

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. As the director, in your own career had you had exposure to immunohistochemistry?

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DR. TORLAKOVIC:

A. I had, as a resident, actually, two ways how I had exposure to immunohistochemistry. It's one through the training program. And at the training program has been established, has been--well, the immunohistochemistry part, I should say, the immunohistochemistry I think at that--at the University of Minnisota was established by Markwick and Paul Swason, those are really internationally, the United States pathologists, but they're internationally known experts in immunohistochemistry. At the time I was a resident they just left couple of years before me, right. But there was the setup with the algorithms, there was, the technology was there, the understanding how things should be done was there. And that, I think I that I had this privileged position of having the exposure to excellence, at the time. And at the same time my research interest involved my personal exposure in the laboratory where I performed immunohistochemistry on my own, but also actually went a step further and combined immunohistochemistry with in situ

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hybridization which was, this is known as fiction. It's not because it is fiction itself, but it is abbreviation that kind of units florescence in situ hybridization with immunohistochemistry. And that's a very challenging technique and at the time I used the technique to show for the first time evidence of unmanipulated cells that the pH chromosome, which is a hallmark of chronic myeloleukemia is also present in benign circulating T and B cells of patients with this disease in chronic phase. And that has been published in high impact journal. And while doing that, I mean, this just didn't happen, there were no simple protocols to follow, I had to be inventive and figure out on my own how to produce technically this part. So I went through lost of methods and lots of hands-on experience and that made me quite aware of what are the components of immunohistochemistry, what can go wrong and how things can be improved or not.

COFFEY, Q.C.:

Q. Okay. And this would be in the mid 1990s going thorough -

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DR. TORLAKOVIC:

A. Yes, yes.

COFFEY, Q.C.:

Q. Looking at your time in Minnisota?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. Kind of, and, I'm sorry, yes, in Minnapolis. You were there, you know, really beginning in '91 to '93, then '93, '94, '94 to '96?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Different positions, but you were there throughout that time?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. So you then in 1997 ended up in Oslo. Were you recruited as the director of immunohistochemistry, were you recruited or asked to--when you first came to that hospital, that was your position?

DR. TORLAKOVIC:

A. Yeah, I was asked to do that specific task. I was also asked if I could prepare a handout that would help pathologists better use immunohistochemistry, not with the sense of to save the money because that's often on minds of many, but with the sense of like because so much literature that is being published in the field then, and even more now, it is difficult for practising pathologists, even for specialized pathologists in certain field, to absolutely follow every published record and focus on the immunohistochemical aspects of their practice. So I actually got as a part of my job to prepare that handout, which I did.

COFFEY, Q.C.:

Q. Okay, and was there a director of immunohistochemistry at that hospital before you arrived?

DR. TORLAKOVIC:

A. No, there was not.

COFFEY, Q.C.:

Q. So this was a new initiative?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

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Q. And did you have any understanding as to why someone in the hospital had already arrived at the idea of obtaining a director, appointing a director of immunohistochemistry? In terms of at the time you arrived -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. What was your understanding about why they wanted a director of immunohistochemistry?

DR. TORLAKOVIC:

A. Oh, but it was clear. I think I mentioned this that this was--Norwegian Radium Hospital is a major cancer hospital and referral centre for Norway. So they diagnose and treat cancer patients. So the emphasis was--it was clear to them that--clear to Dr. Nesland who was the chief of the department that they must have a specialist in this area because this is the area that is critical for diagnosis and establishing appropriate prognostic and predictive markers.

COFFEY, Q.C.:

Q. Okay, and you're the person who arrived there to set it up. He asked you to come and

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oversee it?
DR. TORLAKOVIC:
A. Yes, I was just out of training, but the thing is at the time there was very--in Europe, I don't think there was any place where you could actually obtain official training and certification in this area. I was not certified to practice immunohistochemistry or anything like that, but he--my name was probably recommended to him by some people who knew me.
COFFEY, Q.C.:
Q. Okay. Doctor, then as you've indicated already to the Commissioner, after you got established there, got your office set up and started to work, you realized that or noticed that there was--you said particularly from hospitals, because it was a regional centre -
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. This particular hospital, you noticed that variability in the quality of the material that was being sent to you, or variable results? What was it that caused you then to

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think, well, I have to organize something here so that we're all kind of dealing with the same or approaching this in the same way? What was it about what you saw at the time?
DR. TORLAKOVIC:
A. Often when patients would arrive to the hospital, their diagnostic material would follow them from different hospitals, and that included sending slides and blocks. So what we do usually, and I think it's done all over Canada and United States, and it's part of routine practice, and you have to actually evaluate this material and confirm the diagnosis that was made in another centre before the patient receives the treatment in that hospital--in your hospital. So we had this paraffin blocks and we did immunostaining on our own with panels that we maybe had and they didn't, but also with things that they did, and it often would show that our results were better. So there was a great discrepancy and some of diagnosis were actually missed--not missed, but maybe not completely correct because some of the results with immunohistochemistry were wrong.

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COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. And that for me--that was something that after repeated several times, for me that was a red light that we can do something before patients are sent to us. Maybe we can help them improve.
COFFEY, Q.C.:
Q. Doctor, you've indicated to the Commissioner that you then set about organizing, at least from the Norwegian perspective, an approach to this, and you've indicated as well that DAKO Nordic -
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. As it turned out, who was providing these products at times, the various type of products in use in Norway, did provide some funding to assist this, and you described that. Doctor, what about the other three countries that ended up in NordiQC, I mean, how did you go about not only within Norway, but like across an international border,

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organizing other pathologists to become part of this, how did that work? How did you get the Fins involved and the Swedes? I mean, how did that come about?
DR. TORLAKOVIC:
A. I actually have no direct knowledge who has selected who to invite from each country, but obviously that company has made some choices on their own for who are the leaders in each country. So they picked out representatives of major laboratories from different countries, and it started as, like, nine laboratories and then it shrink to the core group of four with one representative from each country.
COFFEY, Q.C.:
Q. So the actual organization initially was done by whom?
DR. TORLAKOVIC:
A. Actual invitations were done by DAKO Nordic.
COFFEY, Q.C.:
Q. By DAKO itself?
DR. TORLAKOVIC:
A. I believe, yes.
COFFEY, Q.C.:

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Q. Okay, and your recollection is they original started with nine reps from nine labs?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. And then over time it went down to four core labs, I take it, one in each country?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. But that core was actually kind of--that was not what the company did. That core remained there after. Of those nine representatives, things filtered out and we figured ourselves, like, these are the people who are going to take it further.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. And since then, I mean, that core group has remained with one representative from each country and it's still like that.
COFFEY, Q.C.:

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Q. So, Doctor, I take it--do I understand you to be saying, look, DAKO had a hand in organizing this to start, inviting people?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And providing some kind of funding for travel and stuff -
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. So people could come to this initial meeting?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And then when the representatives from the nine labs--nine of 11, sorry?
DR. TORLAKOVIC:
A. Nine laboratories.
COFFEY, Q.C.:
Q. Nine laboratories, showed up, we then took it upon ourselves and from then on -
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:

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Q. It evolved as time went on and it ended up as four of us?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Over time.
DR. TORLAKOVIC:
A. And at the time also it switched from any sponsorship from DAKO to participation fees. So the laboratories that participate, they pay for each run they participate in, and that totally supports the function--all functions of NordiQC.
COFFEY, Q.C.:
Q. So, Doctor, here looking at this, it indicates in the second bullet here, "NordiQC, a core group, you were the Norwegian representative from 1999 through 2004?
DR. TORLAKOVIC:
A. That's right.
COFFEY, Q.C.:
Q. And from 2004 to the present, you're indicated to be an external contributor?
DR. TORLAKOVIC:
A. Yes.

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COFFEY, Q.C.:
Q. You review articles?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. What does that involve?
DR. TORLAKOVIC:
A. That involves that I review certain topics of interest, certain epitopes like CD23, and I look at the literature, current literature, and I write a summary, like, where the--what are the expected results in benign tissue tumours, and I provide images that I think are most useful, most informative, and that part of NordiQC is very valuable because it has an educational role.
COFFEY, Q.C.:
Q. Yes.
DR. TORLAKOVIC:
A. And I think that that part was commented on to me personally from several people who go to NordiQC site. If they want to quickly review what's important about certain epitopes, they go there and then they see the summary, and they also see referenced literature which is

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also helpful.
COFFEY, Q.C.:
Q. Doctor, in relation to that then, I was going to have you, if you would, outline for the Commissioner what it is that NordiQC does, what services do they provide to the four country participants? What services do they provide?
DR. TORLAKOVIC:
A. They provide--well, they are external quality assurance program.
COFFEY, Q.C.:
Q. Now what does that mean in practice?
DR. TORLAKOVIC:
A. And that means that they provide tissue samples that are carefully selected for testing. They send unstained slides to laboratories.
COFFEY, Q.C.:
Q. I'm sorry, they send?
DR. TORLAKOVIC:
A. They send unstained slides to laboratories that stain them with certain antibodies. They send it back. A group of assessors or experts are reviewing the results and scoring them,

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and then telling participants how they can improve their results.
COFFEY, Q.C.:
Q. The staining process, I take it?
DR. TORLAKOVIC:
A. The staining process and the interpretation, if necessary, and also for each of the runs for the epitopes that are being tested, so for the molecules that we are evaluating, these short reviews from experts are also provided as additional education in the area.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. So what it really provides, we can summarize it, it provides them means to calibrate their internal quality assurance program in a sense to make sure that it's calibrated properly, and also it provides education that is necessary to run certain tests in their laboratories.
COFFEY, Q.C.:
Q. For example--so the NordiQC group -
DR. TORLAKOVIC:
A. I should mention--I'm sorry to interrupt, but

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I should mention that they also organize seminars and courses and workshops, which are held typically in a different country at a different site where technologists can come and have direct interaction with expert technologists and pathologists and discuss issues, problems, and anything that they find that they want to do. There is a lecture format where it's presentations and topics are evaluated by experts, but also there is bench type of format, actually technologists being able to interact directly with experts is also an important part of that.
COFFEY, Q.C.:
Q. So NordiQC then provides unstained slides that presumably the people who are doing the providing know what's on the slide?
DR. TORLAKOVIC:
A. Yes, they do.
COFFEY, Q.C.:
Q. They know exactly what's on the slide, the type of tissue that's there?
DR. TORLAKOVIC:
A. They know exactly, yes.
COFFEY, Q.C.:

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Q. And they know the characteristics that it should show?
DR. TORLAKOVIC:
A. Absolutely.
COFFEY, Q.C.:
Q. Or should exhibit if appropriately stained, if the staining process is appropriate?
DR. TORLAKOVIC:
A. Correct.
COFFEY, Q.C.:
Q. And so they send those out to the participating labs, and are they told to stain for particular--do the participating labs understand that they're supposed to stain for particular antibodies?
DR. TORLAKOVIC:
A. Absolutely. Each run has a list for tests that they apply for. They select themselves which test they want to apply for, and, therefore, they get appropriate material for that.
COFFEY, Q.C.:
Q. And then the participating lab, wherever it is, stains the slides -
DR. TORLAKOVIC:

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A. Yes.
COFFEY, Q.C.:
Q. For that antibody, and do they also have their own pathologists, like, in the participating labs, do they give an interpretation of what they see on the slide?
DR. TORLAKOVIC:
A. That depends on the test.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. It is not required for the test--for the usual tests or what we call Class I test, but it is required for Class II test like HER2 test.
COFFEY, Q.C.:
Q. So the Class II tests, the pathologists get involved?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. At participating institutions and give their interpretations as well
DR. TORLAKOVIC:
A. Exactly.
COFFEY, Q.C.:

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Q. Which accompany the slides back to the core group?
DR. TORLAKOVIC:
A. Exactly.
COFFEY, Q.C.:
Q. And for the Class I slides, they're examined in the way you've described for their quality?
DR. TORLAKOVIC:
A. Exactly.
COFFEY, Q.C.:
Q. And they're given feedback, the participating labs get feedback?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And the Class II slides, they're examined for quality by the core group?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And as well, there's a commentary upon the interpretation?
DR. TORLAKOVIC:
A. Exactly.
COFFEY, Q.C.:

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Q. By the participating pathologists?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And indicated that as well NordiQC provides in respect of particular antibodies, educational seminars and, in fact, some of it, I take it, would be electronic, would be online?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Where the participants are able to avail of it, and there are seminars held by time to time, courses, seminars?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Those courses or seminars are for technologists you've indicated that already to the Commissioner, the technologists do go to them?
DR. TORLAKOVIC:
A. Also for pathologists.
COFFEY, Q.C.:
Q. And for pathologists too.

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DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Okay. Is participation in NordiQC mandatory for the labs in the Scandinavian countries?
DR. TORLAKOVIC:
A. No.
COFFEY, Q.C.:
Q. It's not.
DR. TORLAKOVIC:
A. They have in Finland separate program that is their national program, which is obligatory, it's regulated, but that--to my best knowledge, that is the only country that has obligatory participation, but participation in NordiQC is not obligatory. Still many laboratories choose to participate.
COFFEY, Q.C.:
Q. That was my next question, if it's not obligatory, at least up to the time that you left in 2004, what was your sense of how many clinical laboratories--what proportion of clinical laboratories do participate in NordiQC? Would there be a high percentage of participation?

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DR. TORLAKOVIC:
A. High percentage, I think, yes. I know in the beginning there was obviously smaller number, started with nine, but very soon it went to the numbers of 56, and now I think it's range of hundreds.
COFFEY, Q.C.:
Q. And, Doctor, what I'd like to do now is I'm going to come back to where you're coming to Canada and your experience here, I'm going to return to that, okay, but what I'd like to do now is--I'll return to that slide in a little while. In relation to--and you've spoken about here on this slide, the NordiQC program.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. You made a note to speak to the Commissioner about, from your perspective, the history of quality control in IHC in the United States because, of course, you had a time there, quite a number of years as a resident doing different residencies in Indianapolis. What has been your experience in relation to quality control in the United States for IHC,

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what's the situation there?
DR. TORLAKOVIC:
A. My personal experience?
COFFEY, Q.C.:
Q. Yes, and in terms of your observations as a participant in NordiQC -
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Is there any central body in the US that handles quality control for IHC; if so, what is it?
DR. TORLAKOVIC:
A. Yes, there is actually. Of course, there is College of American Pathologists that have a special module also for immunohistochemistry and it's requirement for accreditation--participation in their program is requirement for accreditation of the labs, and I also know that many of the Canadian laboratories participate in that program.
COFFEY, Q.C.:
Q. In the CAP program?
DR. TORLAKOVIC:
A. Yes, in the CAP program. If you want me to

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comment on differences -
COFFEY, Q.C.:
Q. Yes, between the CAP program and the -
DR. TORLAKOVIC:
A. I don't know if I can move the slide.
COFFEY, Q.C.:
Q. Yes, you certainly can.
DR. TORLAKOVIC:
A. Like, here -
COFFEY, Q.C.:
Q. Exploratory--sorry, external laboratory quality assurance, EQA, and you have -
DR. TORLAKOVIC:
A. So you see I have mentioned there is UK NEQAS and CAP program from United States. NordiQC, it's actually the youngest of them, except for the one that we just started--tried to develop in Canada, which is Canadian Immunohistochemistry Quality Control. So there are other programs, of course. This is not total list of all programs around the world, and some of them are smaller, some of them are larger, but these are the ones that will come up for anybody who's practising in Canada, people will see these names, and they have

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contacts with one or the other or all of them. CAP program is structured differently than NordiQC, and it's different than UK NEQAS. What UK NEQAS and NordiQC have in common that they have this assessors component. So there is a group of experts. They don't have to be pathologists necessarily, but group of trained experts who understand how the results should look like, to sit down to score the slides, and it's just not one who would see that. Assessments are typically organized by four people sitting at the microscope, and there is no magic number, whether it should be one, two, three, four or whatever the number may be. The number has been selected as--during these assessments, there is always some kind of discussion that is arising, and as technology is progressing, we are faced with results that we have not seen before, and that's certainly the case even now, not only in '97 when I started to run the laboratory in Norway, but I see still that with new developments we can see different results now. Now that has to be interpreted and discussed between the experts so that we do not make a

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wrong ruling on the success of the staining. We don't want to proclaim something being false positive if indeed it's positive more than previously known because of better technology. So we have to have people with enough background and different type of background and knowledge to be able to assess the complexity of this results. So these assessments are not simple, they cannot be automatized, they cannot be done by machines, they have to be done by experts in various fields actually at the same time.

COFFEY, Q.C.:

Q. So UK NEQAS and NordiQC both use assessor--expert assessor panels?

DR. TORLAKOVIC:

A. Yes, and CAP does not have that component, so this -

COFFEY, Q.C.:

Q. How does CAP go?

DR. TORLAKOVIC:

A. The difference is that there is a self-assessment. So when you receive unstained slides from them -

COFFEY, Q.C.:

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Q. From CAP?

DR. TORLAKOVIC:

A. You sent the slides from CAP and you score the slides yourself, and scoring the slides yourself, it's done to the best possible knowledge, and it's only one person who is doing it and it doesn't even have to be director of immunohistochemistry because not every laboratory has director of immunohistochemistry, so it's the pathologist at hand, let's say, sometimes. So that when these results are received by CAP, they are plotted on graphs that show where do you belong in the overall picture, how many other laboratories have received the same results as your are based on your own judgment what your results are.

COFFEY, Q.C.:

Q. So CAP sends out the unstained slides. They are slide--I'm sorry, they are stained?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And interpreted locally?

DR. TORLAKOVIC:

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A. Yes.

COFFEY, Q.C.:

Q. Wherever the hospital is, the lab is, and then that interpretation is sent back to CAP?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And CAP just plots that result on a graph with all other reported results?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And then the hospital that did the staining and interpretation can see where they stand in relation to everybody else?

DR. TORLAKOVIC:

A. Exactly.

COFFEY, Q.C.:

Q. Yes.

DR. TORLAKOVIC:

A. And that means--that usually means if we agree with the most, that's okay, and if we don't agree, if we are on one or other side of the curve, you're probably not good, but it really doesn't mean that.

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COFFEY, Q.C.:

Q. Okay. What is, from your perspective, what is the weakness with that or potential problems with that, that assumption that if I'm in with the group, I'm fine?

DR. TORLAKOVIC:

A. I mean, everybody can be wrong, too.

COFFEY, Q.C.:

Q. Yes.

DR. TORLAKOVIC:

A. If something that is common and very frequent results, it's not necessarily correct result. So there has to be expert evaluation and decision whether the results are really appropriate or not.

COFFEY, Q.C.:

Q. So from your perspective, I take it, when you compare that aspect of CAP to the expert assessment group and UK NEQAS and NordiQC offer, it's your view that UK NEQAS and NordiQC have a stronger program in that regard?

DR. TORLAKOVIC:

A. In that regard, I would say that I think personally and professionally I would always

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opt to participate in a program that has assessors as a step.

COFFEY, Q.C.:

Q. Expert assessment?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. Now Doctor, does CAP offer any other service related to immunohistochemistry that you're aware of anyway?

DR. TORLAKOVIC:

A. We are not using anything else. Actually, our laboratory in Canada where I work now, we are participating in the program and this is all we do with CAP.

COFFEY, Q.C.:

Q. And now in relation to--I'll ask you now about NordiQC. You've described the process that was arrived at for immunohistochemistry. Do they offer any other service in immunohistochemistry?

DR. TORLAKOVIC:

A. NordiQC?

COFFEY, Q.C.:

Q. Yes.

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DR. TORLAKOVIC:

A. Well, they do in a sense because if you fail the results, you can request additional slides to be retested to see whether you can improve. You have an option of personal communication, not in the sense to complain, I don't like your readings, but you can actually request advice and there is also this educational component that is available on the web all the time, showing what results should look like and so on.

COFFEY, Q.C.:

Q. And in relation to UK NEQAS, okay, what sorts of services are you aware that they offer for IHC? What does UK NEQAS do?

DR. TORLAKOVIC:

A. Well, they test. Also, they assess the results. They send the scores back and their detailed score sheet shows how--what each separate assessor meant, not--like NordiQC gives a common score between the agreed assessor score. UK NEQAS gives each individual and then I think it's average that they go by at the end. They have some other comments talking about--they will comment on

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background staining and details if they know it is something that is immediately relevant, but they will not go into the details of your procedure at NordiQC to identify whether a specific buffer, in their opinion, was wrong and whether the dilution of the antibody perhaps was wrong. But they will give some educational component with this assessor's score sheet.

COFFEY, Q.C.:

Q. And UK NEQAS then, NordiQC -

DR. TORLAKOVIC:

A. They also publish their results. They do, there is a publication and in that publication, there are many good instructive images of the staining. It's similar--that's similar between NordiQC and UK NEQAS, but I think the major difference being that NordiQC is totally internet based, while UK NEQAS is not.

COFFEY, Q.C.:

Q. Nordi, I'm sorry, is totally -

DR. TORLAKOVIC:

A. Is internet based.

COFFEY, Q.C.:

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Q. Internet based?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And UK NEQAS is not?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. As of yet anyway, it's not.

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. Doctor, could you tell the Commissioner, please, from your perspective, what the potential ramifications are of not having appropriate quality control for IHC? What's the down side to not having appropriate quality control?

DR. TORLAKOVIC:

A. If I'm--maybe I'm free to move to some sites?

COFFEY, Q.C.:

Q. Sure, go ahead.

DR. TORLAKOVIC:

A. Well, that's also now, we're going back to the classification of tests because then we have

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to go kind of from the beginning, because it's hard to say -

COFFEY, Q.C.:

Q. Well, that's what we'll do then. We'll go back to the (unintelligible) mostly then take you through because you had at the time--go back perhaps to the history, just go back even further, Doctor, right there. Perhaps you could just take up the narrative then and, because this is done in a chronological organized fashion by subject, and take the Commissioner then through this.

DR. TORLAKOVIC:

A. I think the main point about reviewing the history is to show that it was not before 1989 that these issues about quality control in immunohistochemistry were taken really as something of critical importance that needs regulation. So 1989, that's now about 20 years ago, immunohistochemistry has been in use much longer than that and has been historically considered as an art rather than science, because of so many components that are present in this technique, three major areas. I'm sure this has been mentioned by

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many by now that there is pre-analytical, analytical and post-analytical components and none of the components of these components can be ignored when it comes to what outcome or the result of the testing will be. However, there were no means previously technically that these procedures could be standardized or regulated. So when they become available technically and when the knowledge, accumulating knowledge on the techniques has been--has reached this point, it has been decided that some regulation is possible in the area, and therefore this first workshop from NH in 1989 started this movement and that developed further through various ways, meetings, publications, which--all with the same aim to see how much regulation we can do without harming the procedure, because we do want to avoid over regulation in this area.

COFFEY, Q.C.:

Q. And why is that?

DR. TORLAKOVIC:

A. Over regulation would mean, I think, by definition, too much of a burden for laboratories to do things that have no

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clinical relevance or to tie down a laboratory with numerous tests that would be LAR (phonetic) meaning that they are done on their own without any practical use, clinical use for pathologists, patients, clinicians and so on. So we don't want--and actually, we don't want to over regulate also in the sense that we expect what is not possible, because some of the things are just not possible, even today, even though technology has progressed and some aspects can be regulated.

COFFEY, Q.C.:

Q. Okay, so, I'm sorry, Doctor, go ahead. The narrative then was taken out, I believe, in 1991 with the--go back, there was a biological stain commission?

DR. TORLAKOVIC:

A. Yeah, I was--obviously I was not involved personally in any of these steps. This is the review that I gained from reviewing the literature, reviewing different sites and discussions on this topic and this use and events seem to, in my professional opinion, is worthwhile listing here because they, at the time, made some kind of impact on clinical

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practice. So if I would have to point out some of them here, what they really meant--actually, let us move further.

COFFEY, Q.C.:

Q. Sure.

DR. TORLAKOVIC:

A. I think the one that was, in my personal opinion, the most important one is this classification of IHC devices and this is where Class I and Class II tests and class three tests, for that matter, have been mentioned in the document, and that is a critical point about understanding different impact of different immunohistochemical tests.

COFFEY, Q.C.:

Q. And that's in 1994, this FDA panel meeting to recommendation a classification of IHC devices?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. Okay.

DR. TORLAKOVIC:

A. That, I think, was--and that is still carried out today, and I'm going to talk a little bit

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more about it, how is this important and how this should be taken, you know, into practice through QC programs and so on, because that determines actually everything for the practice of laboratories. I don't think we need to mention specifically more about immunohistochemistry and the definition of it, but I think we need to talk about Class I and Class II tests.

COFFEY, Q.C.:

Q. Okay.

DR. TORLAKOVIC:

A. So that FDA ruled at the time that -

COFFEY, Q.C.:

Q. This is back in the mid '90s?

DR. TORLAKOVIC:

A. Yes, mid '90s, that there are tests clinically that have different clinical impact, and there are tests that are used in conjunction with morphology in conjunction with clinical information and they're interpreted usually in panels, looking at results of other immunohistochemical tests too, and all of this together meant that pathologists are using this, trying to understand the differentiation

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of the tissue to gain additional information about biological aspects of the disease they are looking at, but they are not used alone. They are interpreted in conjunction with this other available information and they are never reported alone as such. So there is, at no time, clinicians will get a diagnosis that says this is 45 positive tumour period or something like that, and that would not--that, in itself, would not carry any clinical information for them. So Class I tests therefore do not stand alone.

Class II tests, we call them, they stand alone and they are reported independently and the best example of that is the example of breast cancer markers. Estrogen receptor, progesterone receptor, HER2, they--we already have the diagnosis, so we already know that the patient has breast cancer. Now we have to give additional information and describe the characteristic of biological (unintelligible) of this disease to tell the clinician whether the tumour actually shows expression of these receptors or HER2 and to what degree. So we have to say something about these molecules.

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We have to tell about their presence and quantitate them. So, and it's all--they can be reported actually not only as a stand-alone conceptually result, but also separate reports are frequently generated just to report on that fact in addition to, as an adjunct report to previously reported diagnosis of breast cancer, or they can be incorporated in the original diagnostic report.

So therefore, the stand-alone tests, prognostic and predictive tests, they can be both at the same time. For example, estrogen receptor is both prognostic and predictive, but it's predictive value to predict the outcomes of the therapy is far more critical for the patient than its prognostic value.

COFFEY, Q.C.:

Q. So generally, tests fall into Class I or Class II and I take it the bulk of tests, in terms of sheer numbers, would be Class I?

DR. TORLAKOVIC:

A. Yes. We have only very few Class II tests and these Class II tests, they can be qualitative or quantitative or both at the same time, and that's--I'm showing this slide to point out

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that there is further classification of immunohistochemical tests. It's not spelled out as such, but many of the Class II tests actually test drug combos or combinations, when you have a result of the test that is ultimately linked to specific therapy and that test drug combination, for example, it's not only breast cancer markers. It could be in lymphomas, CD20 and Rituxan therapy because that special drug is designed to target CD20 molecule, so that's why I call it test drug combination.

COFFEY, Q.C.:

Q. So you have here a classification of IHC tests into Class I, Class II, and in fact, class three.

DR. TORLAKOVIC:

A. In fact, class three too, yes.

COFFEY, Q.C.:

Q. Is there a class--could you just tell the Commissioner about what a class--I take it that ER and PR and HER2/neu would fall into the Class II category?

DR. TORLAKOVIC:

A. This is changing because I think the major

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difference between Class II and class three is whether there is sufficient scientific evidence to validate their use as prognostic and predictive tests. So therefore, the category of ER/PR and HER2, they were all, at some time, would belong to class three without enough evidence and as the evidence is accumulated, they move to Class II.

COFFEY, Q.C.:

Q. Okay, move, okay.

DR. TORLAKOVIC:

A. So at this time, for sure, ER/PR, and to tell you the truth, I haven't look it up at last time, but they are conceptually Class II tests for us because this is how we use them. Whether FDA would define them either as Class II and class three, it's for this purpose irrelevant because what we are talking about are stand-alone tests and are reported separately with this impact on patient care.

COFFEY, Q.C.:

Q. And certainly the ER/PR and HER2/neu fall into that category?

DR. TORLAKOVIC:

A. Yes, absolutely, but there are also a couple

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other tests that have similar impact. I just mentioned CD20, but it hasn't been classified as such, basically because entities that are treated with Rituxan are biologically known to express CD20 and it is rarely that we have to report separately CD20, though more and more now, there is a clinical pressure to do so. So I think that we have to move CD20 also in the category of Class II test now, and CD117 in gist, it's basically used to define biology of the--to use diagnostically so that you arrive to the appropriate diagnosis of gastrointestinal stomal tumour, but because of the relevance for the therapy, the targets actually, imagine if the targets this protein kind is separate, therefore, it is also Class II test. So in Canada, one of the things that we are working on right now, in the National Standards Committee that I'm chairing, is to find the Canadian consensus, like which tests we are going to put in Class II test and request adequate external quality assurance program to follow them.

COFFEY, Q.C.:

Q. Okay, and I'll be coming to that. So in the

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regulatory regime in the United States, under the FDA, there are--you can kind of go onto their site, I take it, and find out whether a particular marker is a Class I, they consider a Class I, or whether they consider a Class II or class three, I take it? Because there's a definition. They have a definition of what is Class I, Class II and class three?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Characteristics. And I take it in terms of just sheer numbers, there are relatively few Class II markers compared to the number of Class I markers?

DR. TORLAKOVIC:

A. Absolutely, very few.

COFFEY, Q.C.:

Q. Very few, and I'll come to that in a bit, in the Canadian context, in particular. And here, you've noted here, panels, undifferentiated tumour panel (unintelligible) panel, in which non-specific tests when used together are considered highly specific versus a single specific test used in the appropriate

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context, having high specificity.

DR. TORLAKOVIC:

A. Specificity.

COFFEY, Q.C.:

Q. Yes, I have a problem pronouncing that. And you've given as examples, ALK1 and CD117. So CD117, would that be a Class I or Class II, in this context?

DR. TORLAKOVIC:

A. In this context, it is Class I.

COFFEY, Q.C.:

Q. Class I, and if we could then, Doctor, go ahead. You were speaking about the--telling the Commissioner the difference between Class I and Class II. I believe here, you have some examples, a paraffin section immuno phenotyping of particular types of malignancies. Would you take the Commissioner just through this?

DR. TORLAKOVIC:

A. Yeah. I have two examples actually for Class I tests, how they work, and these are both taken from this document that is posted by Dr. Markwick on his website and he made it available to anybody for free access and use,

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so I felt free that I can copy this here and show you. It is not exactly how it has to be used. This is not a guideline, but it's an algorithm that can be used, and now you can see that we already have the idea that we are working with hematoporietic malignancy, but we have to arrive to specific diagnosis. So then what do we do? All of the boxes that are presented here are different antibodies.

COFFEY, Q.C.:

Q. That's the box, the black box with the white writing?

DR. TORLAKOVIC:

A. Right. It says vimentin, lyasyme, myloperoxidase, CD34, CD20, other B cell markers, CD45RO, CD45, and therefore, we apply a panel of antibodies and then follow known rules about their distribution in different tumours, but we don't make the judgment based on positivity or negativity of just one of them. So it looks rather complex here and it is a complex process, but generally, it's not that complicated, in a sense, when you work with it. Immunohistochemical diagnosis of small cell tumours, now we already have

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morphological entity. We know it's a small cell tumour. There is just certain number--there is a list of diseases that can be in differential--that is in differential diagnosis of this diagnostic category and then you apply some of the markers, like cytokeratin, leucocyte common antigen, EMA, vimentin, S100 and then based on their positivity or negativity and interpretation of that, one makes the final diagnosis.

However, for Class II tests, there are no complicated schemes like that. You just have single test and you have to give a score on it, if there is a score in that guideline or just say it's positive or negative, and the reports are generally very simple when generated on Class II tests, and the simplicity of the reports is actually what masks, I think, the true biological and technical complexity of the testing, because they are far more complex to regulate and technically optimize than Class I tests, which as you could see from this presentation, Class I tests may appear to have--to be very complex for daily use and interpretation, but it is

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Class II tests that we actually have the most trouble with, despite the superficial simplicity of the reports.

COFFEY, Q.C.:

Q. Could you go on to the next slide, Doctor, yes.

DR. TORLAKOVIC:

A. It's very little that we speak about sensitivity and specificity of these tests. And it is something that in my personal opinion, it is not of lacking, especially the sensitivity of the test, that is lacking from our reports. This reports are generated today and for decades since they started to be used, you never have in the clinical report a statement on the sensitivity of the test. None of the laboratories, to the best of my knowledge, report we have 94 percent sensitivity in detecting estrogen receptors. That does not exist. And there are reasons why that does not exist, but I think as a clinical test that these should be followed and that clinicians who are using that information should have that information. And why is that? We know when we do quality

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assurance testing, if we use large enough of samples to do so, I can tell you for CAP survey now, they use 40 samples for HER 2 tests. 40 samples is a large enough number that one can actually calculate sensitivity of the test in relation to the reference value or one can calculate Kappa-value with reference value or one can calculate the concordance and recommended concordance is 95 percent. So any of these are somehow reflecting the sensitivity of the laboratory, so you know that acceptable pass rate today for Class 2 test, like HER2 is 95 percent concordance by ASCO guideline and that was adopted also by Canadian panel on HER2. So that means that it's not a hundred percent and I think that needs to be clear when this values are reported to the clinicians. It may be that it's even much lower than that from the log that is reporting results. Maybe it's 80 percent concordance, maybe it's not 95 percent, but who knows and since clinicians don't know, they take our reports as for granted a hundred percent sensitivity, which we do not often have. Therefore, I personally

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think that that's a component that is missing from the reports. Once it's there, it allows clinician to think more rightly about their political options and to also take into account other things that most of them usually do, but sometimes they don't. So it enables, gives additional power to oncologist to make decision on the treatments and say, all right, it's 95 percent, it's not one hundred percent, maybe I should treat this patient anyway because there is this other evidence that this type of treatment may be helpful. They don't necessarily need this value, but I think it is a clinical test and such information can be produced and I think it's of value, so it's my personal take on the sensitivity and specificity of this test.

COFFEY, Q.C.:

Q. To your knowledge no pathology laboratories, at least to date, actually do report on that?

DR. TORLAKOVIC:

A. No.

COFFEY, Q.C.:

Q. Of course, if they were to do so, to clinicians, the clinicians would have to

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understand actually the significance of it?

DR. TORLAKOVIC:

A. Right, but that would also mean that they have to participate to such programs that enable them to determine the sensitivity of their tests.

COFFEY, Q.C.:

Q. And would the lab have to do that--the particular lab would have to do that at the beginning.

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And the clinicians would have to understand, in fact, what it is the reports mean?

DR. TORLAKOVIC:

A. Exactly.

COFFEY, Q.C.:

Q. Okay. Doctor, this is entitled "Standards and Optimization", would you just take the Commissioner through this?

DR. TORLAKOVIC:

A. I think that the term standards has been over used greatly in this area. Since it is such a critical issue today in immunohistochemistry

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that we produce accurate results, there is a lot of use of the term standardization. Standardization should be used when we can actually standardize all the components of the procedure. Since we cannot standardize at current time, pre-analytical component, it's just simply not possible, we can go towards that goal of standardizing it, but since we cannot standardize tissue processing, we cannot truly standardize the test. So therefore -

COFFEY, Q.C.:

Q. When you say you cannot standardize, I take it you cannot perfectly standardize it in the sense of -

DR. TORLAKOVIC:

A. You can standardize components but you cannot standardize the entire test.

COFFEY, Q.C.:

Q. Pre-analytic.

DR. TORLAKOVIC:

A. Pre-analytic without standardization of pre-analytical component, all of this other things, if you standardize, will not result with ultimately standard all test.

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COFFEY, Q.C.:

Q. Sure.

DR. TORLAKOVIC:

A. And that's why I have problem with that and an additional problem is that, first I think what we want to do is optimization. In the current state of knowledge, technology and what we have available, we can optimize the test definitely, but I don't think we can standardize. And standardization actually also depends on the ability of a lab to have standardized controls. Even for the analytical component, we cannot standardize fully. We can make it the same every time, that doesn't mean it's standardized. Something if it's the same, it's not-- standards means that we have a point of reference that we use to which we adjust all the protocols and procedures to such product and what is our point of reference? Immunohistochemistry, that's positive controls, so the standardization process should start and it's not complete, but should start with standardization of positive controls and that is the greatest challenge

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right now at this point, historically at this point of time is to standardize positive controls.

COFFEY, Q.C.:

Q. And why is that, Doctor. Why is there a challenge -

DR. TORLAKOVIC:

A. The challenges, one is that--there are several challenges, actually, it's rather complex procedure to standardize the controls, one of them is this tissue processing which we can try to make as uniform as possible. We can try to involve surgery departments in that, but you cannot control, for example why this cannot be fully standardized, let me tell you, because you cannot tell the surgeon how long the surgical procedure will last, you cannot tell them since you claim (phonetic) this vessel and the tissue ischemia is changing our epitopes, did you record that time so that we know exactly when you did that and you know, you shouldn't be doing that for too long because the tissue will become, you know, would alter it and then our immunohistochemistry is not going to work. I

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mean, that's nonsense, that's not going to work, so the tissue degradation starts with the point of when these vessels have been cut or tied and that interoperative part we certainly cannot control at all. And after that, we can try optimizing from the point of tissue procurement to the laboratory and what happens from there on, but it's a rather complex process. I know that in many of the laboratories or hospitals this is being done, they are optimizing every step in the tissue processing now, looking at the best ways how this antigen preservation will be uniform and the best, how antigens are going to be best preserved in the given circumstances of realities of operating room and how pathology departments work with their specimen receiving system and so on. But what are the other challenges? Tissue process is one. The other one is you have to have expert consensus on what are the outcomes and for positive controls, unfortunately still many laboratories what they're using as a reference point is just anything that gives positive reaction and it's rather simple to find that.

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It's simple to find, for example, a tumour of benign tissue that shows high cytokeratin expression or high chromagram (phonetic) expression, yes. But that is not what should be used for positive control and the practice, if it hasn't changed in some of the labs, it has to be changed. And the guidelines should be there that there always has to be composite tissue that has, tissue that presents expression, various expression levels of epitope, including and the most critical one that has very low levels of expression of the protein that we are looking for. That is critical for the calibration of daily QC process. Without it, we don't really know how our procedures are set up, to what level, how they are calibrated and there is no definite and final document that would tell to pathologists or to technologists how to collect those controls. There are some general guidelines I can tell you right away, I like to use these because it's so simple to explain that for some of the epitopes, it's very easy, like CD-23, if you use a tonsil, which most people actually use because it's a

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lymphoid tissue and this is a lymphoid antigen, then you're looking at cells that have very strong expression of CD-23 and those are fully chondrogenic cells and at the same time, the follicle is surrounded with a mantle that has lymphocytes that has a very weak expression. So in the same tissue it's benign and it's predictable, you have this various levels of antigen expression. However, do we have this spelled out for every epitope that we are looking for and there are over hundreds of tests that are used in many of the laboratories, this Class 1 test, you don't. And we don't even have definite guidelines how to create positive controls for Class 2 tests and that's another very important topic is where are the guidelines, how do you prepare actually positive controls for ER/PR and HER2? Any test that has a quantitative component has to have its own quantitative positive controls. So there are some suggestions and, of course, there is industry behind it too that are creating tissue culture controls with given amount of epitope we are looking at, but that's not perfect solution either because

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tissue cuts just do not fully represent what's going on in the tissues. And I just want to, I hope, yeah, perfect, that's the slide we want. This is the last NordiQC round of tests on HER2 and this table is taken directly from their site. You can see these are the results of the cell lines and these are the results of tissues, so their score is either optimal, good, borderline or poor. Now you can see that for some of the samples, here is three, in three labs that was a borderline result with cell lines, but optimal with tissue or a good--so there was no perfect correlation and cell lines did not do better than tissues and some explanations that NordiQC has for this is that this happened because of the impaired morphology of the cell lines and this is possible because of excessive retrieval. But more testing, I don't think this is the final ruling, but I think this is the first evidence that has been shown that cell lines are not necessarily superior to tissue controls and actually the conclusion from NordiQC was, I don't know if it's going to stand the test of time and for the studies, but it is believed

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now by NordiQC that tissue controls actually are better, but there is a value also of the controls from tissue cell lines.

COFFEY, Q.C.:

Q. So the idea of using -

DR. TORLAKOVIC:

A. Kind of both show these.

COFFEY, Q.C.:

Q. - both cell cultures is there, it's out there, it's being looked at and it's still, from your perspective, there's still no conclusion -

DR. TORLAKOVIC:

A. No, that's not a perfect solution and also there is a very high cost of such positive controls and if one is to use such positive controls on every slide that we prefer to use in our current practice, we prefer to use positive controls on every slide that we test. That would be prohibitively expensive. I think it's $40.00 per one slide or so. I don't know the exact value, but I know it's high enough that it's not something that--and since there is no proof that they're better, I don't think they should be recommended at this point

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as an ultimate controls for Class 2 tests. But having said that, I have been involved in trying to create so called perfect tissue controls, so we tried, in collaboration with Jewish General Hospital with Dr. Pilavdzic, she provided numerous samples from tumours with various expression levels of one of the Class 2, with HER2 basically, for HER2 positive controls and we collect--looked at 50 samples and made cores for tissue microarrays and tested the first to see what are their expression levels and also official results were available. So the idea was if you have this information, maybe you can still get, maybe you can sample tissue cores from those tumours that you have well characterized as your positive controls and create, perhaps, small tissue microarrays with the perfect combination of from zero to three plus, so it would be four cores or maybe even 8 just so--because to allow for some tissue hydrogenating, and it works, but it does not work as we predicted because of this tissue hydrogenating, you don't get exactly the same value in each core from the same tumour. You

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do make--you are able to make very good positive controls like that, but each of them have to be again validated, each of them has to be, it's a unique, actually, positive control, has to be photographed at the beginning as a reference value, so that they can be interpreted after each run, in comparison of what their perfect results should look like. So it's a rather complex process and I don't know, we never looked at how many laboratories actually trying to do what other laboratories are doing with positive controls, but I know it's not standardized yet, even for Class 2 tests, not to speak about Class 1 at all.

COFFEY, Q.C.:

Q. So, Doctor, my way of bringing you around to your arrival in Canada, okay, you arrived in Canada, I believe, in 2004, 2005?

DR. TORLAKOVIC:

A. No, actually in December of 2003.

COFFEY, Q.C.:

Q. '03, I'm sorry, and you came here to work where?

DR. TORLAKOVIC:

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A. At the Royal University Hospital College of Medicine at the University of Saskatchewan.

COFFEY, Q.C.:

Q. And what's your position there?

DR. TORLAKOVIC:

A. I'm academically appointed pathologist. I'm currently an associate professor in the Department of Pathology and Laboratory Medicine.

COFFEY, Q.C.:

Q. And, Doctor, when you arrived in Canada and started a practice, what did you find in relation to the situation here in terms of quality control or quality assurance and in particular for IHC testing?

DR. TORLAKOVIC:

A. Well, the first--my first experience was, of course, with the laboratory in Saskatoon.

COFFEY, Q.C.:

Q. Yes.

DR. TORLAKOVIC:

A. So I have looked at, like, what is their practice in daily QC and what's their practice in EQA, their participation in different programs, and despite participation in

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different programs, I found that at the time there were many things about the practice that could have benefited and be improved with some simple measures, but that also showed me that participation in EQA program itself was not sufficient to do this changes for the lab.

COFFEY, Q.C.:

Q. I'm going to ask you about this. So the laboratories in Saskatoon Hospital there where you were working -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Did at the time you arrived, prior to your arrival, participated in EQA?

DR. TORLAKOVIC:

A. Yes, they participated in CAP.

COFFEY, Q.C.:

Q. But based upon what you were seeing, and some observations, and I take it you would be comparing that really to your experience in Europe in the main?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

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Q. That there were some relatively simple things from your perspective could be changed to improve?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Matters--yet they hadn't occurred despite the participation in CAP?

DR. TORLAKOVIC:

A. Exactly.

COFFEY, Q.C.:

Q. Would you go ahead then, Doctor, what then happened? You say you made this observation. What did you do?

DR. TORLAKOVIC:

A. So I made this observations and it gave me a lot of thought about what kind of EQA is necessary for us in Saskatoon, what we would like to have. So, of course, I suggested let's go and participate in NordiQC, but it's an overseas program and Canada is not really--I mean, it takes many days for the specimens to travel from one side of the ocean to another. So it just wasn't a good enough idea. I noticed that actually Canada did not

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have a national program. I heard that somebody is doing something in BC and there is an Ontario program, but there was no program for Canada which I found surprising because Canada is large enough country that--I found it unusual that it's totally dependent on CAP program, and at the same time some provinces have their own, like, they are separate country or something, and it's just--it was unusual that there is such big border between the provinces. I didn't really quite understand how big these borders administrative are until I actually tried to approach some people to see whether we can start developing a national program.

COFFEY, Q.C.:

Q. Okay, so you arrived, you made your observations within your own lab?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Thought about NordiQC, but there is just simply the geographic distance, and shipping times, I take it, and so on?

DR. TORLAKOVIC:

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A. Yes.
COFFEY, Q.C.:
Q. And what then happened? You noticed British Columbia has some kind of a program involving laboratories. You understood Ontario does?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. What then happened?
DR. TORLAKOVIC:
A. Since I didn't know at the time many pathologists in Canada, I did ask my colleagues who would be logical, you know, colleagues to contact to try to set up such a program, and it was very difficult to find people who would be willing or find that interesting enough to try to create, or it was just some of them were very pessimistic about the possibility of a national program in the view of provincial borders.
COFFEY, Q.C.:
Q. Yes.
DR. TORLAKOVIC:
A. But I did find Dr. Blake Gilks from BC who was the--Dr. Blake Gilks from Vancouver General

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Hospital. He was rather enthusiastic because they were in the middle of developing their own provincial program and he thought that provincial program is not a solution, that we do need a national program. So we got together. I actually travelled with my own funds to Vancouver and we discussed this in detail, and made a plan how are we going to start this. I approached the Dean of Medicine at the University of Saskatchewan at the College of Medicine and asking him for his help. I told him I think this is necessary, I think I need help because we need a web page, we need IT support for this, would you be willing to support us, and he said yes. So the College of Medicine provided IT support and the web page was set up, and it was set up in such a nice way that it's very easy to do changes, upgrades. So with administrative powers that I have, I can go easily and since I work with computers, I can do a lot of that on my own, not demanding too much from IT people or from the College of Medicine. The idea was to create a program that is going to have both--provide testing that are adequate

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for immunohistochemistry, quality assurance, but also to provide education, and what we wanted the most, actually, Dr. Blake Gilks and I, is to create a program that will have transparency.
COFFEY, Q.C.:
Q. Yes.
DR. TORLAKOVIC:
A. Because as you can see, and I don't know if anybody try to go into certain programs, pages, and to see the results, you may see some results, you may see some of the good examples of the staining and stuff like that that is presented there, but you actually cannot compare directly the results of your lab with results of other laboratories. You always get some kind of intermediate between this to interpretation from--you either get scores from assessor panels, overall picture, but not direct insight, and we wanted to create program that will give pathologists the ability and technologists to go in and to compare side by side their results with someone else's results and see also a link to that--those results, the protocols that

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produced them. So they can immediately change if they want their protocols and adjust them to improve their results if they need to be improved.
COFFEY, Q.C.:
Q. So if we could, Doctor, on that, just to explore that a bit with you, so there are EQA programs that do exist and are accessible via the web?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Nordic would be an example of it?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And one can go in as a pathologist, particularly if you're a member, you can go in and log in, click, put in your password, and up comes, for example, your own results on the screen, presumably. If you participate, you'd be able to look at your own or you could have them there -
DR. TORLAKOVIC:
A. Actually not. In Nordic, you can't see your

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own.
COFFEY, Q.C.:
Q. Okay, you can't even see your own?
DR. TORLAKOVIC:
A. No, no, no.
COFFEY, Q.C.:
Q. But you can see your own in front of you?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. In a microscope, you know on a microscope?
DR. TORLAKOVIC:
A. Actually, you send it back, so you don't see it ever after.
COFFEY, Q.C.:
Q. So, Doctor, in terms of being able to compare your results, what you're getting for any particular stain, whatever it is -
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. To anyone else's stains, are you able actually to do that?
DR. TORLAKOVIC:
A. Now we are. In CAPs, I mean, let me just show

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you what we have made on this. This is not moving.
COFFEY, Q.C.:
Q. There it is.
DR. TORLAKOVIC:
A. There are some stains here that I would like to go back. I just want to skip now to this program in Canada. This is what we call multi-viewer. I have--we have asked IT specialist to design this program for us specifically with this idea, to make four windows for virtual microscopy, so that we design--the test material that is used by Canadian immunohistochemistry quality control, that's what CIQC stands for, are tissue microarrays. So they're multiple tumours or other tissue samples, so that one can go and zoom in and even under higher power than here, it will be even high close up, and compare. Select the test you want to compare with another lab and see how they do, and then there are the protocols here. They are all coded. The participation is anonymous, so you can link certain result with certain protocol.
COFFEY, Q.C.:

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Q. So the protocol for a particular lab, the lab is not identified?
DR. TORLAKOVIC:
A. No.
COFFEY, Q.C.:
Q. It's given a code number?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. But the actual protocol used to produce that particular slide -
DR. TORLAKOVIC:
A. Exactly.
COFFEY, Q.C.:
Q. Is there.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. It's laid out for themselves and anyone else who participates to look at, and if they look at a particular slide, you can look at the corresponding protocol that the lab that produced the slide used?
DR. TORLAKOVIC:
A. Yes.

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COFFEY, Q.C.:
Q. And then, presumably, compare it to your own or another labs as you go?
DR. TORLAKOVIC:
A. Yes, and in addition to that, we also provide summary pages, and this is very interesting one where this is a quick--this hasn't been done yet in External Quality Assurance programs, a quick orientation where you are at with your concordance rate is spelled out here in this row, and each of the column here is one laboratory that participated in the testing, and you see the positive results are coloured as red, negative are white, and samples that were not possible to evaluate for several technical reasons, they are yellow. So they are taken out of the calculations. So one can quickly see how laboratories compared to each other in regards to positivity and negativity, and also there is a concordance rate that they get right away and this is the value they need if one is to follow ASCO guidelines for Class II tests.
COFFEY, Q.C.:
Q. I'll be coming back to this, but when you set

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out to do this back in the middle of 2000 after you arrived in Canada -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. I take it, that there was--from your perspective, there was no such EQA available that you were aware of anywhere that your lab could participate?

DR. TORLAKOVIC:

A. No, but I--maybe I should go to this slide now when we talk about this in Canada. No, there was nothing like that, and still, I mean, when you look at what--there is a good program, of course, in Ontario, and the program that is now in some other provinces is also very good. So one cannot say that there is no good external quality assurance programs in Canada. I think it's critical to say that there are.

COFFEY, Q.C.:

Q. Yes.

DR. TORLAKOVIC:

A. But there is no national program, so not everybody is in Ontario, not every is--so it has to be also one of--also their programs,

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they don't do this educational component, which I think is critical, and I think that it has to be developed in many ways to enable technologists, not only pathologists, to have very close interactions with experts. Just yesterday we were discussing like we should create something like a hotline question and answer pages where people can quickly answer with their critical questions during the day because you do need -- you need technical support for instrumentation, you also need expert support for all kinds of problems that arise in daily practice of the lab that cannot be sometimes solved by the pathologist who is responsible or by expert technologist they have there. There are some issues we can benefit from interacting with each other and they are actually not rare, if you let people ask. I mean, I have been approached--bombarded with number of e-mails at a time with all kinds of questions, like, why is this, why is that, how to use this, how to use that. So there are so many things that people need help with, and that is because the technology is developing rapidly, that is

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because the publications are--numerous publications in this field are out almost daily and all of this has to be incorporated into practice in the best way possible without significant lag between the current state of the art practises and the real picture in the laboratory.

COFFEY, Q.C.:

Q. Doctor, if we could, you found--you noted here, "No national standards for diagnostic immunohistochemistry". You've pointed out that there's no national accreditation body certainly for immunohistochemical labs. For clinical laboratories, you pointed out there is a program in Ontario. When you arrived, you learned that British Columbia was in the process of setting one up. You prevailed upon your Dean to give you at least a certain basic resource, and talked to Dr. Gilks, met with him?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. I'm going to ask, Registrar, if you would, please, bring up Exhibit P-0412. If we could

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go to page 26, please. Doctor, this is a document that we obtained--the Commission obtained from Eastern Health in the course of preparing for the hearings, and this is entitled, "Proposal for establishment of a Canadian national external laboratory quality control in diagnostic immunohistochemistry".

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And it's--it has your name there, yours and Dr. Gilks, and it's dated 11th July, 2006. This is a two page document. I'll just show you, that's the second page, and if we go back to page 20 of the exhibit--it's the first page of the document here. It's proposal for establishment of a national external quality assurance program for clinical/diagnostic immunohistochemistry, and then this particular document goes on for six pages and the contact person is indicated to be yourself?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Now, Doctor, could you tell us, please--I take

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it, this shorter one, the two page, page and a half here at page 26 of the exhibit, is really just an executive summary of the first six pages?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Doctor, this is dated the 11th of July, 2006. What had happened prior to this? I mean, how far had you gotten or advanced with this effort before July of '06, between the time you first approached your Dean now and produced this?

DR. TORLAKOVIC:

A. To tell you the truth, I don't know exact date how this happened, I just have to say, because I think at the time we already have established web page.

COFFEY, Q.C.:

Q. Okay, you had probably the web page up?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Who was this proposal addressed to? It's a proposal. Who is your target audience here?

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DR. TORLAKOVIC:

A. This was sent to--I believe, to Canadian Association of Pathologists because for us, that was a logical contact in the first place. So we sent it there to the Executive Committee of the CAP to consider this and help us out in creating such a program.

COFFEY, Q.C.:

Q. And if I could, please, Exhibit P-1143. Doctor, this is a couple of e-mails, but look down at the bottom of the page here, the first page. I believe it's an e-mail from Dr. Laurette Geldenhuys, I believe a Nova Scotian, Wednesday, July 12th, 2006. It's addressed to Dr. Banerjee and Dr. Cook and it says--the subject is QC for Immunoperoxidase. She says, "Diponkar and Don, I received these documents from Emina Torlakovic. Since we discussed the issue at an executive meeting recently, I thought you might find these interesting. I attach". Do you know Dr. Geldenhuys?

DR. TORLAKOVIC:

A. Yes, I know she--I think she was -

COFFEY, Q.C.:

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Q. She's at Dalhousie University, I take it?

DR. TORLAKOVIC:

A. Dalhousie, but she was--she's very active in CAP. She's on the executive committee and she also was in charge of, I think, continuing medical education programs with CAP.

COFFEY, Q.C.:

Q. And here apparently in that e-mail, she had sent on to Dr. Banerjee and Dr. Cook a copy of, in fact, what is your proposal for the establishment of a national external quality assurance program for clinical/diagnostic immunohistochemistry, that document, as well as your executive summary. See that? So you had submitted this to CAP?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And apparently this was being circulated within CAP itself, the executive there. If we could look, please, at Exhibit P-2273. This is another exhibit that we obtained. I believe this is from Dr. Cook or Eastern Health, one or other, or both, and this is Dr. Cook's handwriting, "Executive meeting, July

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15th, 2006". Under paragraph five, in particular, items for discussion, paragraph 5.4, it says, "National standards for laboratory/immunohistochemistry testing, Dr. Banerjee noted that a handout was circulated regarding a proposal for the establishment of a national external quality assurance program for clinical/diagnostic immunohistochemistry. This proposal was prepared by Dr. Torlakovic and Gilks. A quick review of their proposal brought forth a few areas of concern. In particular, the last paragraph on page four regarding Class II tests in HER2. The members were asked to carefully read over the proposal and forward their comments by e-mail to Dr. Banerjee", and then, "they need to develop a working group with medical and radiation oncologists, Cancer Societies, CAP, and CCQLM is in progress". Now, Doctor, if we could then go back to Exhibit P-1143. This is one of the copies of a proposal you made. You sent your proposal to CAP. What happened?

DR. TORLAKOVIC:

A. In the beginning, nothing happened, actually.

COFFEY, Q.C.:

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Q. Okay.
DR. TORLAKOVIC:
A. I did not get any comments. I just unofficially heard that this was found as an interesting document and that it was decided that CAP needs to--Canadian Association of Pathologists needs to do something in this area, and then later on I submitted a proposal for a workshop that also takes in diagnostic immunohistochemistry for Canadian Association of Pathologists annual meeting. This was accepted and this year--well, second year and next year will be possibly the last year this workshop is given, but it's one additional thing that I did, but what then happened is that last year Canadian Association of Pathologists decided to form a committee which they decided to call National Standards Committee/immunohistochemistry. As I understand, this would hope that there will be other branches/something else in various fields of pathology. So for this committee try for national standards in immunohistochemistry, they invited several people or interested parties as members, and

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then they invited me, if I could chair this committee, and I accepted that. So that was, I think, in March last year that it happened, and then I started to work with the committee with an idea that we are going to try to identify areas all in an effort to ultimately improve practice of diagnostic immunohistochemistry. Whether we call it standards or not, as I said, I don't prefer to use the word "standards" but I understand that it has to be used sometimes.
COFFEY, Q.C.:
Q. Now, Doctor, you say you were invited to do this last March. Would that be March of 2008 or 2007, March?
DR. TORLAKOVIC:
A. 2007.
COFFEY, Q.C.:
Q. 2007, okay. So it's been now about a year and a half?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Okay. Doctor, if we could look just at this, your original proposal--this is page, yes,

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eight, just looking at that, it's page eight of the exhibit of P-1143, well, it states in the beginning, I suppose, well, it was certainly obvious to you that "Canada does not have a national external laboratory QC program in diagnostic immunohistochemistry. Other countries, including the USA, United Kingdom and Scandinavian countries have established such programs adapted for their own national needs and arena." You write, "Quality assurance in laboratory medicine includes, (a) constant checking of test reliability by internal quality control, ICQ; external quality assessment, EQA, by an independent agency to check performance of a number of laboratories at intervals in order to obtain a retrospective indication of their performance; and (c) proficiency control by supervision of pretest and post-test phases of laboratory work, from specimen collection to delivery of report to the clinician. Currently diagnostic IHC has in excess of 100 tests on the menu and none are currently uniformly assessed since there is no national Canadian external laboratory"--I'm sorry, "laboratory" I'm

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sorry, "independent agency to check their performance." And then you go on to speak about the United States, College of American Pathologists and UK NEQAS. And you note toward the bottom, you say, "Therefore, so far only NordiQC from Scandinavia provides directly applicable information for each participating laboratory as well as direct communication and personal approach in problem solving. However, with the number of experts in pathology and clinical immunohistochemistry there is no reason for Canada not to have its own external laboratory testing in clinical immunohistochemistry. We would like to invite Canadian Association of Pathology to support our intention to develop such a program to serve pathology community in Canada and hope that despite the differences in individual practices the common goal and future benefits of such an organization would unite all interested parties to participate"--I'm sorry, "to contribute in the development of this service. Enclosed is a more detailed proposal with additional pertinent information." So, Doctor, that's what you first sent to the

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Canadian Association of Pathologists. And this, in fact, I'm going to suggest, is a proposal by both yourself and Dr. Gilks? I'm correct on that?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. In fact, it covers everything from the proposed name, which is CIQC for Canadian Immunohistochemical Quality Control, the proposed program; the mechanisms that would be use?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. In a sense of arranging three to four external challenges per year for assessing the performance of participating clinical labs in support of their internal quality control programs. There's a commentary about the American situation, CAP Laboratory Accreditation Program, UK NEQAS and NordiQC. And then you have a paragraph entitled "Background" which I take it, in effect, describes the then current situation in

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immunohistochemistry. Then you talk about Class I tests and Class II tests, explaining what they are. And class three tests, as well. Doctor, here at the bottom of page 4 of your proposal itself.

DR. TORLAKOVIC:

A. Um-hm.

COFFEY, Q.C.:

Q. This, you say here in the second-last paragraph, "No national surveys are available to answer these and many other basic questions relevant to laboratory performance in clinical immunohistochemistry." And the questions you've posed above or suggested above that are "We do not know and are not able to predict what the degree of the problem, if any, on a national level we may have in clinical immunohistochemistry. We do not know if most or all laboratories are using currently available technically advanced methods which provide excellent sensitivity and specificity of the tests. And if these methods are implemented, what is the level of internal and external quality control the laboratories use in daily practice? Are appropriate positive

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and negative controls used? Who is creating optimized positive controls? Are quantitative tests supplied by quantitative positive controls, etcetera?" Suggesting, I'm going to suggest to you, Doctor, really there's almost nothing known nationally about what's going on in the country?

DR. TORLAKOVIC:

A. Exactly.

COFFEY, Q.C.:

Q. At that time?

DR. TORLAKOVIC:

A. Actually, it hasn't changed much since then.

COFFEY, Q.C.:

Q. Yes. I was going to ask you that. I'm going to come back to that. Then you go on at the bottom of this page to say, "Immunohistochemical tests are basically either qualitative or quantitative. Both could be of diagnostic or prognostic significance. While quantitative tests are currently used for scoring of results and determination of hormone receptors or HER2/neu in breast carcinoma which are Class II tests, since Class II tests are very few but require

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particular expertise in both technical aspects and interpretation of the results, it appears most appropriate that additional specialized organization provides a means for their standardization and quality control. These tests would not be the subject of CIQC, which would try to focus on the remaining more than 100 Class I tests."

DR. TORLAKOVIC:

A. Yeah, I can explain that.

COFFEY, Q.C.:

Q. I appreciate that, because that's what I was going to ask you about in terms of that. Because anybody who is reading this, and of course, it's readily available now publicly because it's up, certainly, on the Commission's website.

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. Anybody who has been following this closely. And in any case, I wanted to ask you about your original approach and then how it's evolved.

DR. TORLAKOVIC:

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A. It has changed.
COFFEY, Q.C.:
Q. Well, for the Commissioner to understand your initial approach, of course, I wanted to canvass it with you. Why initially, Doctor, was it your view that CIQC would initially get involved in the Class I tests?
DR. TORLAKOVIC:
A. Because I heard that there is a Canadian panel on HER2 and my assumption was that that panel is also going to deal with all the aspects of Class II tests, meaning also that it will also organize appropriate national program for EQA -
COFFEY, Q.C.:
Q. For -
DR. TORLAKOVIC:
A. And then I thought--for HER2, and that means I hope because these all breast cancer specialists, that they are going to provide, organize such program for breast cancer testing, and so -
COFFEY, Q.C.:
Q. Which would include?
DR. TORLAKOVIC:

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A. Which would include the ER/PR and HER2.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. That was my assumption and it was wrong because that did not happen. What that panel did, they looked at the ASCO CP guidelines for HER2 and then they adopted or slightly changed that for Canadian pathology practice. So they issued Canadian guidelines for that, but they did not -
COFFEY, Q.C.:
Q. For HER2?
DR. TORLAKOVIC:
A. For HER2. But they did not even decide to address EQA. There are some things that are in the guidelines that address EQA, external quality assurance, saying that this 95 percent of concordance is necessary, that optimization or development of the test in the lab, how it has to be done, what number of samples has to be used, that reference laboratory wise--reference laboratory should be used to, you know, to calibrate the test in the beginning, but there is nothing about the program. So

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since that did not happen -
COFFEY, Q.C.:
Q. Okay, so if I could, Doctor, just to give it the context. So originally in the summer of 2006, which is when this proposal was made?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. July of '06, at the time you understood, look, there's some other group that's dealing with HER2/neu, and your assumption, as it turns out, it was not well founded. Your assumption at the time was is they will also deal with, in the course of doing HER2/neu will do other breast markers?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. In particular, ER and PR?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And EQA for those Class II tests?
DR. TORLAKOVIC:
A. Right.

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COFFEY, Q.C.:
Q. As it turns out, ER/PR wasn't dealt with at all?
DR. TORLAKOVIC:
A. True.
COFFEY, Q.C.:
Q. Those two stains. And EQA has not been dealt with?
DR. TORLAKOVIC:
A. No, it hasn't.
COFFEY, Q.C.:
Q. At all either for the Class II tests by that group. They focused on guidelines for HER2?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. For Canada?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. And they published those. And in the meantime, with that in mind, because that was your original mind set while they're off doing that for Class II tests?
DR. TORLAKOVIC:

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A. Right.
COFFEY, Q.C.:
Q. You were going to initially focus on Class I?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Why is that, what did you propose to do about it at the time and why, why Class I?
DR. TORLAKOVIC:
A. Well, Class I tests, actually, large number of tests. And depending on the lab and their particular area of practice they may vary anywhere probably between 10 or hundreds of tests that are done. And -
COFFEY, Q.C.:
Q. Of Class I tests?
DR. TORLAKOVIC:
A. Of Class I tests, different tests.
COFFEY, Q.C.:
Q. Different, yeah.
DR. TORLAKOVIC:
A. And what is important about Class I test is even though we have external quality assurance that is addressing some Class I tests, only those that are most frequently used and only

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very few are being tested. So if you look at even in an ambitious external quality assurance program only about 10 to 12 tests are tested per year.
COFFEY, Q.C.:
Q. Ten to twelve antibodies?
DR. TORLAKOVIC:
A. Yes. Of all possible existing Class I tests, which are almost 100 that are in clinical use. So that was, in my mind, I know it's a lot of work but it's a huge discrepancy that large number of these tests is never tested, will never be tested or addressed, and then nobody will ever tell you how to calibrate this test or help out.
COFFEY, Q.C.:
Q. They're never subjected to EQA?
DR. TORLAKOVIC:
A. Never.
COFFEY, Q.C.:
Q. Process?
DR. TORLAKOVIC:
A. Never.
COFFEY, Q.C.:
Q. So there are 100 plus, easily more than 100

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Class I tests available -
DR. TORLAKOVIC:
A. Absolutely.
COFFEY, Q.C.:
Q. - and in usage?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. But out of that 100 some are far more used than others, more commonly used?
DR. TORLAKOVIC:
A. Exactly.
COFFEY, Q.C.:
Q. And it's the more common ones that are routinely tested in the EQA processes that exist?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. And therefore you were thinking, well, wait now, what about the other 60 or 70 that are-- or 50 or 60 or however many it is that are almost never tested by EQA, that was your concern?
DR. TORLAKOVIC:

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A. Right. Am I free now to elaborate a little bit more on that?
COFFEY, Q.C.:
Q. Yes.
DR. TORLAKOVIC:
A. I have some cites prepared just because if we can go back -
COFFEY, Q.C.:
Q. If we could go back to the PowerPoint, please? Yes, Doctor, go ahead.
DR. TORLAKOVIC:
A. I think we go here, start here. This will do, as well. These are images that illustrate the use of Class I tests in detection of lymphoma, basil lymphoma, which is a malignancy of lymphocytes, that's cancer of the lymphocytes in the bone marrow. Every patient when they get this type of diagnosis has to have bone marrow biopsy which is used for staging to detect how far the disease has spread, whether it's present in the bone marrow or not. So if you bear in mind that I said previously that Class I tests are interpreted in conjunction with morphology, clinical data, other test results. I will show you now that Class I

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tests are not always interpreted in the conjunction of morphology, and actually, that they are critically important for appropriate diagnosis and their significance is no less than any Class II test in that way and cannot be controlled by other parameters. Like, we hope that it should be--that applies biologically to all Class I tests, but it doesn't, and it does not apply in many clinical situations. On the left is the images illustrate black or dark brown staining of the B lymphocytes in the bone marrow. This is evidence of follicular lymphoma. This is minimal evidence of involvement, but nevertheless, for clinical purposes, this is stage four follicular lymphoma for that patient and is important. It's a huge clinical difference between stage one and stage four disease. And that, I'm not going to talk specifically about follicular lymphoma but in general, there are many instances when involvement of the bone marrow is so minimal that only by immunohistochemistry we can detect the disease, not by morphology alone, and so this combination of--these are two

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different patients, so we can see this is not a rare--it wasn't very hard to find examples like this where there is only immunohistochemical evidence. So that means that was the only means by which we have diagnosed this disease.

COFFEY, Q.C.:

Q. And classify it between one and four, for example?

DR. TORLAKOVIC:

A. Well, it's stage appropriate.

COFFEY, Q.C.:

Q. Stage -

DR. TORLAKOVIC:

A. Appropriate staging of the patient, and here, it's even for diagnosis. If you see these two images, these are two on the right, from the same--different patient, but from one patient CD20 that also we interpret in correlation with results of other Class I tests and here it shows that it's not always the case. CD20 is a B cell marker. Pax-5 is also B cell marker. Now we are looking at here very few positive cells and then you are looking at here with Pax-5, it lights up like a Christmas

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tree. So this shows that there is lots of lymphoma that stained with this marker and here, we don't see that lymphoma at all, and it was also something that has not been detected morphologically, and I must say, I have--this is the case I've seen myself. I have been practising hemapathology for many, many years and I don't think that I am a beginner that would not recognize this because of the lack of experience. It just happens that some of the things are difficult to recognize morphologically and immunohistochemistry is frequently being used to enable us to see more than with just H & E staining. So in these two examples, you can see that the interpretation of immunohistochemistry, the use of the it and the result, are critical for the diagnosis.

COFFEY, Q.C.:

Q. And these are Class I tests?

DR. TORLAKOVIC:

A. These are Class I tests. There is another one, even more radical example. This is detecting leukemic cells or blast cells what we call in the bone marrow. Many times, we

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don't have optimal material to detect blast otherwise, but we have to look at the core biopsy. So to detect blast in the core biopsy, we have to use CD34 staining, which detects these immature cells, and this shows actually you can quantitate very carefully four percent, 11 percent of positive cells and 21 percent, 20 percent being a cut off point to diagnose acute leukemia.

So in this, between--it was not possible morphologically to make this distinction, but here we use Class I test to make a critical diagnosis of acute leukemia, yes, or acute leukemia, no, and it has to be quantitated very carefully. So at the same time, it's a quantitative test and it's critically important for therapy decision making. So it doesn't mean that Class I tests are not less worthy, let's say, and there are more than hundreds of them and we don't--and they don't undergo careful testing by external programs and calibration as actually now we are trying to do with Class II tests.

Another example is breast cancer. Of course ER and PR are important, but even more

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important for this patient was just the detection that there is a metastatic tumour in the bone marrow. That would be like Class I test, and then to determine that it's coming from the breast, it's AP-15, again Class I test, and then ER/PR at the end as an adjunct to fully characterize the disease. So I should say that Class I tests have not been appropriately considered in external quality assurance programs, but it's not because people are negligent or they don't want to do it. I just don't know, I have personally no idea how to design a program, external quality assurance program for over hundreds of tests frequent enough so that it's giving the information we need, and at the same time that it's not going to be overburden for the laboratories, pathologists, external quality assurance programs, all of that. I just personally have no vision how to do that.

COFFEY, Q.C.:

Q. As of yet anyway.

DR. TORLAKOVIC:

A. As of yet, yes.

COFFEY, Q.C.:

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Q. Doctor, here, just if we could, just the slide that's there on the screen, the slide in the top left-hand side is a H & E?

DR. TORLAKOVIC:

A. This one, yes.

COFFEY, Q.C.:

Q. Yes, and this is of a metastatic breast carcinoma?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And this is located in, I'm sorry, in?

DR. TORLAKOVIC:

A. The bone marrow.

COFFEY, Q.C.:

Q. The bone, as it turns out.

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. So breast cancer that was understood to have metastasized to the bone. The purpose then of using CK8 and AP-15 are both Class I tests?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

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Q. What is the C--what was the purpose of using the CK8 there?

DR. TORLAKOVIC:

A. CK8 is a type, low molecular rate cytokeratin that detects adenocarcinomas. So it qualifies this disease as adenocarcinoma. So we know now this is adenocarcinoma in the bone marrow and that's not normal. That means it's metastatic lesion.

COFFEY, Q.C.:

Q. Okay, and I take it in doing--in utilizing this here, in looking at it, in order to make that determination -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. - of adenocarcinoma, you would have to be--the pathologist in question would have to be relying upon the CK8 slide making process being accurate?

DR. TORLAKOVIC:

A. Absolutely. If we are going to use this as to be sure that we are dealing with adenocarcinoma, I think we want--should today, in current level of standards of practice, we

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use it frequently immunohistochemistry as evidence of what we may believe that exists anyways. Like I could look at the slide on the left, H & E, and say there is a lesion there and I think it may be metastatic adenocarcinoma, but then often, we would like to confirm that, so it's for medically-based evidence to practice like that. You need the confirmation, and that is what cytokeratin 8 is going here. It's confirming indeed that this is a metastatic adenocarcinoma.

COFFEY, Q.C.:

Q. And I take it then, as a pathologist then, you wanted to be somewhat assured that the CK 8 process is actually working?

DR. TORLAKOVIC:

A. Absolutely.

COFFEY, Q.C.:

Q. If it's not working, if it's giving you an improper result then -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. - you're led down the wrong path.

DR. TORLAKOVIC:

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A. Then you are misled thinking that this is something else.
COFFEY, Q.C.:
Q. I'll go to the next slide here, the AP-15 slide. I'm sorry, it's--you were telling the Commissioner it's used for?
DR. TORLAKOVIC:
A. It's a mark too that is highly specific, not 100 percent, but it's highly specific for breast carcinoma. So it identifies this as organ of origin is breast.
COFFEY, Q.C.:
Q. And again, I take it again, for the same purpose, I take it to see that this metastatic carcinoma is originated in the breast, that's the point of using the AP-15?
DR. TORLAKOVIC:
A. Yes, it is.
COFFEY, Q.C.:
Q. And again, in arriving at that determination, you'd be relying upon the AP-15 being accurate?
DR. TORLAKOVIC:
A. Yes, absolutely.
THE COMMISSIONER:

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Q. Mr. Coffey, we're well past the break.
COFFEY, Q.C.:
Q. If I could, just one more moment, Commissioner, please? Thank you. And then finally then, in this process here, Doctor, with this particular patient, the purpose then of doing an ER and PR on that would be what?
DR. TORLAKOVIC:
A. To provide additional information that is used to stratify the patient for appropriate therapies.
COFFEY, Q.C.:
Q. Therapy?
DR. TORLAKOVIC:
A. Yes, as a predictive markers regarding the use of hormonal therapy or not, Tamoxifen or not.
COFFEY, Q.C.:
Q. And again that's, I take it, it's important, even at that stage, to know that because it may be of some significance to the oncologist -
DR. TORLAKOVIC:
A. Oh, absolutely.
COFFEY, Q.C.:
Q. - as to how to approach the patient?

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DR. TORLAKOVIC:
A. Yes, yes.
COFFEY, Q.C.:
Q. And that would have to be accurate too?
DR. TORLAKOVIC:
A. Absolutely, yes.
COFFEY, Q.C.:
Q. Okay. Thank you, Commissioner.
THE COMMISSIONER:
Q. We'll take 15 minutes.
(BREAK)
THE COMMISSIONER:
Q. Please be seated.
COFFEY, Q.C.:
Q. Thank you, Commissioner. If we could bring up Exhibit P-0113, please? Doctor, this is a memo, the Commissioner has seen this innumerable times now. It's dated April 4th, 2003. It was from a pathologist who practised in St. John's at the time, Dr. Gersham Ejeckam, and I'm not going to ask you to comment upon the memo itself, but there's a certain part of it here. There's certain antibodies identified here, following antibodies. They're, in effect, CK34, I think

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is the short name for it. Am I correct in that?
DR. TORLAKOVIC:
A. No.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. Let's just call it, for this purpose, high molecular rate cytokeratin.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. So it's a special type of cytokeratin which is often used to recognize whether in prostate biopsy there is prostate carcinoma or not.
COFFEY, Q.C.:
Q. Or not, okay, number one. CD3 used for?
DR. TORLAKOVIC:
A. T cell antigen, to identify T cells both benign and malignant.
COFFEY, Q.C.:
Q. CD5?
DR. TORLAKOVIC:
A. It's another lymphoid marker. It's expressed by old T cells frequently lost in T cell

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lymphoma. So the absence of which we use diagnostically, but it's also typically present in some B cell lymphomas in some carcinomas. So we use it for different purposes.

COFFEY, Q.C.:

Q. Depending upon the circumstances?

DR. TORLAKOVIC:

A. Depending on the circumstance, yes.

COFFEY, Q.C.:

Q. CD20?

DR. TORLAKOVIC:

A. This is called a universal pan or pan B cell marker. It identifies B lymphocytes.

COFFEY, Q.C.:

Q. CD79a?

DR. TORLAKOVIC:

A. It's a similar--it's more widely expressed in various stages of development of B cell, normal B cells in various B cell lymphomas and then in some T cell malignancies and even in some cancerous, rarely.

COFFEY, Q.C.:

Q. CEA would be?

DR. TORLAKOVIC:

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A. CEA, it's a marker of--it's a kind of oncogene. It's fetal antigen that is re-expressed with embryonic antigen, it's re-expressed in some carcinomas and it's typically expressed, for example, in colon cancer and it's typically absent in renal cell carcinoma. So it's useful often in evaluating what type of malignancy we are looking at.

COFFEY, Q.C.:

Q. So the six of these then I just looked at here are Class I tests?

DR. TORLAKOVIC:

A. Exactly.

COFFEY, Q.C.:

Q. Now Doctor, as a pathologist, if you were to be told that those six tests were, for an unknown period of time, unreliable, erratic and unhelpful for diagnostic purposes, unbeknownst to you that had been so, okay, but you are now being told that -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. - you know, for an unknown period of time, this is not specified, that those six Class I tests have been unreliable and erratic and unhelpful for diagnostic purposes and you had been utilizing one or more of those six Class I tests dealing with your patients, okay?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Would that cause you any concern about the accuracy of the diagnosis that you'd been given, based upon those tests? Would it cause you to question them?

DR. TORLAKOVIC:

A. This is rather complex question and I'll tell you why, because in practice, this has never happened to me.

COFFEY, Q.C.:

Q. I appreciate that.

DR. TORLAKOVIC:

A. And this has never happened because I cannot be told that this is not--retrospectively, these tests have not been working because wherever I work, we monitor very closely what happens every day. So I have never been in a situation like that, that somebody tells me your test is not--these tests are not working

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for this period of time. But if that would happen that I would come somewhere and where I was not able to use the quality control and quality assurance measures to make sure that I know daily whether they're working or not--I'm not saying that in our lab, all of these antibodies are working all the time, but we'd recognize when they are not and then do something about it right away.

So in that hypothetical situation, if I would have to practice without being able to control their performance, I would be definitely in a state of panic because, as I have mentioned before, Class I tests are extremely important for our diagnostic practice. I just illustrated that you cannot see often without CD20 the presence of B cell lymphoma in the bone marrow. If CD20 was false positive, maybe I have diagnosed B cell lymphoma, something that wasn't and it was otherwise poorly differentiated carcinoma and if I haven't had working high molecular rate cytokeratin in prostate biopsies, that's a particularly bad one to say to have not working because when it's negative, it tells

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us that it's cancer. So maybe I have made some false positive diagnosis based on evaluation of that. Even though we never use just one single evidence, but when you have small glands in a prostate biopsy and you order this test, you ordered it with an idea that it's going to be and it's not going to be there. So you were suspicious enough for cancer since you ordered the test, and then you see the stain is not there, this supports the diagnosis of cancer. So yeah, I would be quite concerned that I have possibly made the wrong diagnosis.

COFFEY, Q.C.:

Q. And you would, I take it then, at least in a theoretical--if you were find, theoretically to find yourself in that position, you'd want to go back to check, well, where did I use them? What period are we talking about?

DR. TORLAKOVIC:

A. Again, this is all hypothetical.

COFFEY, Q.C.:

Q. Yes.

DR. TORLAKOVIC:

A. But what I would do if this would ever happen,

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since it's never happened, what I would do, I would probably go back. I think I would go back. Yes, I would want to know, for my own self, right away to check the things, to make sure even though it's unlikely that the single wrong judgment will be made, but still I would go back to make sure that it hasn't happened.

COFFEY, Q.C.:

Q. Doctor, we were talking about Class I tests, just before the break, and the reason for that being your initial focus in July of 2006 as to where you thought CIQC would, you know, would initially go.

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And you've indicated why that was so, in terms of Class I tests. What then happened? You made your proposal. Initially you didn't hear anything immediately back from the Canadian Association of Pathologists you said.

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. And what then happened? You found out, I take

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it, that the HER2 group were in fact not going to be doing EQA for Class II tests, and then how did this evolve? Perhaps you could take the Commissioner then through how you ended up where you are today, between July of '06 and now?

DR. TORLAKOVIC:

A. If we can go back to the presentation.

COFFEY, Q.C.:

Q. Sure, go back to the -

DR. TORLAKOVIC:

A. I have a couple of slides that I can use to -

COFFEY, Q.C.:

Q. Sure.

DR. TORLAKOVIC:

A. As we can see, we started with run 1. We just started. We didn't have an answer yet, but then we created anyways the testing material and invited several laboratories throughout Canada if they want to participate just on a voluntary basis free of charge, just if they want to -

COFFEY, Q.C.:

Q. Okay, so just so we're clear on that. So you have made your proposal to the Canadian

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Association of Pathologists?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. In the summer of '06?

DR. TORLAKOVIC:

A. Um-hm.

COFFEY, Q.C.:

Q. Initially, you hadn't heard anything back. You had your website up?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. You create Run 1, which is referred to here?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And undifferentiated tumour panel. Who's we? You say "we created".

DR. TORLAKOVIC:

A. It is basically between Dr. Gilks and myself. We created this tissue microarray block with 72 samples, tissue samples, and asked laboratories if they would volunteer and stain them with different markers that are used very

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often in an undifferentiated tumour panel. This is a critical tumour panel to decide on when we have morphologically non-descript entity, so we morphologically don't know what it is, to figure out whether it's--in which group it belongs. Is it carcinoma? Is it lymphoma? Is it sarcoma or what?

COFFEY, Q.C.:

Q. So you create a microarray.

DR. TORLAKOVIC:

A. So that is Class I. That's why we started with Class I.

COFFEY, Q.C.:

Q. Microarray set of slides.

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And in effect, contacted other labs in Canada?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And said "look, would you like to participate?"

DR. TORLAKOVIC:

A. Um-hm.

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COFFEY, Q.C.:

Q. "We'll send you the slides."

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. So what happened initially? How many -

DR. TORLAKOVIC:

A. 12 laboratories altogether participated in this run and so we got some really interesting results. I'm not sure--did I--okay, so I don't have detailed results from Run 1 but I can summarize it, that because we used a large number of tissue samples, we were able, despite the small number of labs, to actually calculate their performance, in the sense of false positive, false negative, and overall success rate and so on. So it was quite surprising for us to see that there was some tests in which you had as many as 30 percent of false positives, a range of 30 percent or so false negative in these tests. So it was -

COFFEY, Q.C.:

Q. And these were all Class I tests?

DR. TORLAKOVIC:

A. Class I tests, and these are very frequently used. These are not some bizarre, rare tests. These are tests that are used daily. Virtually every lab that has immunohistochemistry will use these tests, all of them.

COFFEY, Q.C.:

Q. Okay. So you got the--what then happened?

DR. TORLAKOVIC:

A. After that, the focus shifted on Class II or breast cancer markers.

COFFEY, Q.C.:

Q. Before I go on to that, if I could, Doctor, so initially you got the slides back.

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And they were looked at, and so if I could, perhaps I'd just like to explore that a bit. You sent out the slides, they were stained?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. By these labs?

DR. TORLAKOVIC:

A. Um-hm.

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COFFEY, Q.C.:

Q. They sent back the stained slides?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And they were looked at by?

DR. TORLAKOVIC:

A. Both of us.

COFFEY, Q.C.:

Q. By yourself and Dr. Gilks?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And based upon what you were seeing, you were saying, well, you know, you anticipated that a particular part of the microarray should stain in a particular manner?

DR. TORLAKOVIC:

A. Absolutely.

COFFEY, Q.C.:

Q. Absolutely?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And you were seeing, at times, some positives

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that shouldn't be positive, which were -
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. - classed false positives?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And some that were negatives, visually negative to yourselves, but should have been positive?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Or false negatives, and the rate overall, when you did the calculations is about 30 percent for some stains?
DR. TORLAKOVIC:
A. It varied greatly. Actually, the results were, in summarized format, presented at the-- in Toronto, at the annual meeting of CAP. We had a poster presentation on those results, and they're also--I mean, they're widely available. They're available on our web page for each individual test, and they are

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illustrated in detail.
COFFEY, Q.C.:
Q. If we could, please, Exhibit P-3362? Doctor, there's a summary at P-0276? Is that the -
DR. TORLAKOVIC:
A. Yeah, that's a poster. That's in an abstract format. That was in poster format, this is much larger obviously. The big poster was created with images and more detailed methods and more detailed results.
COFFEY, Q.C.:
Q. Here, Doctor, this was presented at Canadian Laboratory Medicine Congress 2007.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And is this the results of that first run?
DR. TORLAKOVIC:
A. Yes, it is.
COFFEY, Q.C.:
Q. That you were referring to, and this, I take it, summarizes then, in a textual manner -
DR. TORLAKOVIC:
A. It does.
COFFEY, Q.C.:

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Q. - what yourself and Dr. Gilks' observations were?
DR. TORLAKOVIC:
A. Um-hm.
COFFEY, Q.C.:
Q. Then I notice yourself and Dr. Gilks' name. There is a Klassen and -
DR. TORLAKOVIC:
A. That's a resident that was--we tried to--since we have residency program, we try to include residents more in some scientific project. So we included this resident in this project.
COFFEY, Q.C.:
Q. And just looking down through this, Doctor -
DR. TORLAKOVIC:
A. And Klassen is our--Shannon Klassen, she's our expert technologist in immunohistochemistry lab.
COFFEY, Q.C.:
Q. Okay.
DR. TORLAKOVIC:
A. And we do include them as co-authors any time they do extra work that is not specified by their work description, job description.
COFFEY, Q.C.:

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Q. Here, Doctor, just to summarize this, in the middle of it, it begins "15 Canadian clinical immunohistochemistry laboratories were invited to stain tissue microarray slides that contain 76 tissue cores to represent lesions with various expressions of tested epitopes. Selected were tests that are in daily use for evaluation of undifferentiated tumours," and you name them, and then it goes on "in appropriate setting, these markers enable distinction between carcinoma, melanoma and sarcoma. Stains were scored on a scale of zero to three plus with separate scores for pathological or predominant cell population as appropriate and background non-specific staining. Pan cytokeratin," I don't know what you -
DR. TORLAKOVIC:
A. Pan cytokeratin.
COFFEY, Q.C.:
Q. Yes, "staining produced from zero to 30 percent false negative rate with similarly significant differences between the laboratories also for LMWCQ, vimentin and S100. While most laboratories enjoyed

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similar"--sorry, "employed similar detection methods, the differences appear to be secondary to variations in antigen retrieval procedures or dilution of the primary antibodies. The results are a more detailed poster for viewing and visual microscopy at the CIQC website. We conclude that Canadian clinical immunohistochemistry laboratories produce variable results, even with the most commonly used tests and that external QC programs would probably help to achieve standardization in QC programs"--I'm sorry, "standardization in immunohistochemistry," and you've--there's--here, it refers to false negative, but there's--somebody has handwritten here also, false positive, and you did indicate to the Commissioner -

DR. TORLAKOVIC:

A. Yes, that was in the poster itself presented that -

COFFEY, Q.C.:

Q. There were both false positive rates and -

DR. TORLAKOVIC:

A. Right, there were false positives.

COFFEY, Q.C.:

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Q. Doctor, so, I'm sorry, I interrupted you. You did the first run, Class I tests, and then what happened, in terms, if we could go back, please, to the exhibit we were looking at? You were about to tell the Commissioner the focus then shifted.

DR. TORLAKOVIC:

A. It shifted because then we actually, at that time, actually learned about what's happening about false negative results with ER in Newfoundland.

COFFEY, Q.C.:

Q. Yes.

DR. TORLAKOVIC:

A. So, and there was lots of now focus on how ER/PR tests were done, and since nobody else was really doing it for Canada, we decided we are going to create tissue microarrays with a particular purpose to study now Class II tests for breast cancer markers. So Run 2, Run 3 and now we are preparing Run 4 as we speak. They are all focused on breast cancer markers.

COFFEY, Q.C.:

Q. Now here, in the fourth bullet, there's a note "18 labs participated in run 2," which is

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ER/PR and HER2/neu?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And then 23 labs participated in run 3, which was ER/PR. Do you recall when runs 2 and 3 were done, approximately when they were done?

DR. TORLAKOVIC:

A. No.

COFFEY, Q.C.:

Q. Okay.

DR. TORLAKOVIC:

A. I'm sorry, not -

COFFEY, Q.C.:

Q. Sometime since the first, since run 1?

DR. TORLAKOVIC:

A. Well, let me say that run 3 probably was completed three months ago or something like that, and the one before that, five to six months.

COFFEY, Q.C.:

Q. Prior to that?

DR. TORLAKOVIC:

A. Yes, prior to that. I'm not sure about exact dates.

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COFFEY, Q.C.:

Q. Doctor, what were the results, in general, in terms of looking at the results in runs 2 and 3?

DR. TORLAKOVIC:

A. It's quite surprising, and I did want to show you this.

COFFEY, Q.C.:

Q. So this is this -

DR. TORLAKOVIC:

A. This is run 3.

COFFEY, Q.C.:

Q. This is run 3, go ahead.

DR. TORLAKOVIC:

A. I think it is.

COFFEY, Q.C.:

Q. If you could blow that up just a tiny bit, please, if it's possible? See it there, in the top left-hand side, it's run 3.

DR. TORLAKOVIC:

A. Yeah, it's run 3. Yes, it's run 3. I'm sure it's run 3. So this is in the summarized form as to what happened with this, the number of labs, but run 2 was even better. When I say even better, that means that even these

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results are good. Run 2 and Run 3 were designed differently, even though both consists of tumour samples with variable expression of estrogen and progesterone receptors. Run 2 also ran HER2, and the reference values were from FISH, or Fluorescent In Situ Hybridization, and for ER/PR, a most common or consensus why you would use those reference values, but I wanted to tell you that we were very surprised to see in Run 2 that we got extremely good results. We expected much worse results, not because ER/PR themselves are challenging technically, it's just because of historical evidence that there is much more variability than what we achieve. So we wondered why was that, you know, and I think it's because people started to pay attention because that Run 2 was run after people learned about what happened in Newfoundland, and I think that just the fact that this happened and everybody is paying attention now has improved greatly clinical practice in diagnostic immunohistochemistry in Canada. Just as an upshot of this, I think we already have much better practice without any

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additional intervention. So we actually prepared those results to be published and submitted it for publishing in scientific literature and it's currently under review.

COFFEY, Q.C.:

Q. And that's the results of Run 2--Run 2 or Run 3 or both?

DR. TORLAKOVIC:

A. Run 2 only. Run 3 was designed a little bit differently. Run 3 was designed with tumours that were selected with low expression mainly. So large number of low expressors, which is not the case in clinical practice because most tumours, when they show expression of estrogen receptors, they vary, but it is rare that there is a big expression that we detect, compared to strong expression is much less frequent. So this Run 3 was designed with an idea now if we design it like that because the results were so good, maybe we can still see if there are any fine tuning differences that can be detected and the internal quality controls can be further fine tuned not to miss this low expressors. So we did that, and we got also very good results. It was a little

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bit less successful because this is extremely challenging material, and this is usually not the material that you would usually use in ordinary external quality assurance program. So, therefore, it's providing a special type of information to us. I don't think that otherwise they would have an opportunity to discover how exactly, you know, where even the minor problems now should come up after these tests, and it can be fixed.

COFFEY, Q.C.:

Q. And have the laboratories that participated in Runs 1, 2, and 3, were they given feedback on their results?

DR. TORLAKOVIC:

A. Yes. I mean, what they--they can go also on that web page themselves. They can look at--compare their own laboratory with others, all of this. I mean, the major feedback is that you look at the protocols and look at the results, and look at the assessment of what values and look at your concordance rate, and this is what matters. So they have all the information they need to have for their quality assurance purposes.

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COFFEY, Q.C.:

Q. And you had shown the Commissioner earlier, for example, the lab identified with a number, like, lab 102, for example?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. You can go elsewhere on the website and actually look at the protocol used by detail?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. By that lab, lab 102, for their ER?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. And for their PR. You just actually watch it and I suppose then compare it--if you were lab 105, you can compare what you've done in the process to -

DR. TORLAKOVIC:

A. Right. It doesn't mean it gives you all the solutions and it doesn't mean that those that participated did excellent and use these protocols, these are the only protocols that

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will work, or the only reagent that will work. This just means this is what this particular lab was doing and was very successful or not, and if not, I mean, we can identify the problem right away. I can tell you there was one of the labs in Run 2 that was less successful than others in ER. It had, I think, 92 percent concordance rate, which is still good, it's not bad, but it wasn't over 95 percent, and the only difference was it was clear in the protocol that they were using six times higher dilution of the primary antibodies than others, even though they used identical clonal antibody, identical protection system, identical instrumentation. So the point was that was quickly changed. The dilution was re-titrated and the lab was retested and the results were perfect. So that was one of the illustrations how things could be done quickly.

COFFEY, Q.C.:

Q. Doctor, go back to the slide then that--let's see. Just a moment, please, Commissioner. You've indicated you're currently preparing Run 4?

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DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. And Run 4 will involve what types of -

DR. TORLAKOVIC:

A. We thought about two arms of Run 4, it all starts to go back to Class I test also, but to continue to run breast cancer markers because it's so important. So for Run 4, we will have about 50 tissue cores on the block for ER/PR and HER2, and then we will have also tissue microarray for a set of lymphoid markers now for Class I tests.

COFFEY, Q.C.:

Q. Doctor, here on this particular slide, a couple of things I wanted to ask you about beyond what we've already touched on. One of them is the program offered by CIQC provides testing material adequate for sensible statistical analysis currently recommended in new guidelines for Class II test, i.e. for HER2, okay. I take it this has to do with the sheer number of samples in a microarray?

DR. TORLAKOVIC:

A. Absolutely.

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COFFEY, Q.C.:

Q. Okay, can you tell--elaborate on that for the Commissioner a bit as to why compared to, for example, some other programs that don't use microarrays, and the advantage of using a microarray.

DR. TORLAKOVIC:

A. One has to be aware that it's only recently that ASCO or CAP guidelines or even our national Canadian guidelines for HER2 point out the level of concordance that is necessary with reference labs. It's spelled out to be more than 95 percent, and that means that there should be material provided by EQA program that is created--designed as such to enable a meaningful statistical analysis and a meaningful calculation of concordance, or for that matter, otherwise. So to do so, that has to be based on actually proper analysis, taking into consideration the type of statistical analysis or other calculations that need to be done and the type of the material that we are using. So when that comes to that, that means that you cannot really use material from any external quality

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assurance program to fulfil this requirement. For example, NordiQC is right now not providing large enough samples in their material for testing for HER2. I think they are below 10 still, and you cannot calculate 95 percent concordance with 10 samples. I think CAP is providing 40 samples, which is probably sufficient, but my problem with that is they provide it only once a year. So we have to have external quality assurance program that is providing this sensible testing material, but often enough also so that laboratories can -

COFFEY, Q.C.:

Q. Enough at a time, enough samples at a time?

DR. TORLAKOVIC:

A. Enough samples at a time -

COFFEY, Q.C.:

Q. To provide statistically significant results?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. As well as often enough throughout the year -

DR. TORLAKOVIC:

A. Right.

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COFFEY, Q.C.:
Q. To achieve quality control goals--quality assurance goals?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And once a year perhaps is not enough?
DR. TORLAKOVIC:
A. No.
COFFEY, Q.C.:
Q. Because it's another 12 months before it gets done again?
DR. TORLAKOVIC:
A. Exactly. So there is--I think in the United States they go by twice a year as a minimum, and what we want to suggest is three times a year as a minimum for Canada, because I think that would be more like ISO standards or just our own feeling that how--large gap, we want to have for these sensitive and very important sensitive tests to be able to not miss a large number of patients in between.
COFFEY, Q.C.:
Q. If it's twice a year, it's six months before you get around to it again?

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DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. And in the meantime, you process six months worth of patients?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. And potentially if you have had a problem, I take it, for up to six months undetected by outside -
DR. TORLAKOVIC:
A. Except that if this program is used as external quality assurance program should be used to actually calibrate your own lab, so your own positive controls should be constructed like that, and you should notice if there is a problem or not, and you should often demonstrate also that you don't have a problem. So that external quality assurance is not going to be used only so that laboratories can adopt their quality assurance programs and calibrate, but also to have for accreditation purposes as evidence for certification.

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COFFEY, Q.C.:
Q. And here, Doctor, in the third last bullet, "Provides extensive feedback to participating laboratories. Can use this information to improve results immediately", and you gave us the one example of the lab that was -
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. One particular lab earlier involved in Run 2, but here as well at one of the middle bullets here it says, "No funding so far". Now I was going to ask you about how is all this being paid for, CIQC, or is it being paid for at all, and if so, how, and what else is needed from your perspective?
DR. TORLAKOVIC:
A. We had to pay to construct that multiviewer that enables comparison side by side. I think the price was about $6,000.00 or so. So we asked some companies that sell us antibodies and immunohistochemical material if they would want to have their logos displayed on our home page, so we got money from two companies that covered just exactly for that program, two and

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a half thousand from each company, and then otherwise we basically donate totally our time and our work. Why we didn't come up with participation fees; I mean, we are not really well established program, we have no program manager, we have no way how to actually determine what the real cost is, we don't know how large this program may be in the future. So larger the program, smaller the fees would be because you have the same structure to support your small laboratory, so the only additional cost if the lab grows eventually. When it's established, it's just like for mailing of the slides, which is minimal. So I don't really know in that official sense. Like, we have put some calculations together approximately how much it would cost because, as I said, assessment of the results is critical, and I think that face to face meetings--or even maybe not face to face with the current technology. As we scan all the slides, maybe we can do it over teleconference, but it is important that in real time assessors look at the same specimen and discuss the results of the labs and try to

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figure out what the recommendations would be for each individual lab result. So that costs money and it will cost--if we actually travel, it will cost to travel, it will cost for accommodations, for food, and currently if you want to have four assessors as most assessments, that's how they're performed today, that means cost for four people, and if it's three times a year at least. So we have come up with some kind of sum of money that we need. If we would charge participation fees about 20/30 labs, that would be extremely expensive. So we cannot do that, and somehow we do not feel that laboratories kind of should pay for this service, because it's really hard to put a price. You have to have service like this. I think it's--if you mandate participation in such a program, you have to provide such a program available to labs, and I see that--the Class II test, there may be more of them coming up in the future, so there will be even more demands on the labs to participate. Additional fees, I mean, it's just going to crash budget of laboratories because unfortunately pathologists are not--

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labs are not paid fee for service like they are in the United States. They have their budget, and you don't want to crash that budget just because now you mandate something that is expensive.

COFFEY, Q.C.:

Q. For example, participation in something like CIQC if it was -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. If it had to be funded by the participants and it was an expensive program, and it, in effect, would--ultimately if the labs don't have the money in their budgets, they'd have t find it somewhere within their own budget?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. Which would negatively affect, presumably, potentially what they're doing otherwise. Doctor, can you tell the Commissioner have any other funding sources been canvassed or sought, governmental sources, for example?

DR. TORLAKOVIC:

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A. I cannot list for you now agencies, but National Standards Committee for immunohistochemistry from CAP have various committee members and some of them have better understanding of potential sources of funding than myself, and so some of the agencies were shortlisted for the members to consider and contact, and we will try to find some sources, but so far no definite source has been promised or identified. So we cannot say now that this program may be funded by whatever particular agency or source.

COFFEY, Q.C.:

Q. Doctor, it's October 9th, 2008 as we sit here today. As of today you do refer here to, in the second-last bullet, to "This program is adequate to fulfil the criteria for mandatory certification."

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. We've also, of course, heard references to laboratory accreditation?

DR. TORLAKOVIC:

A. Yes.

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COFFEY, Q.C.:

Q. In a wider sense, labs, clinical lab accreditation. Doctor, to your knowledge, where in Canada to date is there laboratory accreditation for clinical labs? I understand Ontario has it, there's mandatory accrediting by QMPLS?

DR. TORLAKOVIC:

A. I think that laboratory--not think. I think I know the answer to this question. There are five provinces that have laboratory accreditation in place, and those five provinces are from, it's BC, it's Alberta, it's Saskatchewan, it's Manitoba and it's Ontario. And they have obligatory participation for immunohistochemistry labs in quality, in external quality assurance programs. And since recently, actually, some of them--and that varies now from one accreditation program to another, when they started to actually mandate these for breast cancer markers, and each of them has their own history and where they are at. And I can tell you for Saskatchewan we are right now in the middle of creating such requirement that it's

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mandatory with Saskatchewan. We have participation for breast cancer markers for a very long time. It hasn't been mandated and it's going to be changed now to being mandatory. But, national standards committee for immunohistochemistry from CAP, one of the immediate tasks that we have on our program is to call for mandatory certification or uniform mandatory certification requirements for all laboratories that practice in diagnostic immunohistochemistry everywhere, even where there are no accreditation programs. It also means -

COFFEY, Q.C.:

Q. Such as, for example, this province?

DR. TORLAKOVIC:

A. Right.

COFFEY, Q.C.:

Q. I'm sorry, Doctor, you were saying, it also means?

DR. TORLAKOVIC:

A. It also means that if there is no accreditation program, I think that it has to be built quickly. And if--for immediate use I think one could use a good external quality

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assurance program and just good practices. And even without accreditation we know that results can be, results can be improved and the quality can rise. We saw that from NordiQC. In Scandinavia many laboratories don't have accreditation but they still kind of certified their tests by participating. So there is a difference between test certification and accreditation programs.

COFFEY, Q.C.:

Q. Yeah.

DR. TORLAKOVIC:

A. So in this case we can go and certify the test even without the accreditation program for the time being.

COFFEY, Q.C.:

Q. And -

DR. TORLAKOVIC:

A. So what would it mean to certify the test? I think it would mean to participate three times a year and with a success rate in the testing in EAQ program for that particular test. That would mean that, say, for ER, three times a year, stain the slide for ER and show that you have more than 95 percent concordance with

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reference wise and that would be certified, that would then certify the lab--the test itself.

COFFEY, Q.C.:

Q. Yes. Is CIQC affiliated with the Canadian Association of Pathologists? Are you a part of that group?

DR. TORLAKOVIC:

A. Not formally, no.

COFFEY, Q.C.:

Q. Yes, and I was going to ask you about the relationship between CIQC and the Canadian Association of Pathologists.

DR. TORLAKOVIC:

A. There is, I mean, I am co-founder of CIQC.

COFFEY, Q.C.:

Q. Yes.

DR. TORLAKOVIC:

A. And I am chairing the committee in CAP and I am now executive committee of CAP, but other than that there is no connection, there is no official connection. They support the program because they think that the program has valid scientific and--all of the principles that we have demonstrated so far show that this

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program is well structured and provides information that is sufficient for laboratory--or that tests can be certified by using this program. It has all the components of -

COFFEY, Q.C.:

Q. If we could look, please--just come down a little bit here, yeah. This is a slide, it's one of the last slides of the presentation. It's the CAP Five-Point Plan?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Could you take us through that, please, Doctor?

DR. TORLAKOVIC:

A. I wanted to say that the committee had a task to create a document for this last summer to--in Ottawa at the annual meeting CAP committee was to present a draft document that contains suggestions like where we should go in regards to standardization in diagnostic immunohistochemistry. So -

COFFEY, Q.C.:

Q. This is a CAP committee?

DR. TORLAKOVIC:

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A. CAP committee, yes.
COFFEY, Q.C.:
Q. Yes, go ahead.
DR. TORLAKOVIC:
A. So that draft document was submitted to executive committee. And out of that draft document some of--most of the points that are listed here as one, two, three, four and five, we had our five points, it's was slightly modified, it's a final CAP document and five-point plan that you see here. So, first of all, we are as a committee or the CAP, actually, is calling for mandatory certification for each prognostic and predictive test performed by a medical laboratory. That means those are breast cancer markers that, that EG4 (phonetic) the CD117 and the CD20 to be included. External validation system where test results from one laboratory would be verified by another independent external laboratory or the participation in EQA is obligatory. Dissemination and use of the Canadian National Checklist for diagnostic IHC. This point actually is extremely important because

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national standards committee is not there to create standards all over, because there are many standards that are published already. So our role was not in creating yet another duplicate document and overlap with major documents that are created for this area. But we found that our role would be in trying to provide standards for implementation of guidelines into the laboratories, because of the only existing guidelines and standards that are published, they are not uniformly transformed or translated into the practice, so we found that as a missing link. And we think that creating checklists would be the way that would help laboratories implement existing guidelines into their practice, and therefore we created two working groups or subcommittees, if you will, in the national standards committee that will work on creating a checklist for Class I and another checklists for Class II tests, that should help in more uniform translation of published guidelines and standards in the practice.
COFFEY, Q.C.:
Q. Into actually laboratory processes?

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DR. TORLAKOVIC:
A. Yes, right. And then point four, "Creation of national body separate from government to accredit all medical laboratories in Canada and ensure they need quality and critical"--"meet" sorry, that "quality and critical mass standards." This is because right now some provinces when we listed out that have accreditation, laboratory accreditation, but some of them don't. And it would be logical, I think, that we should have a national accreditation body that would use the same standards for all labs. How accreditation processes differ from one province to another, I don't know in detail exactly because I'm not involved directly in laboratory accreditation, but I know that there are differences and there are different levels of sophistication that are used for this process. On the other hand, there is no reason why provinces should have different standards for accreditation.
And then the point five, "Immediate and ongoing support from federal, provincial and territorial governments to address the critical workforce and resource shortages

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undermining laboratory medicine." As we all know, I mean, the shortage of pathologists as well a shortage of expert technologists that are working in the labs is something that we cannot easily solve. And that is creating a lot of problems because quality assurance and quality control, they need expertise but they also need time. And I can say my own time, my time and my ability to do what I want to do is actually limited. I am not even able for my own lab to do everything that I would want to do because I just don't have enough time for that. So we do need more resources to be able to actually do this job the way we currently think we can and we know how.
COFFEY, Q.C.:
Q. And in terms of before I come back to the idea of like a national effort here, in number four here there's a reference to critical mass standards. What is that, Doctor, equality and critical mass standards, what is that? Took care of all and ensured that the issue--pointed out, the need should be meet. They meet quality, quality standards, I think is pretty self-evident. Critical mass standards

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would be what?
DR. TORLAKOVIC:
A. For standards, I mean, again, I think that term is overused.
COFFEY, Q.C.:
Q. Yes.
DR. TORLAKOVIC:
A. We need the critical mass of evidence. Critical mass, that's why we need a national body, because some of the places is just simply too small to provide--to create and to have one of their own quality assurance systems. They need to be part of the larger mass, quality mass because at some point, I don't know if it's--I should mention this, quantity at some point becomes quality, and that's the critical mass. You cannot run really good quality assurance programs between two labs in Saskatchewan. There is no quality assurance program that is necessary for--makes, doesn't make sense for two labs. But when you put all the laboratories in Canada together, you get a mass, critical mass that is necessary for such a program to function.
COFFEY, Q.C.:

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Q. And just in terms of the, illustrating for the Commissioner the current state of affairs, if I could, just while it's come up here, Commissioner, here this slide is QC, QA and IHC in Canada. And this is--you pointed out there there's no national list of diagnostic laboratories that perform the IHC testing for patients' care. So I take it to your knowledge there is no actual complete list -
DR. TORLAKOVIC:
A. There's no national list, no, no, there is no complete list. And that is the greatest frustration we deal with because even--when you think about it, how do you know what's going on? How do you know what's happening on the ground when you don't even know who people--where are the labs. Who -
COFFEY, Q.C.:
Q. Who's doing the test?
DR. TORLAKOVIC:
A. - are the constants (phonetic)? Who is doing what? So at the committee, CAP committee that I am chairing we try to do a survey to see where we are and who is doing what, how many tests on their menus to identify how big the

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problem is that we deal with, how are we going to plan for the future, you know, where we are going and so on. There's absolutely no information that we can get because--also, when we were creating CIQC, we wanted to invite as large numbers as possible of laboratories to participate. But just to gain the information who these people are, I mean, and you know that people move from one place to another. What's published in one directory is not necessarily accurate for the current state--for what's currently on the ground. So it took us a lot of time and contacts and phone calling until we get, like, this 12 laps for the first run just to organize that to contact them, to have accurate address, where to send the slides and who's going to take care of them who's going to--that was a huge problem and that still is. So we don't--we have to find a way how to get a list of the labs and then we have to do the survey and then we have to see--to get an insight how big is the problem and then we have to take--plan other steps because before that I don't think we can plan anything.

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COFFEY, Q.C.:
Q. Without knowing who might even be involved or how many?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And where they are?
DR. TORLAKOVIC:
A. We have no idea.
COFFEY, Q.C.:
Q. Doctor, I'm going to end on that note, Commissioner. They're the questions I have.
THE COMMISSIONER:
Q. All right, then. Thank you. Mr. Pritchard?
MR. PRITCHARD:
Q. I don't have any questions for this witness. Thank you -
THE COMMISSIONER:
Q. Mr. Simmons?
MR. SIMMONS:
Q. Thank you, Commissioner. I do have a few questions. I wonder if we might be able to canvas the room and see if Dr. Torlakovic is coming back this afternoon anyway and if she is, I might benefit from an early break so I

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can organize my thoughts a little bit. It's been, you know, obviously, a very interesting and complex (inaudible) testimony so far this morning. But if we could finish Ms. Torlakovic by lunch break, I'll go ahead.

THE COMMISSIONER:

Q. All right. Well, why don't we do that. Mr. Browne, do you have any questions?

MR. BROWNE:

Q. At this point I just have a couple of--there is one area, actually, I wanted to explore with Dr. Torlakovic and I may also benefit from a short adjournment.

THE COMMISSIONER:

Q. Ms. Newbury?

MS. NEWBURY:

Q. I'll probably be ten minutes.

THE COMMISSIONER:

Q. All right. Mr. Crosbie?

CROSBIE, Q.C.:

Q. Five minutes.

PIKE, Q.C.:

Q. No questions for me.

MR. SIMMONS:

Q. It's your call, Commissioner.

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THE COMMISSIONER:

Q. It's my call, obviously. Clearly you feel that you'd benefit from being able to put your thoughts together. Why don't we just take the luncheon break a little early and come back at ten to two, instead of the normal time. How is that?

MR. SIMMONS:

Q. Thank you, Commissioner. It's a valuable opportunity and I wouldn't want to miss the opportunity -

THE COMMISSIONER:

Q. Well, indeed, and I appreciate that. But when we have somebody of the knowledge of this witness, we want to take advantage of it. So we'll take the luncheon break and come back at ten to two. Thank you.

(LUNCH BREAK)

THE COMMISSIONER:

Q. Please be seated. Mr. Simmons?

MR. SIMMONS:

Q. I have a request from Mr. Crosbie, he has an appointment to (inaudible), so I -

THE COMMISSIONER:

Q. All right, then. Mr. Crosbie.

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DR. EMINA TORLAKOVIC, EXAMINATION BY CHESLEY CROSBIE, Q.C.

CROSBIE, Q.C:

Q. Thank you. Doctor, this may be a little off the overall topic that you'd been addressing before the Commission today. But we've heard evidence that in the lab here at Eastern Health there was a period of time, maybe three and a half years, after Dr. Khalifa in the fall of 1999, when the amount of clinical or pathology supervision or input that was available to the IHC lab consisted mainly in the reading of slides and there seemed to be no real resource person with expertise in IHC testing available to the technical people. I'm just wondering if you can say a few words on what you think should be the relationship between the chief technical person in charge of the lab and the clinical side, how should that be structured, set up and what's the division of responsibilities?

DR. TORLAKOVIC:

A. It would also depend a little bit on the size of the laboratory I should start with saying, because if one particular lab is performing

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very limited spectro (phonetic) in small number from your histochemical test, it would be difficult to imagine that you would have a special person, special pathologist dedicated to the function of being a director of immunohistochemistry for such limited volumes. Therefore, there wouldn't be a special person designated with expertise and responsibility for this area.

CROSBIE, Q.C.:

Q. Do you know what the volumes were in the lab here in the period we're talking about?

DR. TORLAKOVIC:

A. No, I have no idea.

CROSBIE, Q.C:

Q. Is it just over 300, have I got that about right?

COFFEY, Q.C:

Q. I'm sorry, you're looking for?

CROSBIE, Q.C:

Q. The volume of ER/PR tests in the lab a year?

COFFEY, Q.C:

Q. About 350 a year.

CROSBIE, Q.C:

Q. 350 a year.

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DR. TORLAKOVIC:
A. All immunohistochemical tests together?
COFFEY, Q.C.:
Q. No, 14,000.
DR. TORLAKOVIC:
A. 14,000.
COFFEY, Q.C.:
Q. Mr. Simmons will correct me if I'm wrong, 14,000.
MR. SIMMONS:
Q. I'm not sure.
DR. TORLAKOVIC:
A. So that -
COFFEY, Q.C.:
Q. That's the figure we've heard.
CROSBIE, Q.C:
Q. 350 ER/PR.
DR. TORLAKOVIC:
A. All right, so that means probably what you said is correct about thousands. So that is volume enough to have a designated specialist to dedicate part of his or her time for immunohistochemistry laboratory alone. And that -
CROSBIE, Q.C:

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Q. Sorry, are you talking on the pathology side now?
DR. TORLAKOVIC:
A. Pathology, pathology side. And that pathologist would have to closely interaction on daily basis with expert technologist who is in charge of immunohistochemistry too. And there should be one person, and preferably, depending on how much volume is--what's the level of automation and so on. But whoever is there, there should be a permanent technology setup of technologists who are the same people, not rotating too much to doing other things because this area is so sophisticated and demanding a special knowledge from the technologist that they cannot, they cannot simply be imported from other areas on temporary basis without clear supervision from other expert pathologists. So you would think that there should be at least one or two, for such number of tests it would be optimally two f u l l t i m e t e c h n o l o g i s t s f o r immunohistochemistry with additional person helping with more simple tasks. And you would have part-time pathologists involved who would

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be daily in contact with the top technologist or whoever is mainly responsible for that.
CROSBIE, Q.C:
Q. What would the responsibilities of the pathologist be?
DR. TORLAKOVIC:
A. Ideally, we can speak only ideally, because this varies greatly from one lab to another, from one country to another. But as I see it ideally, such pathologist would be in charge of making sure that daily quality control systems are functioning correctly and that there is participation in standard quality assurance programs and that even touch base with other pathologists in making sure there is communication that unusual results can be reported to him or her so that any intervention that needs to be done is being done in time.
CROSBIE, Q.C:
Q. I get the sense, listening to various people talking about this, that pathologists themselves have varying degrees of skill and experience with actually how things are done in the lab. In other words, I guess you could

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call it lab or bench experience available to them. Is that correct?
DR. TORLAKOVIC:
A. It's varied. The background of various pathologists in their training level in these areas is extremely variable, extremely heterogenous and the expertise they have, it's usually devised from their personal exposure and experience in their practice, rather than structured education in this area. As I am aware, even today education with residents is lacking in this area, in particular when it comes to quality control and quality assurance issues. I don't think we are educating even the newest generation of pathologists enough on these issues.
CROSBIE, Q.C:
Q. Well, perhaps I could ask this: Would it be a prudent quality assurance measure to actually describe the characteristics or qualifications, which may not be formal ones, they may be based on experience, the sorts of things that the pathology resource person available to a lab with the volume that you've heard about we have here, should be able to

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exhibit and make available to the technology staff in the lab itself? In other words, to describe that formally?

DR. TORLAKOVIC:

A. Again -

CROSBIE, Q.C:

Q. In writing, and when I say "formally", a written description?

DR. TORLAKOVIC:

A. I mean, ideally a pathologist should be a resource for selection of controls, appropriate controls for all the tests that are run in the lab and ideally should be going over the entire communication of the lab on a periodic basis, at minimum once a year, making sure that all laboratory protocols and procedures are updated appropriately. And minimally he should be available as a resource any time because technologists are usually very diligent to bond this, whatever they produce they review, they look at it and they make a judgment. If they notice any potential problems, pathologist should be a first resource for them for discussion and potential intervention.

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CROSBIE, Q.C:

Q. And again, would it be useful to have that sort of, those sort of qualifications that you just described reduced to writing for a lab?

DR. TORLAKOVIC:

A. In writing? I'm not sure that I understand your question.

CROSBIE, Q.C:

Q. Well, you just described for the Commissioner a list of attributes and functions that the clinical side ought to make available to the lab?

DR. TORLAKOVIC:

A. Yes.

CROSBIE, Q.C:

Q. Would it not be a good idea, would it be a good idea to have that in writing?

THE COMMISSIONER:

Q. A job description, you would -

CROSBIE, Q.C:

Q. Yes, indeed, yeah.

DR. TORLAKOVIC:

A. Oh, yes, well, why not. I think that would be actually helpful, since I'm not sure that anybody described ever in such--in a very

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detailed manner like what is the job description of an immunohistochemistry director, you know, of a pathologist who is in charge. I don't think there is an exact and uniform description of what that job should be. But I just told you like from my own experience and practice -

CROSBIE, Q.C:

Q. But that may vary from one lab to another?

DR. TORLAKOVIC:

A. And may vary.

CROSBIE, Q.C:

Q. But at least it helps to reduce the scope for any confusion -

DR. TORLAKOVIC:

A. Absolutely.

CROSBIE, Q.C:

Q. - or lack of clarity about who's responsible for what?

DR. TORLAKOVIC:

A. Yes.

CROSBIE, Q.C:

Q. Another thing I wanted to ask you briefly is, there may be others, but I have this sort of model in my head of IHC testing and I guess

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the testing that you described as Class I and Class II as being done in larger typically university affiliated labs that are part of a health sciences complex with medical schools and the like affiliated with them. You know, we've obviously heard a lot here about Mount Sinai and heard from people from Mount Sinai and whatnot. Are these Class I tests, for example, are they being done in smaller regional labs or outside that kind of environment that I just described?

DR. TORLAKOVIC:

A. Class I is typically done by any lab that is doing diagnostic immunohistochemistry. It's Class II tests that are not often performed by smaller labs because of the level of sophistication that is necessary to do them. But Class I, they are all Class I tests except for ER/PR and HER2, you know, everything else in immunohistochemistry is Class I.

CROSBIE, Q.C:

Q. Yes. So, you know, in a regional centre you might have only two pathologists, let's say, because it's doing surgery and you have to have pathology staff into place in order to do

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surgery. Are we talking--are they doing immunohistochemistry in that kind of a small, small lab?

DR. TORLAKOVIC:

A. That I don't know.

CROSBIE, Q.C:

Q. You don't know the answer?

DR. TORLAKOVIC:

A. I know, I heard of very small laboratories that do like four or five different stains and those would be the Class I tests.

CROSBIE, Q.C:

Q. Yes.

DR. TORLAKOVIC:

A. Some small labs will do that, but that's very unusual. It's usually larger labs that perform diagnostic immunohistochemistry. It is rare that--my belief is to the best of my knowledge it is not common to have very small immunohistochemistry labs.

CROSBIE, Q.C:

Q. But it's hard to be definitive about it because you don't have accurate data?

DR. TORLAKOVIC:

A. No, I don't have.

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CROSBIE, Q.C:

Q. Yes. Thank you.

THE COMMISSIONER:

Q. Thank you, Mr. Crosbie. Mr. Simmons?

DR. EMINA TORLAKOVIC, EXAMINATION BY MR. DANIEL SIMMONS

MR. SIMMONS:

Q. Dr. Torlakovic, I'm Dan Simmons. I'm here for Eastern Health, which is the authority that's operated the IHC lab here. I had a question for you first coming out of the comments that you made about residency training and yours, in particular. Mr. Crosbie has just touched on it, as well. Did I gather that you described yourself as having been privileged in your residency to be able to work with some people who were experts in the field of immunohistochemistry or you regarded them as such? Did I hear that correctly?

DR. TORLAKOVIC:

A. Almost correctly, because what I said is I was privileged to work in a centre that with diagnostic immunohistochemistry that was established by experts who, at the time, when I was a resident, were actually gone from the place.

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MR. SIMMONS:

Q. I see.

DR. TORLAKOVIC:

A. But good practices were in place already.

MR. SIMMONS:

Q. Yes, okay. Would you be able -

DR. TORLAKOVIC:

A. But also not to say that people who I worked with then were not experts also in interpretation and usage and technological aspects. But I just mentioned two names specifically because these are very well internationally regarded specialists in diagnostic immunohistochemistry.

MR. SIMMONS:

Q. Are you in a position to make any comment for us on how your exposure in your residency to immunohistochemical testing would compare to what you would expect of other anatomical pathology residents in other situations? Would you have been more or less exposed, do you think, than others?

DR. TORLAKOVIC:

A. I think that I was more exposed than others, definitely.

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MR. SIMMONS:

Q. Yes, okay. When you were talking about beginning your work in Norway, which I think you began at Oslo in 1997, one of the comments you made in response to some questions from Mr. Coffey was that by that time immunohistochemistry had changed somewhat from years, from a number of years before?

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS:

Q. And did I gather from that that the changes that had taken place may have included the introduction of more and newer antibodies than had been in use previously?

DR. TORLAKOVIC:

A. Absolutely. And more and newer detection methods which enhanced the sensitivity of the test to that degree that the results were-- have become radically different than in the past in the sense that we needed new skills for interpretation of these new results.

MR. SIMMONS:

Q. Okay. So the progress in the technology behind the performance of immunohistochemical

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staining was requiring pathologists to have greater skills and knowledge when it came to the interpretation of those stains, as well?

DR. TORLAKOVIC:

A. Right. And that knowledge actually was not widely available or published because what was published in the literature was based on those previously used methods. So now the whole thing have to be rewritten than normal (phonetic) and it took about a decade, I would say, or so, until things settled down and we think we know approximately or with greater confidence where are we at with the distribution of certain antigens in certain tissues.

MR. SIMMONS:

Q. Um-hm. Now, when would you say that decade transition began and ended?

DR. TORLAKOVIC:

A. Just about at that time. I think it started about '97 because that's about the time when these more sensitive detection systems have been made available.

MR. SIMMONS:

Q. Yes.

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DR. TORLAKOVIC:

A. And that's just about the time when I had at least personally noticed the kind of explosion in new antibody that performed well in formalin fixed paraffin embedded tissues.

MR. SIMMONS:

Q. Um-hm.

DR. TORLAKOVIC:

A. Otherwise numerous antibodies that were available before the time were used in frozen sections and were not applicable for daily practice.

MR. SIMMONS:

Q. Well, ten years, a decade from 1997 would bring us up to 2007 -

DR. TORLAKOVIC:

A. Right, right.

MR. SIMMONS:

Q. - which is just last year.

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS:

Q. So from that can we take it that throughout that decade there has been a continuous period of change and increase in the knowledge

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available to pathologists about how to use and interpret these tests?

DR. TORLAKOVIC:

A. Yes. And it still continues to develop, as it does. There's more and more methods that are being developed. And most recently in our run three in Canadian immunohistochemical quality control we had one lab with far more positive results than any other laboratory for estrogen receptor and progesterone receptor. And when we look at that, they used hypersensitive method. The problem with that -

MR. SIMMONS:

Q. They used?

DR. TORLAKOVIC:

A. Hypersensitive detection methods for -

MR. SIMMONS:

Q. Hypersensitivity?

DR. TORLAKOVIC:

A. Hypersensitive I call them because they are much more sensitive detection systems than those that are routinely used or those that are used for to produce the results that are published in the literature. So we don't really know what is the clinical relevance of

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such results, even though I believe that they have not produced false positive results, those are true positive results, we have no idea what these results mean clinically. So we took them out kind of competition because they are not to be compared, really, for concordance and similar because we don't know what it means yet. I think it yet has to be discovered whether these systems are wisely used in clinical practice or not.

MR. SIMMONS:

Q. Now when you speak of a detection system -

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS:

Q. - is that a commercially available product or set of products -

DR. TORLAKOVIC:

A. Yes, it is.

MR. SIMMONS:

Q. - that a lab can acquire to use in their testing process?

DR. TORLAKOVIC:

A. Yes, it is. It's a system--it's one part of the immunohistochemistry is when you are

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actually using the antibody that is specifically designed to detect the protein of interest. But then, there is an amplification system that is put on the top of that, so it makes a visual signal and that amplification system can be of different sensitivity. It can amplify the type of protein one time, ten times, 200 times, 2,000 times and so on. So depending on the level of amplification, we were read different intensity of staining and then for more sensitive the system is, the stronger the staining, and as I said, with this ultra sensitive systems today, when they can amplify one molecule of one protein in the tissue, we still don't know what that means possibly for clinical use, what's the relevance of that, and therefore that always has to be taken into account when as methods develop whether they have been widely tested for clinical practice or not.

MR. SIMMONS:

Q. So that example you give us though of the one lab whose results you took out of the mix -

DR. TORLAKOVIC:

A. Yes.

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MR. SIMMONS:

Q. - because they were using the newer detection system, would that be an example though of a change in progression in technology which resulted in a lab finding more positive results for this test than they may have found had they used the previous detection system?

DR. TORLAKOVIC:

A. Absolutely, and I would say that I know that still not all the labs in Canada are using normal sensitive, I mean, sensitive methods which are polymer based methods, which give very good, what we call immunohistochemistry signal to noise ratio, so you want to see specifically to find what you are looking for and not to detect background. There are still laboratories that are not using these systems and when they transfer to these new systems, they may yet see that the sensitivity of their tests will increase, and it wouldn't be strange at all if the material from one hospital is being tested in another and you see the huge difference, and that may be because of the detection, different detection system that it's using.

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MR. SIMMONS:

Q. Over the last ten years, have there been other examples of changes in the technology available for this testing that may have had similar results of allowing laboratories to test samples and find that they are getting more positive results than they had before the change, aside from this one you've spoken of, of the detection system?

DR. TORLAKOVIC:

A. Yes, they have. Another good example is development of antigen retrieval methods. So it has been said that some of the epitopes of interest do not need antigen retrieval at all, which may be generally true, but antigen retrieval methods do change results and the sensitivity with which we detect molecules of interest in the tissue, and we have learned, during the last decade or so, that pH of those antigen retrieval buffers matters. It matters whether you are using a pressure cooker or microwave or some other instrument for that purpose. It really makes a difference how this process is done because that is the one that critically alters the structure of the

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tissue, and therefore, I think that only illustrates even more that external quality assurance program is absolutely necessary because these are the programs that will enable people to calibrate their own quality assurance to the level that is clinically applicable, relevant and valid, and this is what we should aim for.

So we don't aim for ultimate sensitivity for sensitivity alone, because we want to have sensitive tests. We want to have tests that is titrated appropriately for clinical use, and therefore, I don't think that laboratories should be left alone to decide what cut off point or calibration is. I think they need to have expert base to have them out to do so.

MR. SIMMONS:

Q. So to just take you back for a second to the antigen retrieval example which you just gave us, do I understand that knowledge about the importance of the pH of the solution used in the antigen retrieval process is something that was acquired during the last ten years? That this is something that was learned or became better understood during that time

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period? Is that correct?
DR. TORLAKOVIC:
A. Of course, and I was personally involved in teaching on that topic. I have personally done no such studies myself, but I used studies from others that illustrated that pH may be critical in highlighting or destroying epitopes of interest and that there are other components of buffers that are important and today, there are many different commercial also antigen retrieval solutions for which we don't even know complete composition, but we know when we use one or the other that some of the epitopes will be better demonstrated. So it's a critical part for--and it's definitely something you learn. It's definitely something you learn also through EQA programs because they show the comparisons, what are results between different laboratories using different antigen retrieval methods too.
MR. SIMMONS:
Q. So then the science behind IHC testing and ER and PR in particular has been progressing, up to the present time. Are we there yet? Have we reached the point where it is--the science

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has optimized the test, or in your view, are there still things to learn and more to be done?
DR. TORLAKOVIC:
A. I think that the level of sensitivity of detection methods will continue to rise and this just last example that I gave and will mention again the lab that had far more positive results for estrogen and progesterone receptors taken out of competition because they are using now another detection system that is not comparable to others and it's not comparable to what's published in the literature too. So it will continue to develop, but in what sense and how exactly, that is difficult to say, but it's something that we will all watch and see how it evolves and then use expert judgments like what of that development needs to be translated into clinical practice, what is relevant and what is not.
MR. SIMMONS:
Q. Okay. Now when you're speaking of sensitivity, it's a term that's well understood by people who work in your field.

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Those of us who come from other backgrounds don't always understand it with the same precision that you do. Am I correct in understanding that sensitivity is a measure of how likely a test is to actually detect the target antigen that you're looking for?
DR. TORLAKOVIC:
A. Right, true positive results.
MR. SIMMONS:
Q. The true positive results.
DR. TORLAKOVIC:
A. Yes.
MR. SIMMONS:
Q. And you measure sensitivity in percentages, I understand, do you?
DR. TORLAKOVIC:
A. Yes, in percentages, but sensitivity itself, as a test sensitivity, is not necessarily the measure we need to use or it hasn't been traditionally used in this area.
MR. SIMMONS:
Q. Yes.
DR. TORLAKOVIC:
A. And if you look at careful language that they are using in ASCO and CAP guidelines and the

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same language can be translated into Canadian guidelines for HER2. That would be our best example where this is commented on specifically is that 95 percent concordance and it says concordance with both positive and negative values. It does not speak of sensitivity of the test, but sensitivity also can be calculated if you have large sample enough and then compare the test results from one laboratory to reference values, yes, it can be.
MR. SIMMONS:
Q. Okay, because you--I understood you to tell us, in relation to the reporting of ER/PR testing, and I may have gotten this wrong, I understood you to say that in your view, sensitivity is something that should be reported to the clinicians who use the test?
DR. TORLAKOVIC:
A. Right, that's in my opinion.
MR. SIMMONS:
Q. And is that a practice that you're aware of is actually in place anywhere now? Is there anywhere you're aware of where the reporting of ER and PR testing includes some statement

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about the sensitivity of that test?
DR. TORLAKOVIC:
A. No, no, no.
MR. SIMMONS:
Q. How -
DR. TORLAKOVIC:
A. It was taken for granted by clinicians, as I understand it. If you tell them it's positive or negative, they take it as granted.
MR. SIMMONS:
Q. Would the sensitivity vary from lab to lab?
DR. TORLAKOVIC:
A. It does. We saw in round, Run 2 testing in Canadian immunohistochemistry quality control, that it actually didn't vary much from one lab to another, but we all know that now everybody is paying attention.
MR. SIMMONS:
Q. Yes.
DR. TORLAKOVIC:
A. But it still varied and still there were labs that were below 95 percent concordance, let's say, for that value and there were some that were--we also calculate sensitivities that were below 95 percent sensitivity.

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MR. SIMMONS:
Q. Right, so how is it that you would like to see the sensitivity reported? How would that be done?
DR. TORLAKOVIC:
A. I think that because it's derived from EQA testing, we don't really know what the sensitivity of the test would be on the lab's own material, because there is no other reference to go by. So it should be reported in the framework of the standing with EQA, last EQA test.
MR. SIMMONS:
Q. I see, yes. So in other words, if a particular lab had a 95 percent concordance on their last EQA test -
DR. TORLAKOVIC:
A. Right.
MR. SIMMONS:
Q. - then you would suggest that that would be something to be included in the pathology report?
DR. TORLAKOVIC:
A. Yes.
MR. SIMMONS:

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Q. We have an ER/PR of this percent, PR of X percent.
DR. TORLAKOVIC:
A. Yes.
MR. SIMMONS:
Q. Our last EQA test done on such and such a date -
DR. TORLAKOVIC:
A. Right.
MR. SIMMONS:
Q. - gave us a concordance of 95 percent.
DR. TORLAKOVIC:
A. Right.
MR. SIMMONS:
Q. So it would give the clinician some measure of how likely this ER/PR result is to reflect the actual positivity?
DR. TORLAKOVIC:
A. Exactly, right.
MR. SIMMONS:
Q. Okay. Now why 95 percent as a target? Because I gather that's a target concordance that you're hoping to see labs achieve.
DR. TORLAKOVIC:
A. Yes.

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MR. SIMMONS:
Q. Why not 100 percent?
DR. TORLAKOVIC:
A. To tell you the truth, I don't know how ASCO, because I was not involved in their expert panel and I don't know all the details how they arrived with 95 percent concordance, but I know from our own, from the experience with NordiQC, there is a small number of test results that fail and you don't know why. We have no explanation. It's unexplained category. For most of the tests that failed, we could always find--it's either wrong antigen retrieval or it's dilution or it's whatever. You find something. But for very small number of tests that are generated, you just don't find the reason why the test failed, but it did. So it's not possible in biological system to have 100 percent, I believe.
MR. SIMMONS:
Q. So for those small number of tests that fail where you cannot find the reason for failure -
DR. TORLAKOVIC:
A. Right.

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MR. SIMMONS:
Q. - would it be fair to say that that small proportion of tests are unavoidable? That the lab will not be able to avoid having a certain number of say false negatives from the test?
DR. TORLAKOVIC:
A. That sounds like a reasonable conclusion. Since we don't know what is causing it, I don't think we can avoid that.
MR. SIMMONS:
Q. Is there any consensus on what percentage of ER and PR testing falls into that unavoidable false negative category?
DR. TORLAKOVIC:
A. I'm not aware of exact.
MR. SIMMONS:
Q. Since we know that 95 percent is the concordance that's been adopted, would it be reasonable to say that five percent is in the range of what would be an unavoidable false negative rate?
DR. TORLAKOVIC:
A. I think that might be the case.
MR. SIMMONS:
Q. Okay. But has there been any real study done

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or any materials in the literature that have really addressed that issue and established a percentage of what would be expected to be the unavoidable false negative rate in ER and PR testing, anything you are aware of?
DR. TORLAKOVIC:
A. I never paid attention to that specific point, so perhaps this was addressed but I'm not aware of it.
MR. SIMMONS:
Q. Okay.
DR. TORLAKOVIC:
A. I remember reading through large number of studies with large number of tumours tested and I don't remember that anybody of them, any of these larger studies were designed as such to address this. We don't--we do know there is correlation with biochemical assays, but then again, we don't have a gold standard. Biochemical assays are not a gold standard and immunohistochemistry tests are again not a gold standard. So while they're approach closely, each of them, to something that is gold standard, we know that in biochemical tests, the nature of the sampling of the

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tissue prevent us from being sure that we are dealing with 100 percent cancer cell population and therefore, the value that we provide is not necessarily the value that is attached to each tumour cell separately or in aggregate, and on the same time, for immunohistochemistry not having a gold standard, again, how do you then adjust your values to something. You know, it's always--our solution to that in CIQC, our reference values were those that were derived from most commonly achieved result, which may be totally wrong in relationship to what ideally this should look like, but we have no means by knowing what the results should actually look like.
MR. SIMMONS:
Q. So it sounds like there still remains some inherent uncertainty -
DR. TORLAKOVIC:
A. There is.
MR. SIMMONS:
Q. - in ER/PR testing which no one yet knows how to resolve or avoid?
DR. TORLAKOVIC:

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A. To the best of my knowledge, there is no given gold standard for ER/PR tests.
MR. SIMMONS:
Q. Okay. You told us about the work that you started with NordiQC starting around 1997, and that that was spurred, I guess, by your observations of variability in testing from lab to lab and also by some initiatives undertaken by DAKO, the commercial supplier of antibodies and materials.
DR. TORLAKOVIC:
A. Yes.
MR. SIMMONS:
Q. Had there been any kind of formal study done in Scandinavia of interlab variability or was this just observations that were made by yourself and others or was there any kind of structured study in advance of the NordiQC work to look at interlab variability?
DR. TORLAKOVIC:
A. In advance, I just started a small pilot study for which actually I have slides here to show, if there is a chance maybe we can go to that, my presentation.
MR. SIMMONS:

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Q. Yes.
DR. TORLAKOVIC:
A. I have a couple of slides from that Norwegian project.
MR. SIMMONS:
Q. Sure, okay, if you could find it, that would be very helpful.
DR. TORLAKOVIC:
A. Here it is. There aren't that many laboratories in Norway, so we started with six and did the very common antigens and one of the Class I test is vimentin. It's widely spread in many tissues, and here, it shows the staining results between the six laboratories in Norway, and you can see from results that are like in the middle part, panel B, it shows you that there is a very strong staining, very clear signal and there is no background. So that's an optimal result, and then you see our intermediate result in some others, and then you see totally negative results in one laboratory, and we speak about vimentin being one of the most commonly used tests at that time, and all of these laboratories that perform this testing were under impression

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that they were doing a good job.
Another epitope, S100, it does look more or less comparable. If you get--I mean, some of the laboratories use red detection system so--red colour so that is equivalent to brown for the signal and you can see that most of these laboratories have rather convincing positivity. But when you look at the tumour sample that was in the benign tissue, you can see again that in this laboratory and partly in this laboratory, and in this one, so three out of six, you have sub-optimal or negative results totally when it comes to tumours. So the system is not--wasn't titrated properly and the result on benign tissue was misleading.
HMB45, it's a marker of melanoma, and there you see also in benign tissues even some of the laboratories were not able to produced expected results and then similarly, in tumours again, one lab totally negative and some producing results that are below the threshold for calling the case positive.
And so finally, not all the labs were using this antibody, melanae (phonetic),

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another melanocyte marker and you can see the huge difference in this and how that relates clinically. What is the point clinically? This was the purpose of the pilot study. This pilot was chosen for ability of the lab to diagnose metastatic melanoma. So it's a metastatic tumour of melanocytes and that's a relatively common problem, because in Nordic countries, people with fair complexion get melanoma and metastatic melanoma is not an unusual clinical scenario.
So we looked at it and we actually see that there are two laboratories that totally failed clinically in the use of this. They would not be able to diagnose malignant metastatic melanoma because they can be morphologically non-descript in the sense that when you see the lesion, you cannot say whether it has any origin--any melanocyte differentiation or not and therefore you absolutely depend on the results of this test and you can see that two of the labs would not be able to make clinical use of their immuno results and you had one laboratory that had full clinical profile that was perfect and

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then some others that could improve. That PI means improvement and PC meaning just minor comment, how they can be modified to be even better, but they were good.
So out of six labs, you had two labs fail. I know this is not a large enough sample to make statistical conclusions, but that was quite surprising that it wasn't--when you put it in the clinical context like that, that it really gives you a larger picture than just when you look at each individual test separately.
MR. SIMMONS:
Q. Right, and were these small community hospital laboratories or were these tertiary care hospital laboratories?
DR. TORLAKOVIC:
A. It's a mixture.
MR. SIMMONS:
Q. Or a mixture?
DR. TORLAKOVIC:
A. A mixture.
MR. SIMMONS:
Q. It was a mixture, okay. Now when the NordiQC program was initiated, did you--I presume

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there was monitoring to see if these results improved over time, once the program came into effect, and would I be correct in assuming that you then saw an improvement in the performance of laboratories?

DR. TORLAKOVIC:

A. Yes, there was, but to tell you the truth, in most laboratories, even with any epitope we test, we still get very variable results, and that's true for--that's true for Canadian immunohistochemistry quality control. Our initial runs show that with the run 1. It's true for any program, and you can see here, on this diagram, this is taken from NordiQC page from run five to run ten, what happened with altogether 23 different epitopes, and we can see an average. There is about 20 to 30 percent of the results are inadequate. They are either red or yellow. That means totally poor or sub-optimal for clinical use. So 30 percent is a huge number for any given test. Were there any improvements further? Yes, and you can see here, these are unexplained category that we were talking about.

MR. SIMMONS:

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Q. Yes.

DR. TORLAKOVIC:

A. False negative, it's six percent. So it's very close to five percent number that we were talking about that we don't know when the test failed, and furthermore, to show like we did recent testing in European Bone Marrow Working Group, which I am a member, to see very commonly used tests from the major laboratories. The members of that group, we track, you know, major labs in European countries and you can see, again, that sub-optimal poor results are anywhere from even 50 percent for CD117, which is huge, and then like 40 percent for CD61. Very--these are basic, commonly used markers, and what's surprising about this, that overall, there is about 35 percent of sub-optimal and poor results in these laboratories throughout Europe.

MR. SIMMONS.:

Q. Now, this 35 percent figure here, that is a figure reflecting results how long after the NordiQC program had been in effect? How long had the program been in effect?

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DR. TORLAKOVIC:

A. This is new. I mean, this is totally new, and this is not from NordiQC, which was a separate study I did as a member of the European Bone Marrow Working Group, and many of these laboratories do participate--some of them actually definitely do participate in NordiQC.

MR. SIMMONS.:

Q. Uh-hm.

DR. TORLAKOVIC:

A. And some of them don't, but the point being is that this value, about 30 percent, poor results when the EQA test--EQA testing just start, it's something to be expected.

MR. SIMMONS.:

Q. Yes.

DR. TORLAKOVIC:

A. And it's something that you're going to see for a very long time until you see the improvement because it takes time, but is there improvement; yes, there was involvement. I think NordiQC website, if you go there, you will see how much improvement was from one run to another in some specific tests. What I want to show with this slide, you can see--I

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also did a survey at the time as a member of European Bone Marrow Working Group, and there is this discrepancy between what people believed that they are doing and what they actually achieve in the real life. So we saw that 95 percent believed that they have excellent or good results over time, but actually only 65 achieved that. So that lack of appreciation that they have a problem is something that education needs to deal with.

MR. SIMMONS.:

Q. Uh-hm.

DR. TORLAKOVIC:

A. So it shows the lack of education in this particular area.

MR. SIMMONS.:

Q. Uh-hm. In the establishment of NordiQC, you told--you described that for us, and I didn't hear anything about the role of government or any government agencies in establishment of NordiQC.

DR. TORLAKOVIC:

A. There is no role of government.

MR. SIMMONS.:

Q. Okay. I didn't hear anything about the role

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of any professional organizations, physicians, or pathologists, or laboratory technologists?
DR. TORLAKOVIC:
A. That actually had nothing to do with any pathologist association.
MR. SIMMONS.:
Q. Okay. We've heard of the UK NEQAS program. Are you familiar with some of the work done, I think, by Dr. Rhodes in the UK where he did some studies concerning interlaboratory variability in the UK?
DR. TORLAKOVIC:
A. Yes, yes, I am. Not probably on everything, but I'm quite aware of his work, yes.
MR. SIMMONS.:
Q. Is it fair to say that this work showed very similar results for interlaboratory variability in the studies that he did in the UK to those that you've described in Scandinavia?
DR. TORLAKOVIC:
A. I think they are very, very comparable.
MR. SIMMONS.:
Q. The UK NEQAS program is the proficiency testing program is available to laboratories

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outside the UK, as you told us, and the laboratory here now participates in it. Do you know how widely used the UK NEQAS external proficiency testing is in Canada among Canadian laboratories?
DR. TORLAKOVIC:
A. How widely used it is?
MR. SIMMONS.:
Q. How widely used? Is it a commonly used proficiency program for Canadian laboratories?
DR. TORLAKOVIC:
A. If I remember correctly, maybe there's nine Canadian laboratories that participate in UK NEQAS.
MR. SIMMONS.:
Q. Okay. In Ontario, we understand the QMPLS has their own proficiency testing program?
DR. TORLAKOVIC:
A. Right.
MR. SIMMONS.:
Q. Is that widely utilized outside of Ontario, do you know, or do you know if other labs are able to use that that aren't Ontario laboratories?
DR. TORLAKOVIC:

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A. I'm not actually--to tell you the truth, I'm not aware that anybody else can participate in their program. I don't think it's an open program. I heard something that perhaps they may be opening up, but I'm not sure about that.
MR. SIMMONS.:
Q. So then for most laboratories in Canada, outside of Ontario, the proficiency testing that has been available to them has primarily been the CAP, College of American Pathologists, proficiency testing?
DR. TORLAKOVIC:
A. Exactly.
MR. SIMMONS.:
Q. Prior to your program?
DR. TORLAKOVIC:
A. Yes.
MR. SIMMONS.:
Q. You've told us about the first three runs in your CIQC program. That the first run was Class I stains, and that you did find a large variability between laboratories?
DR. TORLAKOVIC:
A. Yes.

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MR. SIMMONS.:
Q. In performance. Was the variability that you found what you expected to find, or was it in any way unexpected, given your past experience?
DR. TORLAKOVIC:
A. It was expected, actually.
MR. SIMMONS.:
Q. Uh-hm.
DR. TORLAKOVIC:
A. But the only thing that surprised me was the level of false positive results. It's usually false negative results that are much more common, and false positive results, even though they occur in many laboratories, my previous experience the frequency of false positive was something that I was surprised with.
MR. SIMMONS.:
Q. And this was in the Class I stains in Run 1?
DR. TORLAKOVIC:
A. Yes.
MR. SIMMONS.:
Q. Now in Run 2, you've told us what the result was, that there wasn't as much interlaboratory

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variability as you had anticipated, and I'm wondering what did you expect to see with the ER/PR tests in Run 2?

DR. TORLAKOVIC:

A. I thought that about 30 percent will be sub-optimal or poor, and nobody was poor, and -

MR. SIMMONS.:

Q. Why did you expect that many of those tests would be sub-optimal or poor?

DR. TORLAKOVIC:

A. Because that's published in the literature and that was previous experience that we had in NordiQC, that almost any test you look at, this is what you get when you start EQA program.

MR. SIMMONS.:

Q. Right. So if 30 percent of the tests for ER/PR were sub-optimal or poor, can we then conclude that across all the laboratories being surveyed, there would be a significant number of tests that were being reported incorrectly?

DR. TORLAKOVIC:

A. If indeed the case is that there are so many, some of them will be reported incorrectly,

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yes.

MR. SIMMONS.:

Q. Yeah, okay. Now in other cases elsewhere in the world where these studies have been carried out, and there's been findings that as many 30 percent of these tests have been sub-optimal or poor -

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS.:

Q. Are you ever aware anywhere of there being any steps taken to review past tests in an effort to find those that may have been incorrectly reported?

DR. TORLAKOVIC:

A. No.

MR. SIMMONS.:

Q. In the Run 2 tests that you did for CIQC, I understand that the process used was to send out the slides with the microarray of 72 different -

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS.:

Q. Very tiny tissue pieces?

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DR. TORLAKOVIC:

A. No, 70 something was Run 1. Run 2 had smaller number, about 40.

MR. SIMMONS.:

Q. About 40 -

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS.:

Q. Separate tissue samples, and the participating lab employees had to stain those slides using their own standard protocol that -

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS.:

Q. They had adopted, and presumably optimized for their own testing?

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS.:

Q. Were those slides then interpreted by the pathologists at those institutions and the results of those interpretations reported back to you?

DR. TORLAKOVIC:

A. Yes.

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MR. SIMMONS.:

Q. They were as well, as well as the slides returned to you?

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS.:

Q. So you had an opportunity to evaluate both the staining on the slides and the interpretations of the pathologists?

DR. TORLAKOVIC:

A. Yes.

MR. SIMMONS.:

Q. Okay. On that run, were there any particular conclusions you were able to draw about the quality of interpretation versus the quality of staining, were there any particular issues one way or the other?

DR. TORLAKOVIC:

A. Actually, the quality of interpretation was very good, and that maybe reflects another fact that when interpret this small pieces of tissue in tissue microarrays, what you use as your cutoff point for positivity is just any tumour positive cell.

MR. SIMMONS.:

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Q. Yes.
DR. TORLAKOVIC:
A. And it's a small piece of tissue. It does not show entire tumour where you have to make a decision where to look, how long you are going to look and so on. So it's just--focusing on such small pieces of tissue makes interpretation really easy.
MR. SIMMONS.:
Q. I see.
DR. TORLAKOVIC:
A. And that may not reflect the true interpretative skills and practices in real world, and, therefore, we did not make large emphasis on interpretive part of the test, although we did see some that we considered discrepancies between how it was interpreted and how it was interpreted at the assessment. So there was some difference.
MR. SIMMONS.:
Q. So in the clinical setting then where there are larger pieces of tissue being examined by a pathologist, and the pathologist has to identify the appropriate place on that tissue in which -

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DR. TORLAKOVIC:
A. Right.
MR. SIMMONS.:
Q. To count the cells and come up with an interpretation, there might, in fact, be larger variability in interpretation than would show up in your testing?
DR. TORLAKOVIC:
A. Right. So our testing was not designed to test post-analytical component in detail how it should be done, if that was the focus.
MR. SIMMONS.:
Q. Okay. So in promoting national external quality assurance as an important goal, would I be correct in thinking that one of the big advantages of that approach is the ability to pool resources and expertise around the quality of IHC testing as opposed to leaving individual labs on their own to try and develop their own quality assurance measures?
DR. TORLAKOVIC:
A. Absolutely. I mean, this is the area of high complexity.
MR. SIMMONS.:
Q. Uh-hm.

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DR. TORLAKOVIC:
A. And it is not realistic to expect each individual lab should be able to develop such level of expertise without additional guidance.
MR. SIMMONS.:
Q. Yes, okay. Thank you very much. I don't have any other questions.
THE COMMISSIONER:
Q. Thank you, Mr. Simmons. Mr. Browne.
MR. BROWNE:
Q. Thank you, Commissioner.
DR. EMINA TORLAKOVIC, EXAMINATION BY PETER BROWNE, Q.C.
BROWNE, Q.C.:
Q. Good afternoon, Dr. Torlakovic. We met earlier. My name is Peter Browne. I represent a number of the individual pathologists and oncologists who have been asked to testify before the inquiry. I just want to go back and touch on a couple of areas now. First of all, your comment to Mr. Simmons about, I guess, the changes over the past decade in immunohistochemistry and the advances in, I guess, the--I took the impression, the immense volume of information

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and changes in antibodies and in detection kits, and I guess also the literature in terms of dealing with all the issues surrounding IHC. Is that a fair description of what has occurred in the past decade?
DR. TORLAKOVIC:
A. It is. I mean, it has been developing before, but since this technical advances in the last ten years are so remarkable, the upshot of that is that we are today using very powerful technique with different results than before.
BROWNE, Q.C.:
Q. And Mr. Crosbie asked you about in terms of selecting a medical director for an IHC lab and so on. In terms of getting a person to do that, would it not be important to have a couple of things in place; one, someone who has had basic training in IHC, first of all, and you talked about the fact that there is that sort of gap within the residence program here in Canada.
DR. TORLAKOVIC:
A. Yes.
BROWNE, Q.C.:
Q. Secondly, I guess, if there's a problem with

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recruitment and retention, you need to try to recruit someone who has that skillset, and then providing them with resources to be able to keep on top of all this information that has occurred over the past ten years?

DR. TORLAKOVIC:

A. Absolutely, but since there is a lack in education, there is a lack in perception, like, what's going on and what's necessary, there is going to be, of course, lack in providing means to get to the point where we should be.

BROWNE, Q.C.:

Q. Okay.

DR. TORLAKOVIC:

A. But it's necessary, yes.

BROWNE, Q.C.:

Q. Now you mentioned interestingly, and, Registrar, if we could enter P-3365.

EXHIBIT ENTERED AND MARKED P-3365

THE COMMISSIONER:

Q. So entered.

BROWNE, Q.C.:

Q. Doctor, this is actually--I had spoken to you over the lunch break about this article, and I

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mentioned I may enter it. This is the results of the Royal College of Pathologists quality assurance program, I think an audit that was performed between 2004 and 2006 of their labs and sort of the results were published.

DR. TORLAKOVIC:

A. Yes.

BROWNE, Q.C.:

Q. Have you--are you familiar with this particular article?

DR. TORLAKOVIC:

A. Yes, I'm familiar. I think it's very interesting article that shows when audits are done a larger scale, what they can possibly find.

BROWNE, Q.C.:

Q. Right.

DR. TORLAKOVIC:

A. And I read it with great interest. Especially there is a table. I don't know if we can move down there -

BROWNE, Q.C.:

Q. Yes. If I could walk you through because there are a number of comments you made, and I just want to point out, first of all, a couple

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of points. Mr. Simmons asked you about the fact about these changes that have been noted and so on, has there ever been a look back as a result of it. Given--and this is now in relation to estrogen progesterone receptors, particularly.

DR. TORLAKOVIC:

A. Yes.

BROWNE, Q.C.:

Q. And in the conclusions section here, I just want to point out it says, "A number of individual laboratories do not meet the target values", and we'll talk about that. As a matter of fact, I'll show you, I think in a paragraph just below here, they as well found 30 percent variability, poor results, which is I guess similar to the experience you had in the Nordic program, but more importantly, "A number of individual laboratories did not meet the target values and variation results, which would impact on patient treatment decisions". So they recognized that this problem would have an impact on treatment decisions?

DR. TORLAKOVIC:

A. Right, and I'm not aware that they went back

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and they actually did anything with that.

BROWNE, Q.C.:

Q. Okay. As well, I was noticing in reviewing this over the lunch hour, they started, the specimens just note right there, "The specimens consist of routine formalin fixed paraffin embedded material that has been supplied to the QAP by participants". Sorry, just above here, "The original material was a composite block, but this has been changed to tissue microarray construct for the past two years". So they started using as part of this -

DR. TORLAKOVIC:

A. Yes.

BROWNE, Q.C.:

Q. Tissue microarray construct as well.

DR. TORLAKOVIC:

A. Yes, I think that is now prevailing practice for this province when it comes to Class II tests, and in general, it is recommended. I think it was Dr. Gilks who first published actually on use of tissue microarrays for quality control/quality assurance purposes, and logically this was quickly implemented in

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many ways because it's a very powerful approach for QA.

BROWNE, Q.C.:

Q. I think the table you were looking for, we'll just find here now, those are the results, but there may be further on--here, is that the table you're looking at?

DR. TORLAKOVIC:

A. That's the table.

BROWNE, Q.C.:

Q. Yes. Now it's quite--I'll let you--if you want to sort of refer to anything in particular there.

DR. TORLAKOVIC:

A. When you look at positivity for ER, the variability, and if I can correctly remember some numbers here--I think it's in the middle of the column or so. There are few--here it is, laboratory 49, 30 percent, and then you have laboratory 24, 90 percent, and then for PR, below 30 percent for some labs, and then over 80 percent, and even 96 percent by other labs. So this extreme variation in the results, you can see obviously that something is wrong. I mean, there are laboratories who

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are producing large number of false negative results.

BROWNE, Q.C.:

Q. If we can just go back for a minute as well--I'm going to go back to your observation about changes over the past ten years because there is a note here as well by the authors.

DR. TORLAKOVIC:

A. While you're looking for that, I just would like to comment on overall percent, like there is a variation between 30 or 90 percent in ER results, but overall 75 percent, which if you would take them overall, you would come probably to the number that is expected for breast cancer in general.

BROWNE, Q.C.:

Q. Right, we've heard that, so -

DR. TORLAKOVIC:

A. So overall picture doesn't give you exact information what's going on in each individual laboratory.

BROWNE, Q.C.:

Q. And that's why the importance is participating in the process so you can get this feedback from the -

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DR. TORLAKOVIC:

A. Exactly.

BROWNE, Q.C.:

Q. - Quality Assurance Program. This comment right here in the conclusion section, it says, "Over the last decade IHC has moved from"--and this is a 2007 article -

DR. TORLAKOVIC:

A. Yes.

BROWNE, Q.C.:

Q. --"moved from a qualitative test brown or not brown to a quantitative test that determines selection of patient therapy and treatment outcomes with a development of new targeted therapy imperative to identify predictive tests will increase. IHC may be able to fulfil this role, but the data from this and other studies indicate it is fraught with difficulties. The difficulties with predicting response to epidemial growth factor receptor by tyrosine kinase inhibitors and monoclonal antibodies based on IHC graphically illustrates this point." So does that sort of summarize what you are saying, we start out with this notion of brown--is it brown or not

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brown to this more, as you are now talking about, the notion of probably putting into your reports the sensitivity as a communication tool to clinicians?

DR. TORLAKOVIC:

A. But I can warn you that my view may not be shared by everyone because even today you have articles published in which experts in immunohistochemistry say that they do not believe in quantitation, in formalin fixed paraffin embedded tissues and they published, particularly an article by Dr. Nadji.

BROWNE, Q.C.:

Q. Nadji, we've seen that article, the Commissioner has seen that article.

DR. TORLAKOVIC:

A. And there is another review article very recent from the same author who says again that the quantitation is not reliable in paraffin embedded tissues. I object to that scientifically and object to that they might publish research in which I--as I was interested in B cell lymphoma and transcription factors and their target genes, I wanted to see whether we can quantitate in

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tissue defects some of the transcription factors so in my studies for my PhD one of the things that I did, I wanted to see how--whether there is any correlation between P1, which is a transcription factor that regulates expression of some other genes, so I picked up those that we know that these transcription factors should regulate, that's proven, those that are hypothetical possible targets for this transcription factor, those that the factor knew that this transcription factor does not regulate at all. And my results clearly showed that there is perfect correlation between those genes that regulate it, so it's a winner. I also constructed tissue microarrays with different lymphomas and this was particularly useful for, you can call it dosage of the gene, so more staining you see, then you think there is more of the product, so we think quantitative in that sense. So we measure the intensity, so we measure the intensity of the transcription factor and then we measure the intensity of the staining of these target genes and we notice more transcription factor, more target

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gene expression. That means we have biological proof that we indeed can quantitate when using histochemistry for quantitating analogies and we also showed that, when that P1 was up, that genes that are not regulated by this, by this transcription factor, that were not up in those, in know, in those lesions. So I believe that, strongly believe that the techniques that we are using today enable us to quantitate very, very precisely, so not in this way. It's always semi quantitating, we are not talking about picamoles or actual measurements in that sense, but can we distinguish between weakly, weak expression of tumour and strong expression of tumours. I believe we can.

BROWNE, Q.C.:

Q. Okay, and we've heard from Dr. Dabbs, Dr. David Dabbs from the United States on this point, the notion of--are you referring now to the use of a H score, that type of approach to reporting?

DR. TORLAKOVIC:

A. Yes, H one was exactly the score I used in my studies and I used this for specific reason.

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This is not the score that is used perhaps for a measurement of ante--we know Allred score is more frequently used in Northern America for measuring, for scoring estrogen progesterone receptors and in my personal opinion H score is better because it gives you more information, it does not artificially make--it does not categorize artificially as Allred score does in a way. So with H score what you do is, actually you're looking at the percent of positive cells for each intensity and then you multiply and derive the score from zero to 300 and that is the score that was originally published was that McCarthy, I believe was the author, where biochemical tests for ER and PR were related to, correlated with the results in the tissue sections and it was proven that you can actually do excellent job with immunohistochemistry in identifying ER/PR. So my personal opinion, there is no need for yet another type of scoring, I would use the one that actually showed this perfect correlation with biochemical ones if it were up to me, and I know that there will be different approaches as to which score to use and I'm not here, an

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expert to say, to make a judgement about that, but it is just my personal opinion that my preference would be to use H score.

BROWNE, Q.C.:

Q. And that's the Harvey article, I think, is it, Dr. Harvey's work in that area, is the H score Dr. Harvey or -

DR. TORLAKOVIC:

A. McCarthy I think is the original from 80's, so when it was first time published that one could use immunohistochemistry as means of determining the quantity of ER in tissue sections.

BROWNE, Q.C.:

Q. But I take it from your answer, though, Doctor that this is a subject of great debate still, today?

DR. TORLAKOVIC:

A. It is still debateable and still there is no definite rule on this and there will be laboratories that are using one score system over the other because it's in guidelines, this is not something that really a standard. In standard you have to perform it all the way, all the time the same way. When using

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guidelines, one has a freedom to modify some parameters in the guidelines.

BROWNE, Q.C.:

Q. Now just one last area I wanted to cover with you and this was covered somewhat by Mr. Simmons and that is sort of looking forward and the Commissioner has to look at making sort of recommendations. The Australia, I guess in terms of its legal structure has a Federal and Provincial arrangement. Would you see your work in the CIQC as being sort of ideally, now let's look at ideals here for a minute, in an ideal world, something which is funded by governments or certain bodies, regulatory bodies, to allow that work, as you talk about getting that critical mass to both disseminate information and then to evaluate material forwarded?

DR. TORLAKOVIC:

A. Absolutely because as I said, I believe that this type of testing should be free and this type of expert knowledge or hotline should be also provided. It is not realistic, as I said, to expect each individual laboratory to be able to gain that type of expertise in

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daily routine work.

BROWNE, Q.C.:

Q. Do you know whether the UK NEQAS Program that was under discussion here a few moments ago, is that government funded or -

DR. TORLAKOVIC:

A. I think it's government funded, I think it's government funded for UK, but then participation is paid by other countries, other labs from other countries who want to participate.

BROWNE, Q.C.:

Q. But for United Kingdom itself, it's -

DR. TORLAKOVIC:

A. I think it's government.

BROWNE, Q.C.:

Q. And I think you mention as well that in relation to the UK NEQAS experience, literature has sort of shown a sort of discrepancy in terms of improvements. The volunteer participants have not improved as well as the UK labs, is that my understanding?

DR. TORLAKOVIC:

A. That's correct, that's their result--that's their own, you know, published evidence.

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BROWNE, Q.C.:

Q. Are you able to indicate to the Commissioner any, at least your observations or your knowledge as to why that may be so?

DR. TORLAKOVIC:

A. Well, obviously, I mean one of the reasons why this may be so, I don't know exactly why is that so, but I would guess that a success in this test in the UK is kind of mandatory because accreditation of the lab depends on it, so they will--they will be given some time to make corrections and to improve, but they will have to pass this test to actually continue to be accredited. How exactly this is used in their accreditation process, I cannot tell you the details, but I know that they are expected to correct and they do correct and they become better. But that is because of the accreditation. Additional role that they also have is educational role and that is more obvious for UK labs than for other labs that participate in UK. How much and exactly what they do, I don't know, but I am certain that the education component must play a role.

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BROWNE, Q.C.:

Q. Lastly, Doctor, just in terms of the experience, the findings of programs such as UK NEQAS and NordiQC and I guess the Australian RCPA Program, were there any particular areas that were identified to explain the interlab variability of results, do you know, in terms of the whole analytical process? Were there studies to indicate where, if there were any problems where those problems lay? For instance, antigen retrieval, antibody concentration, is there any literature -

DR. TORLAKOVIC:

A. No, I am not aware of, other than to show you again, like from, if I am free to go to my presentation -

BROWNE, Q.C.:

Q. Sure.

DR. TORLAKOVIC:

A. Of some of the things that are very obvious, for example, this is how it's done at least in NordiQC. This was a run where this particular anti-smooth muscle antigen, CD15 EMA estrogen receptor and progesterone receptor, this

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illustrates several things, this type of presentation here that I am showing you. It shows that ER was good and PR was poor and it shows that if you do good, well with one test, there's no guarantee you're going to do well with another test. And it also tells you now that this one was considered false negative, first it says it could be false positive or false negative if it's poor, so this one was false negative, but it tells you suggestions for improvement that come from this judgment was to optimize antigen retrieval, use different pH because they look--the look was different to low pH and possibly increase primary antibody concentration and this is the result that this is how it looked before and this is how it looked after this improvements were done. And they solved really the problem, so that shows you how in most efficient way external quality assurance can help. To give exact precise instructions for what can be done, I think that's done, the success is obtained. Now in the summaries format, I also have one slide to show you what was the results of false negative and false

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positive test and you can see here that there are different reasons for false negative tests and different reasons for false positive and different percentages were given to that. So very often it's through diluted primary antibody and so one third of cases that the reason for failing, having false negative result. Inappropriate primary antibodies, you're using, selecting the one clone that will not do as good job, but you didn't know before you participated that that's not a good clone, it's a reason for additional 13 percent of false negative test. Insufficient antigen retrieval, so what happens to the tissue before it goes to the test, it's one forth of the cases, so that's a large number too and then inappropriate epitope retrieval, so using not only insufficient, so not long enough or not even a high temperature but just using wrong, for example, enzyme digestion instead of cooking in the EDTA buffer and that would be the example, or just the lack of epitope (unintelligible) for additional 14 percent and then unexplained, this is about that magical five or six percent value, we don't know why.

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So those are the false--and false positives again, there are some reasons but they were not that common. So then you kind of summarize, you see, it's the experience of NordiQC for those three runs, those eight to ten, eight, nine and then, but were there any larger studies done in that sense? I'm sure that UK NEQAS looked at that and so on, but I don't know their numbers at hand, but they should not be too different from these.

BROWNE, Q.C.:

Q. So if I--to take away any sort of particular message on the quality assurance or quality, CIQC that you're looking at right now, there's both sort of a national, global sort of information sharing that labs across the country will know particular global issues, but also on the local level, feedback from, for their particular lab -

DR. TORLAKOVIC:

A. Yes.

BROWNE, Q.C.:

Q. Would that be the sort of the two, the two-tier focus of that type of program?

DR. TORLAKOVIC:

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A. Yes, you could say that.

BROWNE, Q.C.:

Q. Thank you.

THE COMMISSIONER:

Q. Thank you, Mr. Browne. Ms. Newbury? Mr. Pritchett, I don't think you were here this morning when we did the rounds of the room, so I skipped over you just then, did you have any questions for this witness?

MR. PRITCHETT:

Q. No, we don't have any questions, thank you, Commissioner.

THE COMMISSIONER:

Q. Thank you.

DR. EMINA TORLAKOVIC, EXAMINATION BY MS. JENNIFER NEWBURY

MS. NEWBURY:

Q. Good afternoon, Dr. Torlakovic, Jennifer Newbury, we met earlier. I represent the Newfoundland and Labrador division of the Canadian Cancer Society. I wanted to ask you first of all about a comment in the Exhibit P-1143 please? This is the proposal from July 2006 for quality assurance and you were shown that earlier today, so this is the proposal for the establishment of a national EQA

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program. And on that very first page, item No. C is the one I'm interested in, so quality assurance in laboratory medicine includes, and then down to item C, "Proficiency control by supervision of pre-test and post test phases of laboratory work from specimen collection to delivery of report to the clinician." And I wonder if you can elaborate a bit on that particular point?

DR. TORLAKOVIC:

A. I could, I mean it's not something that I am intimately involved in all the phases of pre-test, post-test phases, but we--we cannot over emphasize the significance of tissue processing and reporting of the results and this is also, I mean, it's one thing that EQA can deal with directly is exactly the test itself and then looking at the slides, but also cannot be forgotten there are pre-analytical and post-analytical components and they have to be somehow incorporated and regulated in any clinical laboratory and that is what it refers to. It refers to--and we know that it's a novel thing, actually, it's from 2007, first time that officially

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guidelines address pre-analytical component. This has never been done before and it's huge news for our practice, so it introduces totally different components that we, as pathologists, have to now deal with. It introduces, it actually incorporates surgery department now in the whole process of testing and it will--it requires their co-operation and several changes in the laboratory and tissue or specimen receiving that enable careful tracking of tissue through all these steps before it comes for the testing.

MS. NEWBURY:

Q. And sorry, who did you say introduced that in 2005?

DR. TORLAKOVIC:

A. No, it's 2007, actually first time, ASCO CAP guidelines on HER2 testing, it's first time that this was put from an expert panel that it was officially address--when for many years, of course, you could read in the literature and many distinguished immunohistochemistry experts around the world would write about the significance of tissue processing. But that has never been put into guidelines before, so

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that directly would have to be addressed by laboratories and hospitals, as they should be now.

MS. NEWBURY:

Q. Okay, and in talking about the CIQC program and the fact that it doesn't focus on the interpretation by pathologists, although it can pick up some problems, but it's not--because of the sample size of the tissue on a microarray -

DR. TORLAKOVIC:

A. Right.

MS. NEWBURY:

Q. It's certainly not going to be the target, I guess, of the CIQC program, do I understand that correctly?

DR. TORLAKOVIC:

A. Not necessarily because we are just starting and these I call like baby steps at this point, it's a very modest approach. I think that it is also necessary for CIQC to address the post-analytical component and to enable, to actually put on the ramp of scan slides that it was the idea that what I would like to see in next year or next two years, developing

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in this year to put, to scan the slides with variable results and to have expert scores on one side and then to have people log in and they can test by virtual microscopy the steps on line and the large number of specimens and see their own average score and they can improve if they--so it would enable them self evaluation and training also, that material should be available for resident training too, because if it's on line and if it's already scored and if it's already prepared for this particular purpose, it would enable a large number of people to use it if some specimens that may not be so easy to prepare for every centre or every residency program separately.

MS. NEWBURY:

Q. So it's both a quality assurance type tool as well as an educational -

DR. TORLAKOVIC:

A. Yes, yes.

MS. NEWBURY:

Q. So, while that hasn't been done yet, that is something that you're -

DR. TORLAKOVIC:

A. We have the idea that we would like to put

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that in -

MS. NEWBURY:

Q. And would you anticipate perhaps varying the types of specimens that are posted from year to year or expanding upon the type of a program just to get a the post-analytical or the interpretation aspect?

DR. TORLAKOVIC:

A. I mean, definitely, one would focus on those specimens that post-analytical component is critical and that means scoring again prog--predictive Class II test. That would be the first focus. And secondly, also, it should not be forgotten that the interpretation of Class I tests may be very difficult. And it's difficult to learn if somebody is not constantly exposed to large number of such specimens. One of the reasons, one of--my main motivation for example for the book that I recently prepared and it will be out early, I think, 2009, Bone Marrow Immunohistochemistry, is knowing that in general practice, it's very difficult to train residents who come and rotate for two, three months without exposing them to some kind of

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reference point and what good result is or what you expect in different types of specimens. That type of image collection was never available and it was my motivation to put that book out, to show that, of the spectrum of possible results, what people can--and this is what I think is the idea, is to produce such source, whether it's total internet based or not, but to produce such sources easily available to anybody who wants to learn, see quickly. We don't need to have pathologists learning two decades about something that can be presented and taught, you know, in matter of hours.

MS. NEWBURY:

Q. Okay. And in addition to guidelines that may be available about the pre-analytic phases of testing, particularly as it relates to ER and PR testing, are there any techniques or tools that CIQC is going to explore as to how you could have some sort of quality assurance program to focus on that or is that something that you think is possible or -

DR. TORLAKOVIC:

A. No, but I am aware that as part of

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accreditation of the laboratory, those that have accreditation, that some of the things that they look at is actually tissue processing and when the inspections are coming, they look at how the tissue was processed, how the recording was done and so. How uniformed that is applied in different provinces and to what extent, I cannot comment on.

MS. NEWBURY:

Q. Okay. And are you referring then to having standard operating procedures in place that are -

DR. TORLAKOVIC:

A. Absolutely.

MS. NEWBURY:

Q. - known to produce good results.

DR. TORLAKOVIC:

A. Yes, absolutely.

MS. NEWBURY:

Q. And there are no programs available, that you're aware of, that someone could work up a slide through the tissue processing stage to compare it with other laboratories to see how it compares?

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DR. TORLAKOVIC:

A. I'm not aware of that. That doesn't mean it does not--it hasn't been done, but I'm not aware of it.

MS. NEWBURY:

Q. And in terms of--there are a variety of programs that you've spoken about earlier today, the NordiQC, the UK NEQAS CAP, your new CIQC program and there was some reference to QMPLS which is the Ontario program.

DR. TORLAKOVIC:

A. Yes.

MS. NEWBURY:

Q. Do you know much about the QMPLS?

DR. TORLAKOVIC:

A. No, and I kind of feel embarrassed because it's Canadian, you know, and I know so little about it. The thing is also, as I said, like our time limitations, how much time we can invest into learning about--and it's not something that is easy to figure out. I can tell you that just most recently I learned more about what's happening in Alberta. We are working on something in Saskatchewan and who else knows about it? Nobody knows about

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it. It's just--not even pathologists in Saskatchewan all know exactly what we are working on. So, it's not a type of information that is widely posted and available.

MS. NEWBURY:

Q. Right. So there's no sort of clearing house -

DR. TORLAKOVIC:

A. No, no.

MS. NEWBURY:

Q. - as to all of the types of programs that are available.

DR. TORLAKOVIC:

A. No.

MS. NEWBURY:

Q. Would you think that there are any advantages to a laboratory perhaps enroling in several programs just to take advantage, I guess, of the benefits that one might have over another particular program or is that something that you think might already be done by some laboratories?

DR. TORLAKOVIC:

A. I think that laboratories participate in more than one program for several reasons. One of

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them is that these programs are not identical and they offer different type of information for the laboratories. I already pointed out some differences between CAP program and UK NEQAS program and then other differences with NordiQC and with CIQC again, we provide different type of information and education and insight than others. So I don't think that these are necessarily competition to each other or that even when you look at just Canada, CIQC is right now small addition to other programs and I think that all of them are valuable and all of them should be supported and I don't think that any of the programs should be extinguished or closed at this time, just in the contrary.

MS. NEWBURY:

Q. You think that they perhaps complement one another?

DR. TORLAKOVIC:

A. Absolutely.

MS. NEWBURY:

Q. Okay, and in light of the fact that at this time, the CIQC doesn't have any particular focus on the interpretation issue or the post-

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analytic testing, is there a program there that you think that might be particularly beneficial for that particular aspect of testing?

DR. TORLAKOVIC:

A. NordiQC I think looks at that, at the interpretation too, and I think it's also UK NEQAS that looks at interpretation. I think that in Ontario, QMPLS, I don't think that they look at interpretation.

MS. NEWBURY:

Q. Okay.

DR. TORLAKOVIC:

A. And CIQC, as I said, we have the data, but the time itself prevents drawing of larger conclusions out of that, but we will go into that direction. I don't think there is a perfect program to address that because a perfect program would have to have not only testing abilities, to see the performance of the pathologists, but also this training component, as I said, and also what people try to emphasize in this post-analytical component is that not everybody should be interpreting the results, for example, of ER/PR if they're

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not sufficiently exposed to it in their practice to a certain number of tests that would make them proficient, but having that said, I think if you made available online large number of tests and if the pathologist can prove that they are competent, they should not be prohibited from doing this practice. That's my opinion.

MS. NEWBURY:

Q. Thank you. You were just shown or you actually pointed to a slide, and I wanted to bring that up again just for some clarification. It's Exhibit 3361, please, and I believe it's page 31 of the presentation? And this is the NordiQC run, three particular runs. Could you just clarify what those runs related to? What was the scope of the testing in that case?

DR. TORLAKOVIC:

A. I don't remember what were exact epitopes, but if one wants to know, they are all the time available online. I don't know if we have online capability in this computer to go to NordiQC site and maybe open that.

MS. NEWBURY:

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Q. Okay. I don't know if we -
DR. TORLAKOVIC:
A. Can we do that?
MS. NEWBURY:
Q. Actually, I just wondered if that related to ER and PR testing?
REGISTRAR:
Q. What's the web site reference?
DR. TORLAKOVIC:
A. It's NordiQC, N-O-R-D-I-Q-C.org and then go to assessments.
MS. NEWBURY:
Q. Assessments?
DR. TORLAKOVIC:
A. Yeah, I can do that actually, and you were interested whether that estrogen -
MS. NEWBURY:
Q. I think they were 8, 9 and 10, I believe, were the numbers. The ones are numbers 8, 9 and 10.
DR. TORLAKOVIC:
A. And you were specifically interested in estrogen receptor, correct?
MS. NEWBURY:
Q. I was wondering if it included ER and PR

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testing, those results?
DR. TORLAKOVIC:
A. No, that was called 1B5, so no, it didn't.
MS. NEWBURY:
Q. Okay.
DR. TORLAKOVIC:
A. I don't think it did. Maybe we can also read through this. No.
MS. NEWBURY:
Q. Okay, and how about PR, would that -
DR. TORLAKOVIC:
A. No.
MS. NEWBURY:
Q. Okay, so it's something other than ER and PR testing?
DR. TORLAKOVIC:
A. Yes.
MS. NEWBURY:
Q. Okay. Could you indicate what factors, if any, could negatively impact on the specificity of testing for ER and PR?
DR. TORLAKOVIC:
A. What factors specifically?
MS. NEWBURY:
Q. What types of factors? And just again

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referring back to that slide, there are some references there, and I don't know if they would equally apply to ER and PR testing. If you've got--I understand that if there's a problem or a lack of specificity with testing, then that might lead to false positives.
DR. TORLAKOVIC:
A. Yes.
MS. NEWBURY:
Q. And here, there are a list of factors that could possibly contribute to false positives, and I'm wondering if they would equally apply to a problem with false positives in ER and PR testing?
DR. TORLAKOVIC:
A. Yes, you can say generally speaking. I do not have a reference to support this what I am saying, but generally speaking, these are the factors that are widely applicable as a cause of false positive results.
MS. NEWBURY:
Q. Okay. So in terms of whatever the test that was being run here with runs 8, 9 and 10, you did have, I think, about ten percent of all of the insufficient staining were related to

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false positive results, as opposed to false negatives?
DR. TORLAKOVIC:
A. But the false positive result, specifically when you think about it, also as they are being reported, that's a different thing than actually when you have a slide and you have--you see that, that the nuclei are really positive and they should not be positive. That's a different thing. False positive results sometimes are reported because of the interpretive component.
MS. NEWBURY:
Q. Okay. So if you have excessive background staining, as an example?
DR. TORLAKOVIC:
A. Excessive background staining or, you know, inappropriately interpreted staining might end up as false positive in patient's report, yes.
MS. NEWBURY:
Q. Okay, and so it might be a positive result for a particular test. It's not valid for that particular specimen and it's due to interpretation?
DR. TORLAKOVIC:

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A. Yes.
MS. NEWBURY:
Q. Or a combination of interpretation and perhaps background staining?
DR. TORLAKOVIC:
A. Right, right.
MS. NEWBURY:
Q. Okay. If you have absent negative controls during a test, would that be a factor that might contribute to having a wrong result or an inappropriate result for an ER or PR test?
DR. TORLAKOVIC:
A. Yes. I mean, and there are different types of negative controls that should be taken into account. Generally speaking, there is a rule that should be followed that from the block that is being tested piece of the tissue, there should be one negative control for each type of tissue processing. For example, if I do three different tests and they all have different antigen retrieval, I'd say for one, the best one would be process digestion. Another one would be buffer and another one would be nothing. I need negative controls for all of them, so I would need three

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negative controls. But there is also internal negative control that has to be interpreted with knowledge and skill of the pathologist that are looking at this, at the tissue. You know what to expect. It should be negative and when it comes to the critical test, the tissue sections that enable you to identify internal negative controls are designed as such, are selected for the testing, if possible at all. So once you take into account two types of controls, negative controls that are used for interpretation, and certainly I thank you actually for pointing-- for asking me about them because it's frequently thought that we are overusing or that negative controls are not an important part of the testing because we are wasting money because to test one negative control, it's expensive thing. You have additional slides and as I said, even for just one, this particular patient, you need three negative controls that some people think that that's not reasonable to do in clinical practice. But I think, in my personal opinion, it is critical that one follows such rules.

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MS. NEWBURY:
Q. Okay, and that would help to detect, by using a negative control, whether there's any inappropriate staining of the slide that might lead to a false positive result?
DR. TORLAKOVIC:
A. Yes, but there is no perfect system.
MS. NEWBURY:
Q. Sure.
DR. TORLAKOVIC:
A. There is no perfect system, but it does help, it definitely helps.
MS. NEWBURY:
Q. Okay, and just back to what you were saying there a minute ago, that background staining, I think your evidence is that that wouldn't necessarily be a true false positive result and would a true false positive result be when you have nuclear staining that should not have occurred?
DR. TORLAKOVIC:
A. Right, if your expected result is true false positive is the one that when your evidence that you have on the slide looks like a specific staining but it is not.

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MS. NEWBURY:
Q. Okay.
DR. TORLAKOVIC:
A. I'll give you one example of that, that is a nuclear staining. There was a viral epitope that sometimes people are interested in looking at medical practice. I don't want to say any specifics about it, but I can tell you that the clone that was available on the market for a while was the one that actually cross reacted with histones in the nucleus, human histones, but not histones for on which epitope it was designed originally. So when it was used in renal transfer and pathology, you would get like positivity in the nuclei and it really looked like a true specific result, and it was true false positive because it just looked like it should look like, very specific, just some nuclei stained and it was only nuclear. There was no cytoplasmic and it looked like there is perfect signal to know its ratio, but it was the result of cross reactivity with human histones in the nuclei.
So that is the thing that reflects true

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false positive result, but when it comes to ER and PR, it can happen, but I think it's extremely rare.

MS. NEWBURY:

Q. Okay, and are there certain types of procedures that might be more apt to cause false nuclear staining? And there's been some reference to -

DR. TORLAKOVIC:

A. Yes, when there is too much antigen retrieval, that can happen.

MS. NEWBURY:

Q. Too much antigen, okay.

DR. TORLAKOVIC:

A. Yes.

MS. NEWBURY:

Q. And that's also referred to as over antigen retrieval, is it?

DR. TORLAKOVIC:

A. Yes.

MS. NEWBURY:

Q. Okay, and is that more common with one technique over another?

DR. TORLAKOVIC:

A. How do you mean?

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MS. NEWBURY:

Q. The avidin biotin method versus the PAP method or some other type of antigen retrieval.

DR. TORLAKOVIC:

A. Well, I don't--I'm not aware of a systematic study to look at that. Perhaps there was, but I just don't remember anything, but I can only tell you that some--when you think about antigen--avidin biotin systems, of course, they are generally prone to endogenous biotin and false positive type of results, but that would not apply to ER/PR because these are nuclear antigens, so endogenous biotin activity would not cause false positive ER test.

MS. NEWBURY:

Q. Okay, and are you aware--you just mentioned a clone that caused a particular problem, just because of the--I guess the studies that didn't translate as well from animals to humans. Are you aware of any of those types of clones that might be used for ER/PR testing?

DR. TORLAKOVIC:

A. No.

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MS. NEWBURY:

Q. Okay. Are you aware if there might be any possible problems with a false positive test or inappropriate positive test if there's inadequate fixation of tissue followed by exposure to alcohol, either through tissue processing or tissue reprocessing? Is that something that you have ever encountered?

DR. TORLAKOVIC:

A. No, I cannot comment on that. I don't know that.

MS. NEWBURY:

Q. If you discovered, I guess, in participating in a quality assurance review that there had been instances of excessive background staining and that this background staining was inappropriately interpreted to be a positive test result, what recommendations would you make to the laboratory that was involved in providing those results?

DR. TORLAKOVIC:

A. Well, generally they are made all the time, from NordiQC when such specimens come. Background staining is something that is looked at carefully. It's immediately

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commented on and recommendations are given based on what is thought to produce that background staining. It's very difficult. If we see that it's endogenous biotin staining, clearly we'll say switch to another detection system that is not based on avidin biotin, you know, interactions, but otherwise, there will be different sources of background staining. Sometimes it's obvious that some lab is using too high primary antibody concentration, so we would say well, dilute the antibody further.

MS. NEWBURY:

Q. And that's one of the factors listed here on this NordiQC.

DR. TORLAKOVIC:

A. Right.

MS. NEWBURY:

Q. Run 8, 9, 10, the too high primary antibody concentration. It's the first item there under false positives, and that would be, I guess, a technique that would have to be adjusted in the laboratory by the technologist or whoever is involved in optimizing the particular techniques. Is that correct?

DR. TORLAKOVIC:

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A. Right, correct.
MS. NEWBURY:
Q. Okay, but in terms of the combination of having the background staining and then having a pathologist interpret that as a positive result, would there be any additional steps to rectify that part of the problem? I assume that sometimes there might be background staining, but the pathologist doesn't interpret it as a positive result. They still interpret it as a negative result.
DR. TORLAKOVIC:
A. Right.
MS. NEWBURY:
Q. What happens if you have the background staining and in addition to that, the pathologist interpreted that to be a positive result?
DR. TORLAKOVIC:
A. Then you have it reported as false positive test obviously. I don't know what else to say.
MS. NEWBURY:
Q. Okay. No, I'm just wondering in terms of corrective actions.

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DR. TORLAKOVIC:
A. Of correcting, I mean, you would have to have somebody first notice that that has happened in the first place, and if pathologists didn't notice that, then it's hard to imagine--to me, it's hard to figure out how, except for the wide audit, who would go back and review those specimens again, I don't know.
MS. NEWBURY:
Q. Okay. So really, it would just have to be a review just to make sure that that's not a common problem?
DR. TORLAKOVIC:
A. I know that in some instances, where the breast pathologist--it's responsibility of certain pathologists in the department if there is breast cancer expert. Those are the people that will frequently review such--you know, go back and review what other people in the department are doing and take, you know, actions when necessary.
MS. NEWBURY:
Q. Okay, and are those types of quality reviews--those would be in addition to a program such as CIQC or -

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DR. TORLAKOVIC:
A. Right, definitely, yes.
MS. NEWBURY:
Q. Okay, or UK NEQAS?
DR. TORLAKOVIC:
A. Yes.
MS. NEWBURY:
Q. And what types of programs, are there any sort of informal programs or guidelines as to how that would be done, you know, within a particular institution?
DR. TORLAKOVIC:
A. See when you have breast carcinoma experts working with this, you know, with breast cancer in the department, they will take into account all available guidelines and knowledge that is there published, and they will be sure to monitor that well differentiated carcinomas are positive, do they expect that all papillary carcinomas will be positive for ER, that all medullary carcinomas will be negative, and will look for things like that, there is evidence, accumulative evidence. For example, in Saskatoon, we have breast pathologist, Dr. Rees. She's following for

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many years now in an extensive database exactly what is the histologic type and what's the percent of positivity just to see that, yes, we are on the line with published evidence and that is what is expected in that, and she goes back and retests, reviews, and re-scores a certain number of specimens throughout the year and so on to make sure that we don't get--that you notice trends if they are developing at the time.
MS. NEWBURY:
Q. Okay. So your monitor trends -
DR. TORLAKOVIC:
A. Yes.
MS. NEWBURY:
Q. As to what will be statistically expected?
DR. TORLAKOVIC:
A. Right.
MS. NEWBURY:
Q. I guess, based on a certain type of cancer.
DR. TORLAKOVIC:
A. Yes.
MS. NEWBURY:
Q. And you would also have reviews by other pathologists just to verify?

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DR. TORLAKOVIC:
A. She organizes occasional throughout the year meetings with other pathologists and circulates the material for them to score and so on, so that we have an idea that the whole group is--how the whole group is performing the scoring and everything, and understanding of the topic and so on. So it is something that that particular pathologist has a responsibility for, and can I do that, in theory, I could, but it's not really my job. I'm not doing it, you know.
MS. NEWBURY:
Q. Okay.
DR. TORLAKOVIC:
A. So this is a kind of ideally how it should be, that in the department there are certain responsibilities for certain areas that we take care of. Even though I oversee immunohistochemistry, she still makes sure that results fall into the trends. She's the one to monitor the trends. I'm not doing it.
MS. NEWBURY:
Q. Based on tumour site?
DR. TORLAKOVIC:

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A. Based on the tumour--yes.
MS. NEWBURY:
Q. And if the expertise were not available at a particular institution, if there was no one there at that particular time who had that wealth of knowledge, I guess, in breast carcinoma, are there any other sort of informal or formal programs that are available for that type of review of interpretation results?
DR. TORLAKOVIC:
A. I'm not aware of that, no. There is literature available, but I don't think there are any set programs.
MS. NEWBURY:
Q. Thank you, Dr. Torlakovic, those are all my questions.
THE COMMISSIONER:
Q. Thank you, Ms. Newbury. Anything arising, Mr. Coffey?
MR. COFFEY:
Q. Yes, just a couple of questions for Dr. Torlakovic.
DR. EMINA TORLAKOVIC - RE-EXAMINATION BY BERNARD COFFEY, Q.C.

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COFFEY, Q.C.:
Q. If we could bring up, please, Exhibit P-3365. Doctor, this is this article that Mr. Browne referred you to. I just note that it is published online, January 26th, 2007, and you recall Mr. Browne asked you about Dr. Rhodes publications, and just in terms of time frames, Doctor, here foot reference #2, the Rhodes publication is there in 2000, another one published in 2000, footnote #3, footnote #5 is a publication in--another publication in 2000 by Dr. Rhodes, and footnote #19 is another publication, again by Dr. Rhodes in 2000, and these are all, I believe, in the Journal of Clinical Pathology. Just look down through them. Doctor, I'm going to ask you, in terms of the findings that Dr. Rhodes made in relation to his study in the UK and he published them in the main in 2000, I think one or two of them in 2001, that Journal of Clinical Pathology, is that widely known in your world? Is it a journal that's widely available?
DR. TORLAKOVIC:
A. It's widely available--well, it's widely

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available, of course. I mean, it's accessible on internet, that's not a problem, but it's widely read in Europe, it's not widely read in North America, to the best of my knowledge.
COFFEY, Q.C.:
Q. And the next question, the second one is there's a reference to Layfield in this article, buried in the actual journal publication itself out of Australia, and here footnote 18 is by Dr. Layfield, I believe, and we've seen the actual--the Commissioner has been shown the actual article itself. This is Breast Journal 2003. His article dates from that time, dealing--Dr. Layfield, dealing with a study in the UK and the US in terms of ER and PR. Finally then in relation to this, doctor, I wanted to ask you about this. Here in the last paragraph actually the publication or article says, and to put it in context, in the paragraph before they point out for HER2 there's always, if necessary, FISH testing available as confirmatory testing. Then they conclude, "However, for ER and PR, no alternative methodology to IHC is available. Therefore, it is essential that the clinician

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and laboratory are at all times aware of the potential impact reporting of IHC has on patient treatment and outcome. Internal audits should be performed in the laboratories to ensure results are as accurate as possible and referral laboratory should be considered for laboratories performing small numbers of cases".

DR. TORLAKOVIC:

A. Yes, I agree with that.

COFFEY, Q.C.:

Q. This is the beginning of 2000 in Australia, this particular article is published out of Australia in 2000--2007, I apologize.

DR. TORLAKOVIC:

A. 2007, yes.

COFFEY, Q.C.:

Q. As a European at the time, like, going back to the time of Rhodes publication or publications in 2000, in the European context, what's stated here in this paragraph, anybody who followed the journal that Dr. Rhodes published in, would they have been aware of this, in the sense of this sentiment, the idea of the necessity for being careful with ER/PR?

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DR. TORLAKOVIC:

A. I can tell you that I was present at his original presentation in Europe when he first time was at a meeting talking about his results, and everybody was kind of shocked, but everybody said we knew this, you know, but they were shocked that this information was actually publicly displayed and scientifically supported now and it's going to be published. So it was like a bomb really, even though despite the knowledge that something is wrong and that not everybody is getting good results with ER and PR, people just didn't pay attention to it. They didn't--I don't know what is this inertia, why is that happening, but it seems like that an intervention in immunohistochemistry is not something that is easily done. So people somehow don't know where to start, and that is what we are seeing now. Now it's clear that we now are crystallizing the role of internal quality assurance, external quality assurance, accreditation. We have come to the point where things are understood, we know how to do it, and we're going to do it, and we are doing

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it, but some years ago this was not clear at all.

COFFEY, Q.C.:

Q. Doctor, in relation to a question Mr. Simmons asked you about concordance and he referred to 95 percent is -

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. The minimum acceptable.

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. In relation to that, Doctor, is there such a thing as having a higher concordance than 95? Like, can you have a 98 percent concordance or a 100 percent concordance?

DR. TORLAKOVIC:

A. Oh, yes, we have 100 percent, and 98, in some of the laboratories with reference value, yes.

COFFEY, Q.C.:

Q. So I take it, the higher the better?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

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Q. And 95 being kind of an accepted minimum, but if you're up to 99 or 100, better still?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. Okay, and finally if I could, both Mr. Simmons and Mr. Brown asked you questions about the development of, in particular, ER/PR, IHC and ER/PR in particular over the past ten years. If we could go to the PowerPoint presentation please. If we could go to--let me see, it's page--blow it up, thank you. Doctor, this is this Run 3 you referred to, and I appreciate that things have changed over the years, but at the time this Run 3 was done which was, in effect, I take it, within the past six months or so?

DR. TORLAKOVIC:

A. Yes.

COFFEY, Q.C.:

Q. By CIQC. Just looking down through the headings here, the lab numbers are obviously different. Antigen retrieval being used is "yes" all the way down, so that's fine, they're all using--instruments, the type of

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instrument being used in these various laboratories.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And I believe I counted up--let me see, 23 labs are listed here, I think is what it is. There are a number of different types of instruments that are utilized?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Different types of instruments. There are a number of different temperatures used?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. For antigen retrieval. There are certainly a number of different antigen retrieval times used.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. It varies all over when you look down through it. There are certainly quite a number of

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different types of buffers used?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. There are quite a number of different types of primary antibody clones used? I shouldn't say quite a number. There are relatively few here.
DR. TORLAKOVIC:
A. Relatively few in this particular case, but if it were even large number of clones, that would be still okay.
COFFEY, Q.C.:
Q. Suppliers, of course, will vary. The dilutions of the primary antibodies vary somewhat in terms of the dilution ratios. You can see that throughout?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. And some are premixed--are prediluted, I'm sorry. The dilutant types vary somewhat. The incubation times vary. In fact, at times somewhat considerably depending upon which one you look at. Detection systems vary, a number

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of different types of detection systems?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And from different--using different names. The incubation time for the detection systems vary somewhat, if you'll look down through that, would you agree?
DR. TORLAKOVIC:
A. Uh-hm.
COFFEY, Q.C.:
Q. And what I want--what I wanted to ask you then is this, having drawn yours and the Commissioner's attention to that, is--and I appreciate this is Run 3.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. Was there a similar table done for Run 2? Would there be a similar table existing?
DR. TORLAKOVIC:
A. Yes, yes, of course.
COFFEY, Q.C.:
Q. Okay, and there would be similar sort of variability at the time?

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DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And yet in Run 2, you said that all the labs that participated, the dozen or so who participated at the time, all got -
DR. TORLAKOVIC:
A. Very good results. It was -
COFFEY, Q.C.:
Q. Very good results.
DR. TORLAKOVIC:
A. Excellent, yes.
COFFEY, Q.C.:
Q. Right across the board?
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And despite all that variability?
DR. TORLAKOVIC:
A. Right.
COFFEY, Q.C.:
Q. Recorded as to protocols and so on and so forth.
DR. TORLAKOVIC:
A. Do you want me to comment on that?

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COFFEY, Q.C.:
Q. Yes.
DR. TORLAKOVIC:
A. I will do that. It's not actually difficult to explain because that illustrates that more than one method can lead to optimized result as long as you know what is your target, what is your goal, and this is the start point for any standardization. You have to know the goals before you try to standardize the procedures. So even if you used all the same procedures, maybe select one best procedure that we think is best, and make it the standard, the outcome may not be standard for each of the labs. So my point would be that my preference for standardization is standardization of the results and expected outcomes of the methods, not methods themselves. By the way, in this process, we end up doing less and less different methods, and they appear to be more and more similar. That is all right, or not, I really don't think that emphasis should be put on methods so much as it should be on the results.
COFFEY, Q.C.:

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Q. And getting the correct result?
DR. TORLAKOVIC:
A. Getting the correct result.
COFFEY, Q.C.:
Q. As often as possible.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And, Doctor, one final point, if I might be allowed just a little bit of latitude, Commissioner, you did differentiate between Run 2 and 3.
DR. TORLAKOVIC:
A. Yes.
COFFEY, Q.C.:
Q. And this is Run 3--well, the actually protocol that was used at the time, and you do refer to the fact that in Run 3, though, the results were more--were not as -
DR. TORLAKOVIC:
A. Not as good.
COFFEY, Q.C.:
Q. And that you attributed to this low--you utilized in Run 3, low expressors.
DR. TORLAKOVIC:

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A. Exactly. There was -
COFFEY, Q.C.:
Q. Which makes it more difficult?
DR. TORLAKOVIC:
A. This was designed to be very challenging. It was not designed to reflect daily practice. It was designed with the purpose to detect deficiencies of the staining, even define deficiencies of the staining systems.
COFFEY, Q.C.:
Q. And so assuming that generally the same protocols were being utilized, you know, generally, and I appreciate there were more people involved in -
DR. TORLAKOVIC:
A. Yes, some people changed the protocols perhaps little bit. But again, the same protocols could have been used and then you would, yes, you end up with more differences between the labs.
COFFEY, Q.C.:
Q. Thank you, Commissioner. I appreciate it.
THE COMMISSIONER:
Q. Thank you very much, Doctor, for having come and assisted us today. I'm sure everyone in

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the room joins me in saying how very much we appreciate your contribution. People suggest we take the afternoon break and then we'll continue.
(BREAK)
MR. TERRY GULLIVER, EXAMINATION BY SANDRA CHAYTOR, Q.C.
(CONTINUED)
CHAYTOR, Q.C.:
Q. Good afternoon, Mr. Gulliver. Commissioner, there's two new exhibits this afternoon that I'd ask, please, to have entered. P-3038 and P-3036?
THE COMMISSIONER:
Q. Entered.
EXHIBIT ENTERED AND MARKED P-3036.
EXHIBIT ENTERED AND MARKED P-3038.
CHAYTOR, Q.C.:
Q. And if we could bring up, please, Registrar, P-0080? And this is again is a note from Dr. Williams' notes, and it's dated August 20th, 2005. And at this point the key notes, key points that he notes are that Mount Sinai is to do all new cases. And secondly he says, "Waiting for Ventana technical expert for Canada to phone Terry Gulliver to arrange an

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early site visit." And thirdly, "Heather Predham to start QI review process in the a.m." And he goes on with the fourth point being some results, it appears, from retests that were done. Mr. Gulliver, the technical expert from Ventana coming in, you were involved, obviously, in arranging that. And what was the purpose for that visit?

MR. GULLIVER:

A. The main purpose, Ms. Chaytor, was obviously at this time when all of the discussions were, you know, surrounding the ER/PR, there was some concern expressed that we had been using the Ventana system by this time, you know, for almost a year and a half and there was some question about are we getting more positives, higher staining than we should expect. So we felt it was important that we have the Ventana technical expert come in to St. John's and do a complete review of the Ventana system to make sure it is operating as per the specifications provided by the vendor.

CHAYTOR, Q.C.:

Q. And the third note here, "Heather Predham to start QI review process in the a.m." what did

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you understand Ms. Predham was to do?

MR. GULLIVER:

A. I think Dr. Williams had asked Heather to, you know, to go into the pathology laboratory, in particular, IHC lab--I mean, from Heather's portfolio and her role in the organization I guess there's been many events in other parts of the organization where she had done what they call, I think, roots cause analysis and those kinds of things. I think he asked Ms. Predham to go to the lab and see if we could start that kind of process.

CHAYTOR, Q.C.:

Q. Okay. And you ultimately, I take it, arranged to have the Ventana expert come in. And what was the result of that?

MR. GULLIVER:

A. Well, I made contact with Ventana. And in Canada the person we dealt with who set the instrumentation up originally, her name is Carole, I think it's Quevillon out of, she's based out of Quebec, and she came in and she came in to, you know, review the whole Ventana system.

CHAYTOR, Q.C.:

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Q. Okay, and if we could look, then, please, at P-0552? And this is Ms. Quevillon's report to you dated August 5th, 2005. And she writes, "As per your request, I checked the Ventana benchmark instruments, the procedure and protocols used for the ER and PGR stains, the knowledge and the capacity of the technicians to troubleshoot and run the instrument." And so in contacting her what was it--what did you explain to her and what did--the issue to be and what did you ask her to do?

MR. GULLIVER:

A. I didn't ask her to do anything specifically. We just asked her to do a complete review of the Ventana system to ensure everything is operating properly.

CHAYTOR, Q.C.:

Q. Okay. And she concludes that she feels confident that the technicians knew what they were doing. "They know how to use the instruments and that the benchmark instruments are staining as they should be." She did find that the recommended maintenance procedures, monthly and quarterly, were never done on the instruments. And "We did it monthly and

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quarterly on one benchmark yesterday and they are doing the second one today." So there was an issue in terms of the recommended maintenance being carried out, but otherwise -

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. - the system was in place?

MR. GULLIVER:

A. Yeah.

CHAYTOR, Q.C.:

Q. And upon receipt, then, of her report what did you do?

MR. GULLIVER:

A. Well, I brought the report Dr. Williams. And I think that Dr. Williams met with Carole before she left.

CHAYTOR, Q.C.:

Q. Yes. And did you attend that meeting, as well?

MR. GULLIVER:

A. Yes, I did.

CHAYTOR, Q.C.:

Q. Okay. And was there anything different discussed in the meeting than what we see in

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her report?
MR. GULLIVER:
A. I don't think so. I think she, you know, verified in person to Dr. Williams that, you know, the Ventana system that we had been using since April, '04, it was operating as it should. She validated some of the antibodies on it, she looked at some of the slides, and she said to Dr. Williams that our staff are well trained. And I remember she made a point saying that Mr. Dyer was one of the best troubleshooters on the system she had encountered. Because during the system being set up originally, Ken Green, who was our sort of lead tech in IHC and Barry Dyer had went to Phoenix, Arizona for a week of sort of in-depth training on the instrumentation and that kind of stuff.
CHAYTOR, Q.C.:
Q. Yes. And so other than you and Dr. Williams, did anyone else meet with her?
MR. GULLIVER:
A. Well, she obviously spent time with our technologists. I mean, she was in the lab with them physically doing the reviews and

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checks with them.
CHAYTOR, Q.C.:
Q. And did Dr. Cook attend the meeting with her?
MR. GULLIVER:
A. I think he did, Ms. Chaytor.
CHAYTOR, Q.C.:
Q. And did you communicate the results of her review to anyone else?
MR. GULLIVER:
A. You mean other than Dr. Williams and Dr. Cook?
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. Well, I mean, obviously the pathology manager and the technologists.
CHAYTOR, Q.C.:
Q. Yes. So, for example, the issue regarding the recommendation for maintenance procedures to be carried out, you communicated that to Mr. Dyer, I would take it?
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. Okay. And that was attended to, was it?
MR. GULLIVER:

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A. To the best of my knowledge, yes, yeah.
CHAYTOR, Q.C.:
Q. If we could have, please, 0542? Mr. Gulliver, did you inquire of Mr. Dyer as to why that wasn't happening in any event, why they had not been carrying out the recommended maintenance schedules?
MR. GULLIVER:
A. I don't know if I asked Barry that directly. I mean, I know I've been over in that part of our laboratory in pathology, because I remember seeing they have by the instrumentation on the wall, there is a big chart there where they tick off the maintenance and those kinds of things. But, no, I don't know if I asked Barry or not.
CHAYTOR, Q.C.:
Q. So you didn't ask, you didn't follow up with that to find out -
MR. GULLIVER:
A. I don't remember if I did or not. I could have and I could not have.
CHAYTOR, Q.C.:
Q. Then we have 0542 is a memo of Dr. Cook to all pathologists and to yourself and Mr. Dyer

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dated August 2nd, 2005. And it indicates that "Dr. Ejeckam is currently our resource person for immunohistochemistry. All inquiries regarding immunohistochemistry should be referred to Dr. Ejeckam and in the event that he's not available, then Dr. Fontaine." Mr. Gulliver, was this discussed with you before this memo was sent out?
MR. GULLIVER:
A. Yes, I do believe myself and Dr. Cook and Dr. Ejeckam met in my office. It was just basically Dr. Cook, you know, asking Dr. Ejeckam, he had--by this time he had been in our lab for two years and while he had been performing in the role of our lead pathologist for IHC part of our lab, it was never really formalized.
CHAYTOR, Q.C.:
Q. So this was formalizing what, in fact, was -
MR. GULLIVER:
A. Pretty well, yes.
CHAYTOR, Q.C.:
Q. - the situation?
MR. GULLIVER:
A. Yeah.

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CHAYTOR, Q.C.:
Q. And telling it to all the pathologists in a formal manner, I take it?
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. And in terms of the communications issues that we spoke briefly on about in early on in your evidence about technologists receiving different advice from different individuals, once this was done and the memo was sent out, did that seem to make any improvement in the communications issues that the technologists were experiencing?
MR. GULLIVER:
A. I certainly think it made, I guess it made improvements in several areas. It certainly made improvement in from a technologist's perspective. They were quite clear now that Dr. Ejeckam has been officially appointed in that role and that's who the technologists would consult for advice or any issues. And then the pathology manager, Mr. Dyer, would know now Dr. Ejeckam is the lead pathologist. I think the staff seen some overall

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improvement. I don't know if they seen, you know, a full improvement in still the numbers of pathologists that would make direct phone calls to the lab and say I'd like this done this way or a pathologist going into that part of the lab, you know, physically and asking to have something done this way or that way.
CHAYTOR, Q.C.:
Q. And is that something -
MR. GULLIVER:
A. But this was the beginnings of really implementing that sort of direct line communication.
CHAYTOR, Q.C.:
Q. So over time it's further improved, I take it?
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. And to the point now where Dr. Elms is in the position and those lines of communication are clear, everybody understands that any questions about immunohistochemistry are directed through Dr. Elms?
MR. GULLIVER:
A. Today?

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CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. If we could have, please, 0940? And this is an e-mail from Heather Predham to Doctors Cook and Williams and it's August 4th, 2005. And it says, "Hi, just wanted to let you know that I met the technical expert from Ventana this a.m. with Terry and Barry. We went over the issues and what we needed from her." So I take it there was a meeting with Carole Quevillon and yourself -
MR. GULLIVER:
A. I think I remember that Heather was in the lab, actually. I think Heather had to be there doing her thing that Dr. Williams asked her to do, to do like a quality review.
CHAYTOR, Q.C.:
Q. Okay. And in terms of going over the issues and what we needed from her, do you recall what was discussed?
MR. GULLIVER:
A. Other than just the basic do a complete review

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of the system.
CHAYTOR, Q.C.:
Q. And it says, "Terry told her we would be meeting with her tomorrow to hear her assessment of our system. During our conversation with her Terry questioned whether the 58 cases that we retested were all negatives or did they include weak positives, as well. He had a feeling that Dr. Carter may have included weak positives in this group when the slides were pulled. If that is the case, then we haven't had 41 out of 58 convert and that was the reason we began questioning the Ventana system. Barry is going to recheck these cases to see if they were all negative. He should know this by this afternoon." What's that about, Mr. Gulliver?
MR. GULLIVER:
A. Oh, this is not discussion with the Ventana person. This is Heather's e-mail, I guess, telling Dr. Williams here's some of our discussion yesterday afternoon. There was some question about the original, the 2002 cases that were first identified, you knew the index case from 2002, and there were three or

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four other patients that the oncologists specifically asked Dr. Carter to review and retest and then Dr. Carter did a broader retest of the 2002 negatives. There was some confusion over at that point in time were those 58 cases all sort of like zero, zero negatives or in that 58 cases were some of those reported earlier as ten percent, 15 percent positive and were they retested.

CHAYTOR, Q.C.:

Q. And why did you--what difference would that have made, why were you querying that?

MR. GULLIVER:

A. Oh, because, well, you see there they were saying of the 58, 41 converted.

CHAYTOR, Q.C.:

Q. Um-hm.

MR. GULLIVER:

A. There was no assessment done to see of those 41 did they convert from zero, zero to positive or did they convert from 15 percent to 25 percent.

CHAYTOR, Q.C.:

Q. Now, were you of the understanding that the PRs were also being looked at when you say

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zero, zero as opposed to -

MR. GULLIVER:

A. To my understanding, yes. But obviously the ER was the main focus.

CHAYTOR, Q.C.:

Q. So your understanding at that point in time, at least, was that the 58 cases were, you were thinking they were zero, zero, zero ER and zero PR?

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. And did you come to learn anything different from that or was that, in fact, the case?

MR. GULLIVER:

A. I think it was later on that we learned, Ms. Chaytor, that some of those 58, they weren't all zero, zeros, like the true negatives.

CHAYTOR, Q.C.:

Q. And were they all zero ERs?

MR. GULLIVER:

A. I don't think so. And again, I can't swear to you 100 percent, but I don't think so.

CHAYTOR, Q.C.:

Q. And it says, "As well, Barry will pull the

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cases tested between June 29th and November 1st to confirm that all results in that period of time were negative." Now, is that the six-month or thereabouts time period that you were referring to that came up in the issue with Dr. Carter on August 1st?

MR. GULLIVER:

A. I'm not sure exactly if that's the time frame. I don't know if she means Barry will pull or if we had already pulled.

CHAYTOR, Q.C.:

Q. Because this is now August 4th and I believe you indicated that you did that immediately the evening of August 1st?

MR. GULLIVER:

A. It was done--yeah. Well, I'd say within that few-day period.

CHAYTOR, Q.C.:

Q. Okay.

MR. GULLIVER:

A. I couldn't tell you the exact day, time.

CHAYTOR, Q.C.:

Q. So this might be, in fact, that. Do you recall any other period then for which Barry would have checked a time period to see if

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they were -

MR. GULLIVER:

A. No.

CHAYTOR, Q.C.:

Q. - negative?

MR. GULLIVER:

A. No.

CHAYTOR, Q.C.:

Q. So this must be in reference to the issue raised by Dr. Carter?

MR. GULLIVER:

A. In all likelihood. But what we did pull was the whole year.

CHAYTOR, Q.C.:

Q. Okay. "I'm at a meeting at St. Clare's this afternoon. If you need me, page me. I had a long chat with Barry and Terry after we got the Ventana lady settled away .... Heather." And what do you recall about that, having a long chat with Barry and Terry, do you recall what that would have been about?

MR. GULLIVER:

A. I don't remember anything in particular, no.

CHAYTOR, Q.C.:

Q. So this is August -

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MR. GULLIVER:
A. We spoke to Heather like almost every day, sometimes three or four times a day. I can't tell you -
CHAYTOR, Q.C.:
Q. This is August 4th and this is shortly after the issue arose with Dr. Carter and she resigned her position on August 2nd. Does that help in any way indicate what it was that you may have spoken with with Ms. Predham?
MR. GULLIVER:
A. I really don't believe I would speak to Heather about, you know, what had just transpired, you know, the couple of days before with Dr. Carter.
CHAYTOR, Q.C.:
Q. Do you think it had anything then to do with quality initiatives in the laboratory because that certainly would be within her -
MR. GULLIVER:
A. I'm thinking that's more likely what the conversation would be. I can't verify that 100 percent, but I know Dr. Williams had asked her to do some kind of quality review. And I think Heather does some kind of review and

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report. I think really what Heather tells Dr. Williams is that, you know, this is so technical that really it's out of her experience level, type of thing. Understand, I mean, you know, this is still within a few weeks of all this issue starting, you know, and people like Heather who now have been at this for a long time were just really starting to understand just laboratory in general.
CHAYTOR, Q.C.:
Q. If we could have, please, P-0941? This is another e-mail from Ms. Predham, August 8th, 2005. And you're included in this. It's to Doctors Williams, Cook, yourself and Ms. Pilgrim. "Overall Database." She writes, "I've got the lab database and NCRTF database combined, but I still have issues to clarify. There are data quality issues such as people with the same name and address, different MCPs" and she goes on from there. "Also, there are a lot of individuals with incomplete MCPs" and she's going to work on that. What would the lab database be that she's referring to here?
MR. GULLIVER:

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A. There was no database. It's, I think what she's referring to is, you know, by this time myself and Mr. Dyer, we have all the surgical pathology reports that we had searched Meditech for where we were going through then a process of reviewing patients, making those spreadsheets, what you refer to now as the spreadsheets that actually Dr. Carter is the one who created the spreadsheet. You know, that's what we used when we took over doing this project. And I think that's more to what Heather is talking about.
CHAYTOR, Q.C.:
Q. Okay, so it would be the spreadsheets that -
MR. GULLIVER:
A. That's by this -
CHAYTOR, Q.C.:
Q. - Dr. Carter had started?
MR. GULLIVER:
A. - this is what we had done by this--well, Dr. Carter didn't really start them. By this time myself and Barry are doing them.
CHAYTOR, Q.C.:
Q. Okay, so that's what this would be referring to?

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MR. GULLIVER:
A. I'm pretty sure, yeah.
CHAYTOR, Q.C.:
Q. The spreadsheet that you worked from in then identifying the patients?
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. Okay. And she goes on to say, "There are a couple of issues that have come to light"--"that came to light, though, during this process." And she says, "Rough numbers from the combined database now show 4510 people overall." Do you know where that number would have come from?
MR. GULLIVER:
A. No idea.
CHAYTOR, Q.C.:
Q. How many people did you identify?
MR. GULLIVER:
A. Well -
CHAYTOR, Q.C.:
Q. Or approximately?
MR. GULLIVER:
A. Yeah. My search identified from 1997 up

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until, well, until we stopped testing in the end of July of '05, it was like 2860, it was roughly around that number that our lab Meditech system had identified of the number of specimens that were--had ER/PR testing done.

CHAYTOR, Q.C.:

Q. So your number of about 2800 would have included -

MR. GULLIVER:

A. All ER/PR tests that had tested -

CHAYTOR, Q.C.:

Q. - all ER/PR tests done -

MR. GULLIVER:

A. Breast primaries and non-breast primary.

CHAYTOR, Q.C.:

Q. Right, for whatever reason, all ER/PR tests completed that you could pull off Meditech and what you could pull off Meditech would include which centres, which institutions?

MR. GULLIVER:

A. Those numbers included the specimens refer--as you know, the Health Sciences was the only lab in the province doing the testing, so we would have received blocks, i.e. specimens that were

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already fixed and grossed and processed in other labs, and sent them to the Health Sciences for the ER/PR test, and there were nine--at various times, there were as many as nine pathology labs in the province. But when the specimen came in to the pathology lab at the Health Sciences, there would be a record into our Meditech system that we received a block on patient so and so from Gander or Grand Falls or Corner Brook. We did an ER/PR test and it was sent back then for interpretation. But we had that level of documentation. So my numbers would have included any patient from around the province that had an ER/PR test ordered in our system.

CHAYTOR, Q.C.:

Q. From 1997 up through to 2005?

MR. GULLIVER:

A. Yeah.

CHAYTOR, Q.C.:

Q. Okay. So you're not able to say what the 4500--we'll have to ask, I guess, Ms. Predham about that. "The Cancer Registry does not identify almost 2100 of individuals who had ER/PR testing. Current status, living or

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deceased, is only identified in 1245 of those people. ER/PR status is indicated in 1230 people with an overall ER positivity rate of 55 percent" and -

MR. GULLIVER:

A. And all those numbers, Ms. Chaytor, are not from the lab data.

CHAYTOR, Q.C.:

Q. Okay.

MR. GULLIVER:

A. This is the information she's getting at this time, information getting back from the Cancer Registry.

CHAYTOR, Q.C.:

Q. Okay. So then these numbers that we see here, because you were working of course on positivity rates yourself -

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. - overall ER positivity by year, and she says "and remember, this is rough" and she gives "2003, 61 percent. 2002, 48. 2001, 46. The Cancer Registry only indicates P and negative or positive and negative, not percentage." So

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you're saying that's not your figures.

MR. GULLIVER:

A. No.

CHAYTOR, Q.C.:

Q. That must be coming from the Cancer Registry.

MR. GULLIVER:

A. I had nothing to do with that.

CHAYTOR, Q.C.:

Q. Okay, and at the time then that you received the e-mail, did it catch your attention, the difference in those figures as compared to what your data was indicating?

MR. GULLIVER:

A. Oh, I was certainly well aware, and that's why--read the next sentence, where Heather says now she's "going to pick up from Terry the spreadsheets that he and Barry worked on over the weekend and incorporate this information as well."

CHAYTOR, Q.C.:

Q. Yes. So then, did you discuss this issue with her and the discrepancy in the positivity rate?

MR. GULLIVER:

A. I don't remember specifically. I'm sure we

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had just basic general conversation about it, and I know that Heather would have--was saying to us that, you know, information she's able to gather from the Cancer Registry side, you know, wasn't complete information. Again, she identified there that they had 4,500 people and 2,100 didn't have ER/PR testing. I think the Registry just registered patients who had like a breast specimen done and not specifically patients who were positive for cancer and had ER/PR testing done. There was a big debate over that also.

CHAYTOR, Q.C.:

Q. Okay, and if we could look, please, at P-2375? And this, Mr. Gulliver, I believe to be a copy of one of the spreadsheets. Is that right?

MR. GULLIVER:

A. Yeah.

CHAYTOR, Q.C.:

Q. And this is indicated to be in 2002. So this is the type--this is the spreadsheet that you and Mr. Dyer used in going through the pathology reports?

MR. GULLIVER:

A. Yeah, and Dr. Carter actually had--this was

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her original intent when she was going to do the review of the patients, and we just took it from her.

CHAYTOR, Q.C.:

Q. Okay, and so she's the one who came up with the headings, I take it, surgical number and MCP number, hospital of origin?

MR. GULLIVER:

A. Yeah.

CHAYTOR, Q.C.:

Q. Okay, and the printing on this, is this your writing?

MR. GULLIVER:

A. That's actually not my writing. That's Mr. Dyer's.

CHAYTOR, Q.C.:

Q. Okay. We see over, and then up on top, the total tested, those numbers, is that your writing?

MR. GULLIVER:

A. That's my writing, yeah.

CHAYTOR, Q.C.:

Q. Okay. So you've got 2002, total tested 189; negative, negative, 48; and is this weak positive?

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MR. GULLIVER:

A. Yeah.

CHAYTOR, Q.C.:

Q. Less or greater than ten percent ER, what does this say? What does this tell us?

MR. GULLIVER:

A. 30.

CHAYTOR, Q.C.:

Q. So weak positive, you're calling what?

MR. GULLIVER:

A. The ones that are positive but didn't meet the clinical threshold.

CHAYTOR, Q.C.:

Q. Okay. So weak positive, and what does it mean that you've got in brackets, greater than ten percent ER, and then the number?

MR. GULLIVER:

A. That probably should be just a written--that should be less than probably.

CHAYTOR, Q.C.:

Q. Okay, and there were 30 of those cases you're saying?

MR. GULLIVER:

A. Yeah.

CHAYTOR, Q.C.:

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Q. And 48 negative, negative?

MR. GULLIVER:

A. Zero, zeroes.

CHAYTOR, Q.C.:

Q. Okay, and those are the ones to be repeated, you're indicating?

MR. GULLIVER:

A. Retested, yeah.

CHAYTOR, Q.C.:

Q. Out of the entire -

MR. GULLIVER:

A. Of the 189 though, Ms. Chaytor -

CHAYTOR, Q.C.:

Q. 189 would include the positives too, I take it, is that right?

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. Yes.

MR. GULLIVER:

A. And these are--understand now that in our Meditech system, in reading all the pathologists reports and identifying patients and putting them on the spreadsheets, we could only spreadsheet patients that were tested and

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interpreted in St. John's.
CHAYTOR, Q.C.:
Q. Right.
MR. GULLIVER:
A. While we did have a list, another list generated of out-of-town specimens with no interpretation. So the numbers you see on top, that 189, would be--reflect the sort of St. John's Health Care Corporation patients.
CHAYTOR, Q.C.:
Q. So this 189 is just St. John's?
MR. GULLIVER:
A. Right. We're doing our St. John's -
CHAYTOR, Q.C.:
Q. St. John's area hospitals.
MR. GULLIVER:
A. - we're doing the St. John's patients and St. John's sheets during this time.
CHAYTOR, Q.C.:
Q. So the ones you have results on?
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. And even though you would have had a stack of pathology reports or not--a stack of Meditech

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records -
MR. GULLIVER:
A. What we call out of town.
CHAYTOR, Q.C.:
Q. Yes, which included the out-of-towns, but you wouldn't have had the results for those?
MR. GULLIVER:
A. No.
CHAYTOR, Q.C.:
Q. I guess except for the period of time when Dr. Khalifa was doing the reporting?
MR. GULLIVER:
A. Well, '97 would be a bit different, because in '97, where Dr. Khalifa was doing pretty well most of the reporting or all reporting for the province, in our Meditech system, we did have both the test documentation and we had the patients interpretation as provided by Dr. Khalifa.
CHAYTOR, Q.C.:
Q. What did you call negative, negative? What did you define as being -
MR. GULLIVER:
A. Zero, zero. What you see here, see the negative, negative?

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CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. What we logged in here, see ER/PR?
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. Whatever the original report said is what we put in there. So that stroke minus, minus, is like zero, zero, negative, negative.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. But they would be all zero, zero.
CHAYTOR, Q.C.:
Q. Okay, and so then you call weak positives anything, and this you're saying should be less than ten percent?
MR. GULLIVER:
A. Right, and actually, when we did all these here, we kind of erred on the side of caution that any patient that we thought could even be on the borderline, we put them on--this is--you probably got all the sheets for '02?
CHAYTOR, Q.C.:

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Q. Okay, yes, the next page then.
MR. GULLIVER:
A. If you continue on.
CHAYTOR, Q.C.:
Q. We have the next page, and again -
MR. GULLIVER:
A. Right, and you see what's--and you see this next line, controls and original?
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. This is if we actually read in the pathologists interpretation that they said in their report positive controls were viewed. We made a notation of the times that was documented in the pathologist's report. But these are all the zero zeros, the negative, negatives.
CHAYTOR, Q.C.:
Q. Okay. Then the next page then, so page three.
MR. GULLIVER:
A. Again, all negative negatives.
CHAYTOR, Q.C.:
Q. And page four is all negative negatives?
MR. GULLIVER:

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A. Yeah.
CHAYTOR, Q.C.:
Q. And page five?
MR. GULLIVER:
A. And then that would be the end of the negative negatives for '02.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. Then we started new sheets where anybody reading reports that we thought could be debatable, to have them reviewed then after, once the sheets were done. So you see that first patient there, it was zero for ER, 20-25 for PR.
CHAYTOR, Q.C.:
Q. Right, okay.
MR. GULLIVER:
A. And even though we had, you know, some oncologists had said well--some had said we would still treat somebody if they had a 40 or 50 percent PR but negative ER, that still wasn't sure and it wasn't standard. So we just put anybody that could be possibly reviewed on those next set of sheets. All the

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zero, zeros were a guarantee retest.
CHAYTOR, Q.C.:
Q. And did you understand that it was standard and it was firm that if somebody was -
MR. GULLIVER:
A. Zero for ER -
CHAYTOR, Q.C.:
Q. - over ten percent ER, after January 1st, 2001 -
MR. GULLIVER:
A. 2001.
CHAYTOR, Q.C.:
Q. - that they would have been treated?
MR. GULLIVER:
A. That's what we were told, but you will see lots of cases where even after the 2001, if the report said even like 10 to 15 percent, we put them on the list to be reviewed.
CHAYTOR, Q.C.:
Q. Okay, and what about beyond 15 percent? What about the patient who was, say, 20 percent in March of 2002, did she end up on your spreadsheet?
MR. GULLIVER:
A. If it was 20 percent ER, no. No, they didn't.

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CHAYTOR, Q.C.:
Q. So you used a bit of discretion and said 10 to 15 percent?
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. And that was just on your initiative, as opposed to anything told to you by the physicians?
MR. GULLIVER:
A. No, I--no, myself and Dr. Cook had talked about it.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. And we just both decided, "look, anything--anything even close to the cut offs, put them on the list so we can review them."
CHAYTOR, Q.C.:
Q. And close to the cut off, you interpreted as being about a five percent difference?
MR. GULLIVER:
A. Around five to ten. Sometimes it said 10 to 20 percent, and we would put them on the list.
CHAYTOR, Q.C.:

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Q. Well then that's what I was wondering. What about the woman who was 20 percent ER?
MR. GULLIVER:
A. But if someone said just 20 percent, there was no ten percent, you know what I mean?
MR. SIMMONS:
Q. I think there's probably a bit of confusion here. I think Mr. Gulliver is referring to -
THE COMMISSIONER:
Q. It's clear between the difference between a number and a range.
MR. SIMMONS:
Q. - a pathology report. I think Mr. Gulliver is referring to a pathology report when the report is 10 to 15 percent on this one report.
CHAYTOR, Q.C.:
Q. Yes.
THE COMMISSIONER:
Q. Yes. I don't think there's any confusion.
MR. SIMMONS:
Q. Sorry.
CHAYTOR, Q.C.:
Q. I didn't think I was confused.
MR. GULLIVER:
A. I don't know.

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THE COMMISSIONER:
Q. Mr. Gulliver is indicating that if it specifically said 20, he treated it as 20, and that wasn't in a--that wasn't doubtful.
MR. GULLIVER:
A. It wasn't from a range, yes.
CHAYTOR, Q.C.:
Q. Right.
THE COMMISSIONER:
Q. But if you put in 10 to 15, he didn't know whether it was on the 10 end or -
MR. GULLIVER:
A. Or 10 to 20, yes.
THE COMMISSIONER:
Q. - on the 15 end, so that was doubtful.
CHAYTOR, Q.C.:
Q. Right.
MR. GULLIVER:
A. You see one here, Ms. Chaytor, it says 15 and 20 percent.
CHAYTOR, Q.C.:
Q. Yes, that's right. So 15 to 20 percent, you considered that 15 and so you included it?
MR. GULLIVER:
A. Right.

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CHAYTOR, Q.C.:
Q. Right, yes, okay, all right. We're all good.
MR. GULLIVER:
A. And you can see that one is crossed off.
BROWNE, Q.C.:
Q. Commissioner is (inaudible).
THE COMMISSIONER:
Q. Pardon?
BROWNE, Q.C.:
Q. (Inaudible).
THE COMMISSIONER:
Q. Is that what it is? No, I just might be months of being back there, Mr. Browne.
CHAYTOR, Q.C.:
Q. Okay. So one moment, please.
THE COMMISSIONER:
Q. Mr. Gulliver, I'm taking these things literally, because the little dash you're saying is zero, but I'm assuming that if it's--either it said zero or said negative only on your report?
MR. GULLIVER:
A. Yes, you're correct.
THE COMMISSIONER:
Q. And if there was a percentage at all, you put

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that percentage in?
MR. GULLIVER:
A. Yes.
THE COMMISSIONER:
Q. Okay.
MR. GULLIVER:
A. And sometimes, Judge Cameron, the report might have said WP for weak positive. If it said WP, we wrote WP on the sheet.
THE COMMISSIONER:
Q. Okay, all right.
CHAYTOR, Q.C.:
Q. Okay, so for an example, the one here that we're looking--that you just pointed to, Mr. Gulliver, where it was 15 to 20, and then it's crossed off. Why was that person crossed off?
MR. GULLIVER:
A. All the ones you see--once we got to the stage where the spreadsheets were done for each year and any patients that were questionable, I brought them to Dr. Cook's attention. So he would speak to the oncologists. I think what they did, Ms. Chaytor, is just verified if that person--like that 15 to 20 percent person, did that person receive therapy back

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in 2002? If they did receive therapy, then they weren't sent for retesting.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. So that's the kind of verification went through, but the ones--when we got ready to send them all off in these batches, Heather Predham was working with the Cancer Centre and she provided to us the list of patients who had already passed away, and our first focus was the patients who were still living, and all the ones you see with a cross marked going through and see deceased written over on the end?
CHAYTOR, Q.C.:
Q. Yes, so this patient was crossed off because you had determined -
MR. GULLIVER:
A. They were crossed off -
CHAYTOR, Q.C.:
Q. - she was deceased?
MR. GULLIVER:
A. - at that time, yes, at that time.
CHAYTOR, Q.C.:

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Q. Based on the list that Ms. Predham gave you?
MR. GULLIVER:
A. Right, and as you know, all the deceased patients went together as one batch later on, after all the living patients in town and out of town were retested.
CHAYTOR, Q.C.:
Q. So you, for your purposes, you put everyone on there and you understood anyone who was ten percent or greater -
MR. GULLIVER:
A. And 30 percent or less up to 2001.
CHAYTOR, Q.C.:
Q. Right, up to 2001, and then after 2001, ten percent or greater, and you put in a little bit of a buffer, in terms of after your discussions with Dr. Cook, that well, let's have some leeway, anyone close to the cut off.
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. So if you saw 15 to 20 percent, you put that person in. But someone who was just 20 percent ER, that person wouldn't have gone on your spreadsheet?

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MR. GULLIVER:
A. I don't--I don't think so. If it was 20 percent ER and negative PR, I might have put it on the sheet just to make sure.
CHAYTOR, Q.C.:
Q. Okay. So you used some discretion yourself in terms of coming up with who should go on your spreadsheet, and then you understood there was going to be a further vetting after you passed in your spreadsheet and that people who had already been treated, that would be determined, and those people would also not be sent for retesting?
MR. GULLIVER:
A. Well, Dr. Cook then reviewed those particular patients and reports.
CHAYTOR, Q.C.:
Q. And so you understood they wouldn't be sent? Or the intent was not to send them if they'd already been -
MR. GULLIVER:
A. If they already had received treatment, yes.
CHAYTOR, Q.C.:
Q. Okay, and did you ever learn anything different from that?

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MR. GULLIVER:
A. No, not to my knowledge, no.
CHAYTOR, Q.C.:
Q. Okay. So the fact that people who had received treatment were in fact sent for retesting, you weren't aware of that?
MR. GULLIVER:
A. No.
CHAYTOR, Q.C.:
Q. Okay, and -
MR. GULLIVER:
A. Now again, you know, the other labs outside of St. John's who were doing, I guess, a similar kind of review, you know, I don't know if they were doing the exact same thing that myself and Barry were doing. Again, if they had a questionable patient, I'm assuming they contacted the oncologist or the pathologist, spoke to the oncologist and made a determination at that point in time.
CHAYTOR, Q.C.:
Q. Okay, and Mr. Gulliver, who gave you the criteria by which you were to search? Whose decision, I guess, was it to say ten percent from January 1st, 2001 and 30 percent before

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that? Who gave you that criteria?
MR. GULLIVER:
A. At one of these meetings, you know, we've seen. You've seen lots of them.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. At one of the meetings where it was a meeting with the oncologists were there, you know, Kara Laing was there, Joy McCarthy was there, and I think that one too, I think Dr. Kwan was at that one, and I guess to go back to the beginning, there actually originally, there is debate about who should identify the patients over this time frame that required retesting. That was the first decision, of who should actually do all this process and all this work. You know, I had indicated to the oncologists, pathologists, Dr. Williams, that you know, originally when the decision was made to retest patients, you know, I had told them that, you know, lab practice is that we keep patients blocks and slides for 20 years. So that we actually do have the capability to go back and retest. Of course, the next step

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is then who are you going to retest? And that was a debate and a decision that was made at one of those meetings.

It was my viewpoint originally that the oncologists were working--by this time, were working with Dr. Carter and Dr. Cook. The oncologists were pretty well reviewing patients and picking out key patients and giving them to Dr. Carter and Dr. Cook and they were being done as a consult, as a retest, and that was my first opinion, well, the oncologist should go and review all their patients, whether it meant reviewing clinical charts or I had no idea what computer records the Cancer Clinic kept, and I thought that would be the best method to--for them to review their own patients and then give us a list by year of who they felt should be retested.

But Dr. Kara Laing said that, you know, the computer systems at the Cancer Clinic, you know, they weren't up to date. There were oncologists who had come and gone. You'd have to go and read every single patient's clinical chart, and this was--time was of the essence,

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type of thing, and you know, I had--and they asked, "well, how would the lab do it?" and I said that well, the lab does keep a computer record on Meditech of every patient that comes in for an ER/PR test. So everyone pretty well agreed that that was probably the most complete way and probably the quickest way to be able to identify patients who had an ER/PR test done, and in that discussion, the guidelines that were given to me by the oncologists and everyone in the room was there, was that, you know, the 30 percent cut off and the ten percent cut off time line.

CHAYTOR, Q.C.:

Q. Okay, and so the oncologists set those parameters?

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. Was there any oncologists in attendance who disagreed with the parameters or said that his or her practice was different than that?

MR. GULLIVER:

A. I know, and that's why I remember Dr. Kwan was there, because Dr. Kwan had made a statement.

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He said that he has treated people with--who were zero, zeros, depending on the age of the woman, the clinical history and other factors, and yes, that was stated at that meeting.

CHAYTOR, Q.C.:

Q. And was there anything--was Dr. Alidina there or did he have any opinion?

MR. GULLIVER:

A. Who?

CHAYTOR, Q.C.:

Q. Is it Alidina? No? Okay.

MR. GULLIVER:

A. No.

CHAYTOR, Q.C.:

Q. So Dr. Kwan indicated he had treated people zero, zero?

MR. GULLIVER:

A. That's why I remember him being there, because he actually made that statement.

CHAYTOR, Q.C.:

Q. Okay.

MR. GULLIVER:

A. And there was also some discussion, you know, other oncologists said that if it was a negative ER but a high positive PR, they

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looked at the hormone receptor in total. Others, I think, said that we're practising at strictly with the cut offs. So that's how the decision was made to, well, we should apply the 30 percent, 10 percent rule.

CHAYTOR, Q.C.:

Q. Okay, and so in terms of how far then to go back, and to start at 1997, who decided that? Whose decision was that?

MR. GULLIVER:

A. I don't think that was decided first, Ms. Chaytor. In that discussion, this is 2005, I think it was Dr. Laing, you know, who pretty well, I mean, she's the oncologist expert. She was the one that said that, you know, literature shows and clinical trials show that women who had not had hormonal therapy, even if it's four or five years that's gone by, they can still be helped by giving them hormonal therapy. So the original thing was looking over a five-year period and it was just pretty well decided--I said well--and they actually asked a combination of when did we start doing ER/PR testing by IHC method, and then they asked would we have blocks even

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back to the testing even began. Of course, the answer was yes, because we keep them for 20 years, patient records. And the decision was to do--start with the current year, you know, in trying to assess who should we do first. It was start with the most current patients and work back. So that's why you might see some of my stats didn't include '97, '98 and '99.

CHAYTOR, Q.C.:

Q. Yes, you add to that as time went on.

MR. GULLIVER:

A. We did 2000 and 2004. So we got current, that five-year group of patients done first.

CHAYTOR, Q.C.:

Q. Uh-hm.

MR. GULLIVER:

A. And then went back and started the patients from '97,'98, and '99.

CHAYTOR, Q.C.:

Q. And you could have gone back, I guess, even beyond that, but the decision, I take it, was made to start with IHC testing?

MR. GULLIVER:

A. Well, we couldn't go back beyond that.

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CHAYTOR, Q.C.:

Q. You had blocks beyond that. So if you wanted to test, for example, people who had had their test done by way of the biochemical method, there were blocks available that you could have done that?

MR. GULLIVER:

A. Not really, no.

CHAYTOR, Q.C.:

Q. Why not?

MR. GULLIVER:

A. Well, when the biochemical method was being performed in biochemistry--again it's not my area of expertise, but I do know a little bit about it, that that methodology meant that--at that time, if you--if a woman found--if there was a lump in a woman's breast, in the old methodology, the surgeon had to do an invasive procedure and remove part of that lump, which hopefully included the tumour. That tumour then was submitted to the biochemistry lab. That tissue was snap frozen in liquid nitrogen and it was stored for a period of days and weeks, and then it was unthawed and you put it into a bowl, like a crucible, you added

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solutions to it and you mashed it all up.

CHAYTOR, Q.C.:

Q. Yes.

MR. GULLIVER:

A. And then you try to measure how much supernatant came out of the tissue. When that was done, the tumour tissue then is gone.

CHAYTOR, Q.C.:

Q. Right, so you didn't have -

MR. GULLIVER:

A. And this methodology, it was more--now you can do an non-invasive procedure and do a biopsy of the lump and send it for IHC. So it was a different--whole different.

CHAYTOR, Q.C.:

Q. So unless you had other -

MR. GULLIVER:

A. Unless you had other tumours and stuff there.

CHAYTOR, Q.C.:

Q. If all of the tumour was used -

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. If all the tumour was used up in that process, you wouldn't have it?

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MR. GULLIVER:

A. Right.

CHAYTOR, Q.C.:

Q. So it would only be for any patient that there was additional tumour and tissue available, for example, if the patient had a mastectomy and only part of their tumour had been used?

MR. GULLIVER:

A. Right.

CHAYTOR, Q.C.:

Q. Okay. So the decision was made to go back to 1997 and that's when the IHC method had begun?

MR. GULLIVER:

A. Right.

CHAYTOR, Q.C.:

Q. Okay. Then if we just continue on here with your 2002 records--I think that might actually be your--no, it's another page. Then on page eight of this exhibit, P-2375, we'll see there's some here where you write in again 10 to 20. Those are, I think, Dr. Cooks records of the same. So if we go back then -

MR. GULLIVER:

A. Well, I guess once these sheets were finalized and any patients that were in question that we

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spoke to Dr. Cook about, the next step was the time consuming process then to go and retrieve all these original blocks and slides from the filing cabinets.

CHAYTOR, Q.C.:

Q. Yes, and I'm going to ask you about that. First of all, though, before we leave the exhibit, this "reviewed May '07", is that your handwriting?

MR. GULLIVER:

A. That's my writing, yes.

CHAYTOR, Q.C.:

Q. And why--what does that indicate, what happened in May of 2007?

MR. GULLIVER:

A. I think I reviewed those, Ms. Chaytor, just to verify the exact numbers. I think there were some questions coming from Heather and Susan Bonnell about what was the exact number of patients that were sent for retesting and those kinds of things, and I think these are reviewed again another time through the NLCHI process.

CHAYTOR, Q.C.:

Q. Yes. So in May of '07, it was Ms. Predham and

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Ms. Bonnell who asked you about exact numbers. So your review at that time was just to count up what you put on your spreadsheets, is that what happened?

MR. GULLIVER:

A. Yes. Oh, yeah, it wasn't recheck patients, if they were sent or not sent.

CHAYTOR, Q.C.:

Q. So you weren't checking names -

MR. GULLIVER:

A. Right.

CHAYTOR, Q.C.:

Q. To see if there was a patient on your list that--was or wasn't on your list?

MR. GULLIVER:

A. It wasn't a cross-reference. It was verifying the numbers because people were worried about the numbers, the numbers.

CHAYTOR, Q.C.:

Q. Okay, all right. Well, then tell the Commissioner about how you went about then, first of all, identifying all the approximately 2800 people who had had ER/PR tests, and then you've told us how then you reviewed to try and figure out who would end

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up on your spreadsheet. So what did you have to do? After finding out there was 2800 approximately people who had the test--you wouldn't have had, obviously, pathology reports on all those people?

MR. GULLIVER:

A. No.

CHAYTOR, Q.C.:

Q. Because you wouldn't have the out of town people. So what did you next have to do in order to end up with people to put on your spreadsheet?

MR. GULLIVER:

A. Well, I guess, I mean, what I did, in the Meditech hospital system there is a separate laboratory information system, and within that, there is a separate anatomical pathology module, and the pathology module actually has a fair bit--has more search capabilities than all the other lab modules in the system. So what I did, I went in by year and did a search on Meditech and I asked the computer system could you please identify every patient who had an ER or PR procedure performed. From that, I would get the total numbers. Then I

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printed off hard copies of every single patient report, and then by year would read the reports and I would separate them into key piles. So, obviously, you can see here all the negatives, the 0/0 were in a pile, all the ones that were questionable, like, what we called the weak positives were in a pile, all the strong positives were in a pile. We made a pile then for the non-breast specimens, and then we made a pile for the ones that were sent out of town that we had no results or idea if they were positive, negative, weak positive, and--that was just documentation that test was performed.

CHAYTOR, Q.C.:

Q. What did you define as strong positive? Who went in that pile?

MR. GULLIVER:

A. Well, again, I mean, anybody you don't see here, anybody who had 70/70, 90/90, 50/90, all those ones, yes.

CHAYTOR, Q.C.:

Q. Anyone above 10 percent or the range that you used?

MR. GULLIVER:

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A. The range was--yes.
CHAYTOR, Q.C.:
Q. The 10 to 15 kind of thing?
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. So they were--the strong positives got put to one side and didn't end up on your spreadsheet?
MR. GULLIVER:
A. Right.
CHAYTOR, Q.C.:
Q. And the out of town people, did you then at least make a list of their names and whatever centre they were from?
MR. GULLIVER:
A. I had the computer print off that came off the pathology module that would say--it would indicate the patient's name and demographic information. The surgical number and the specimen that was assigned in the referral hospital, and then the surgical number that was assigned when it arrived in our lab for the procedure to be performed, and then generally most of them just had a specimen

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comment that said, "return back to Gander for interpretation" or "return back to Corner Brook", and even at times return back to St. Clare's, or the Grace when they were open.
CHAYTOR, Q.C.:
Q. Yes, and did you make a list of them, though, of those people?
MR. GULLIVER:
A. No, they weren't on no spreadsheets. They were just--they were put together sort of in a group as "other, out of town".
CHAYTOR, Q.C.:
Q. And was that grouping then ever used at any point in time afterwards? For example, when samples were coming in from other regions -
MR. GULLIVER:
A. No, no, it wasn't.
CHAYTOR, Q.C.:
Q. Was there any cross checking to make sure your stack--they had everyone that was in your stack?
MR. GULLIVER:
A. No, because I would have no idea -
CHAYTOR, Q.C.:
Q. Yes.

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MR. GULLIVER:
A. Because I--I had no results, so I would have no idea. If I had 50 -
CHAYTOR, Q.C.:
Q. You didn't know if they were positives or negatives?
MR. GULLIVER:
A. Exactly.
CHAYTOR, Q.C.:
Q. Fair enough.
MR. GULLIVER:
A. So if I had 50 patients that were, say, in the year 2002 that were, say, from Western Memorial, and from their region, could be Stephenville or Corner Brook, but their responsibility, if I had a list of 50 patients and Corner Brook sent me in 35 for retesting, which came in like maybe September/October -
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. I would have no idea if the 35 they sent -
CHAYTOR, Q.C.:
Q. Right, who was what?
MR. GULLIVER:

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A. Who was what on the list.
CHAYTOR, Q.C.:
Q. And you didn't provide them with the complete list?
MR. GULLIVER:
A. I know, and I've actually said that to my--well, not just to myself. I've actually said that many times since that, you know, when we were doing this here, I mean, understand we were doing this night and day up until midnight most nights, weekends, for weeks. It was such a time consuming process that--I really wish that--I don't know why I never thought about it, that the list that I printed off of us having a record of a test performed from the regions, that I could have just sent that list out to the regions.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. And another strange thing is, and I did have some contact with the regions, and no one in the region ever asked, you know, do you have a list in your records of who was sent in from Corner Brook, Gander, or Grand Falls.

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CHAYTOR, Q.C.:
Q. Mr. Gulliver, does that list still exist that you had of all the -
MR. GULLIVER:
A. They're still in my original files, yes.
CHAYTOR, Q.C.:
Q. You still have that?
MR. GULLIVER:
A. I think you've got copies of all that.
CHAYTOR, Q.C.:
Q. Copies of all that?
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. Including -
MR. GULLIVER:
A. All those repots that were copied, they're in there under "other category" or they might say "out of town".
CHAYTOR, Q.C.:
Q. Okay, I see what you mean, yes.
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. Why were you keeping track of

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negative/negatives. Was that of any significance to you?
MR. GULLIVER:
A. Well, the significance is we're also looking at these spreadsheets, looking at how many patients were--the whole positive/negative issue too was ongoing. So the negative/negative, true 0/0, to me that's true lab--that's a negative test.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. There was no staining whatsoever.
CHAYTOR, Q.C.:
Q. So if we could just go to P-0514 for a moment, please, and this is a document I showed you yesterday, Mr. Gulliver, and this is the first, I think, of these sheets that you came up with on stats for positivity rates, July 20th, 2005 document.
MR. GULLIVER:
A. And the spreadsheets aren't done by this point.
CHAYTOR, Q.C.:
Q. Right, okay.

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MR. GULLIVER:
A. This is earlier.
CHAYTOR, Q.C.:
Q. I'm just wondering, though, when you were then figuring out who to put in these categories -
MR. GULLIVER:
A. Well, just go to 2002.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. Which we just seen.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. So you would see there that we had 344 tests that were found in our system.
CHAYTOR, Q.C.:
Q. Right.
MR. GULLIVER:
A. Of those, 155 were sent in from -
CHAYTOR, Q.C.:
Q. Were from out of town.
MR. GULLIVER:
A. From all the regions outside St. John's. There were 189 St. John's tests that we had

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results on.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. And then of those, 95 were positive, which means they were clearly positive.
CHAYTOR, Q.C.:
Q. Uh-hm.
MR. GULLIVER:
A. There were 33 cases that we called weak positive, i.e. that list you see, the second list.
CHAYTOR, Q.C.:
Q. Uh-hm.
MR. GULLIVER:
A. It could have been 1 percent ER, 80 percent PR.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. We called them a positive under the weak positive category.
CHAYTOR, Q.C.:
Q. So these are the under 10s?
MR. GULLIVER:

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A. Right.
CHAYTOR, Q.C.:
Q. For 2002.
MR. GULLIVER:
A. And then there was 32--sorry, 61 of them that were clearly no staining, zero, zero.
CHAYTOR, Q.C.:
Q. So you were looking at zero, zero?
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. But what about if 0/40?
MR. GULLIVER:
A. That would be in our weak positives.
CHAYTOR, Q.C.:
Q. So they're under weak positives?
MR. GULLIVER:
A. Yeah, the hormone receptor test had a certain degree of positivity reported.
CHAYTOR, Q.C.:
Q. So regardless--so it's not just ER negativity we're talking about here.
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:

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Q. We're talking--in order to be come classified as negative here -
MR. GULLIVER:
A. It was zero, zero.
CHAYTOR, Q.C.:
Q. It had to be both estrogen and progesterone negative?
MR. GULLIVER:
A. They were both negative, yes.
CHAYTOR, Q.C.:
Q. And under here under this 33 is where I would find my--what might be classified ER negative, but PR positive, and I would also find in here the people who were 10 percent or under for ER positivity?
MR. GULLIVER:
A. Right, yes.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. And when you--then you see the bottom, I just added up and said "overall, we can see the strong positives, the weak positives", and again you can call the weak positives the low expressors, if you like, and then the true

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zero, zero, and we're saying for that year there were--when I did this at this point--now this may change 1 percent after it's been refined several times, but we're saying overall for that year, 68 percent of the cases that we had results on that we could document from St. John's, 68 percent were reported with some degree of positivity.
CHAYTOR, Q.C.:
Q. In either -
MR. GULLIVER:
A. Either/or -
CHAYTOR, Q.C.:
Q. ER or PR.
MR. GULLIVER:
A. Strong or weak, and 32 percent of all cases were zero, zero.
CHAYTOR, Q.C.:
Q. Were zero, zero?
MR. GULLIVER:
A. Yeah, and again you're highlighting 2002.
CHAYTOR, Q.C.:
Q. Right.
MR. GULLIVER:
A. And if you look at the--all the years, you

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know, three years later, you've circled--and 2000, you're pretty well looking at -
CHAYTOR, Q.C.:
Q. This came to us. We didn't do the circling.
MR. GULLIVER:
A. I know, and that might have been mine who did this.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. I mean, you're looking at the two years that had the highest numbers of specimens that were zero, zero.
CHAYTOR, Q.C.:
Q. Okay, and then for 2000, under your weak positives, you would have been using the 30 percent cutoff?
MR. GULLIVER:
A. Exact same--same criteria, except for the 30 percent.
CHAYTOR, Q.C.:
Q. 30 percent cutoff.
MR. GULLIVER:
A. Well, no, not really.
CHAYTOR, Q.C.:

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Q. No?
MR. GULLIVER:
A. It would still be--if there was a percent of positivity, you know, 5 percent, 10 percent--yes, you're right, less than 30 percent.
CHAYTOR, Q.C.:
Q. Okay. Are you sure?
MR. GULLIVER:
A. Yeah, yeah.
CHAYTOR, Q.C.:
Q. Okay. Just have a look at--there was a new exhibit. I think this might be an updated version of what you had done. Let's try 3036, please. This is then into January--January 28th, 2008, and it's an e-mail from yourself to Ms. Predham, and you call it an update, and you'll see here--I don't know if you can read that, Mr. Gulliver, the print is a bit small, but it's positive/negative rates for St. John's and your numbers when I looked at--well, we were just looking at 2000, 2001, 2002, onwards, and when we look at those, they appear to be the same as what I was showing you on your original. If we could go 514 again, please, Registrar.

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MR. GULLIVER:
A. This was--I think I did this, Ms. Chaytor, after--during the NLCHI exercise.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. One of the questions was these original tables, you know, and I had said to them that these tables change and updated.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. Myself and Reza, who was assigned that task, we went back and reread every single report just to make sure. Again it was a numbers game, it wasn't reviewing patients who might have been missed for retesting.
CHAYTOR, Q.C.:
Q. Right, okay. No, that's--okay, that's what I understood the exercise to be, it's a positivity rate.
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. If we could just go back, Registrar, to 3036,

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and again so your numbers seem to be, I believe, consistent through this time period. So there was no--even though this is an update, your numbers didn't change. Your numbers appear to have been accurate back in July of 2005.
MR. GULLIVER:
A. I think 2000 the numbers might have changed a bit.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. During this here.
CHAYTOR, Q.C.:
Q. Okay, and -
MR. GULLIVER:
A. We came across some cases that we had included in our positive category.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. For statistic purposes, and they were positive, but they weren't necessarily a breast primary, so we kind of took those away from our stats.

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CHAYTOR, Q.C.:
Q. And then the number of tests, strong positive, those are the ones that didn't end up on your spreadsheet, as you say?
MR. GULLIVER:
A. Right.
CHAYTOR, Q.C.:
Q. All right, and then we see the breakdown number of tests, weak positive, and then that's defined. Number of tests, negative/negative, and that's straightforward. Number of tests reported with positive staining, strong, plus weak, what was that referring to?
MR. GULLIVER:
A. That's the two--see strong positive and a weak positive, that's just adding them together.
CHAYTOR, Q.C.:
Q. Oh, that's adding them together, sorry, yes.
MR. GULLIVER:
A. Right.
CHAYTOR, Q.C.:
Q. Yes, okay. Number of tests reported negative, no staining, percentage.
MR. GULLIVER:

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A. Right.
CHAYTOR, Q.C.:
Q. And your total tests than are 2,726?
MR. GULLIVER:
A. For the breast primary specimens.
CHAYTOR, Q.C.:
Q. And that's just for -
MR. GULLIVER:
A. That's DAKO and Ventana for the whole time period up to August--July 31st, '05.
CHAYTOR, Q.C.:
Q. Okay, just for St. John's?
MR. GULLIVER:
A. No, no, no, the total tests for the province.
CHAYTOR, Q.C.:
Q. Okay, so this up here where it says positive/negative rates for St. John's, that includes the tests carried out in St. John's, I take it?
MR. GULLIVER:
A. Right.
CHAYTOR, Q.C.:
Q. But it's for the entire province?
MR. GULLIVER:
A. See the total--with results?

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CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. Those would be the total St. John's patients, 1529, that we had documented results in reports that we could do statistics on.
CHAYTOR, Q.C.:
Q. Right.
MR. GULLIVER:
A. Our total positives reported for those totals for St. John's, 77 percent were reported as some positivity, and 23 percent were reported as zero/zeros.
CHAYTOR, Q.C.:
Q. So that's just for your St. John's -
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. Because those are the only ones that -
MR. GULLIVER:
A. That we have documented information on.
CHAYTOR, Q.C.:
Q. Okay. Now where you would have had--right, okay. So that's all you would have had at that point, but certainly in January, 2008,

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you would have had somewhere within your system the records for everyone else, but that's not included in what you've done here it's just St. John's?
MR. GULLIVER:
A. Right, and I still--I still don't have any records of the positive/negative rates for outside St. John's. I have not been privy to those results.
CHAYTOR, Q.C.:
Q. Okay, Dr. Cook would have them, but you wouldn't, on his spreadsheets?
MR. GULLIVER:
A. No, Dr. Cook only has results of the ones that were retested. This is all the patients who were retested or not retested in this file.
CHAYTOR, Q.C.:
Q. Okay. The -
MR. GULLIVER:
A. And again, we were still doing, you know, some comparisons, Ms. Chaytor.
CHAYTOR, Q.C.:
Q. Uh-hm.
MR. GULLIVER:
A. Looking at, you know, the total DAKO specimens

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that were done and the total rates by year, positive, negative and then the overall average of 75.8 and 24.2 and then comparing to the year and a few months of the specimens on a Ventana that we had results on, we seen that the overall rate there was an 86.14 percent.
CHAYTOR, Q.C.:
Q. Okay, and you got one person from James Paton added on, why was that person included in your numbers?
MR. GULLIVER:
A. I think--this is now 2008.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. You know, I think by this time there was patient who wasn't originally on the list or retested who was added to that list, so we added one number to 97.
CHAYTOR, Q.C.:
Q. Okay, were you keeping a list--you said you kept a list of the out-of-town patients and how about the list of what you determined to be strong positives? Was a list of those -
MR. GULLIVER:

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A. They were all kept too, yes.
CHAYTOR, Q.C.:
Q. That's all kept.
MR. GULLIVER:
A. Yeah, that's all in your, in everything provided.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. And they're separated by yellow sheets, all the different years and by the sheets in front.
CHAYTOR, Q.C.:
Q. And if we could just go back, please, to I think it's P-2375, that's your 2002 stats.
THE COMMISSIONER:
Q. Mr. Gulliver, when the out-of-town information came in, did you take it just as it was and send on or was there any kind of assessment done of those lists that you received from, say Grand Falls?
MR. GULLIVER:
A. No, you mean like a clinical assessment?
THE COMMISSIONER:
Q. Well, no, in the sense of--well I am making an

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assumption now, I should back up. My understanding is that in Grand Falls, for example, they would have pulled a particular number of blocks, sent them to you -
MR. GULLIVER:
A. Correct.
THE COMMISSIONER:
Q. And then they went on through some method to Mount Sinai?
MR. GULLIVER:
A. Right.
THE COMMISSIONER:
Q. Would you just have transmitted to them directly to the Mount Sinai or would you have for any reason excluded a number of them?
MR. GULLIVER:
A. We didn't exclude any, but we did--myself and Mr. Dyer and some of the technologists who were doing this, we actually then made a list for ourselves of what we received from, for example, Grand Falls and documented what was sent and then we packed it up and sent them in the same manner as all the St. John's patients. But there was no secondary review process by us to either add or exclude -

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THE COMMISSIONER:
Q. Yes, for example if in that group of, not slides, blocks which had been sent to you thee were a number of people who were deceased, you would not have -
MR. GULLIVER:
A. We had no idea.
THE COMMISSIONER:
Q. You would not have culled those out because you were keeping deceased until later -
MR. GULLIVER:
A. No.
THE COMMISSIONER:
Q. You would have sent it on then.
MR. GULLIVER:
A. No.
CHAYTOR, Q.C.:
Q. And if there were also people who were 30 percent throughout the whole time, if someone used the 30 percent cut-off throughout -
MR. GULLIVER:
A. They were sent.
CHAYTOR, Q.C.:
Q. - and sent them in, you sent it all on?
MR. GULLIVER:

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A. Yeah.
CHAYTOR, Q.C.:
Q. You didn't do any further vetting?
MR. GULLIVER:
A. No. As you know, Dr. Cook sent out some criteria to the other laboratories and pathologists of what they should do to review their patients.
CHAYTOR, Q.C.:
Q. Yes, and whether or not they stuck with that or decided to do something different, there was no further or secondary check, as you say -
MR. GULLIVER:
A. No.
CHAYTOR, Q.C.:
Q. - done in St. John's.
MR. GULLIVER:
A. I know during the timeframe that--I know Corner Brook called me, you know, the lab director in Corner Brook and generally just talked about to make sure, what are you doing in St. John's, what should we do out here? And pretty well walk through over the phone, you know, to make sure they are clear what

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they're doing and I think--I don't know if it was Gander or Grand Falls, someone else called too just to be clear on what they're supposed to be doing type of thing.

CHAYTOR, Q.C.:

Q. Okay. And I just want to be clear too again on lists because I know what we've received in terms of receiving pathology reports and having it broken down into categories. But did you actually compile lists of the peoples' names who would be in those categories?

MR. GULLIVER:

A. No.

CHAYTOR, Q.C.:

Q. Okay. That's where I'm -

MR. GULLIVER:

A. No, the only people you see in a list or spreadsheet are the ones we identified that could possibly be retested.

CHAYTOR, Q.C.:

Q. And those are what we are looking at here on the screen.

MR. GULLIVER:

A. And that's what you're seeing there, yes.

CHAYTOR, Q.C.:

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Q. So, there's no actual list of the names of the people deemed to be strongly positive, lists of the people from out of town, that list doesn't exist.

MR. GULLIVER:

A. No, and when we started the NLCHI exercise, you know, in July of '07, that was actually my recommendation, that if we're going to do a database, we should do every single patient who was ever tested for ER/PR, but again time was of essence and it was decided to do the patients who were retested and put those in the database.

CHAYTOR, Q.C.:

Q. Okay. So, you were wanting to put all the positives in the database for example, as well.

MR. GULLIVER:

A. Correct.

CHAYTOR, Q.C.:

Q. Put everyone in, okay. Did you, at any point too, Mr. Gulliver, suggest that everyone should be retested?

MR. GULLIVER:

A. No, I didn't, no. Again, as you know, that

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was discussed with various experts and we've seen lots of literature where false positives are very rare and there was no concern expressed from the oncologists. So, it just wasn't never decided to do.

CHAYTOR, Q.C.:

Q. Okay. Were you of the opinion that the original slides should have been re-read along with the test being--the blocks being turned into new slides and re-tested?

MR. GULLIVER:

A. I think shortly after Dr. Banerjee had come in to do his first review, you know, I had the privilege to spend an afternoon with him, myself and Mr. Dyer, and it was--so, after he left, that's one thing that struck me, that we should engage someone like him to actually re-read every single original slide. We were in the process of sending out original blocks to get re-tested and get re-interpreted somewhere else, but I thought--I suggested that. That we should have -

CHAYTOR, Q.C.:

Q. And who did you suggest that to?

MR. GULLIVER:

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A. To Dr. Cook and Dr. Williams.

CHAYTOR, Q.C.:

Q. Okay. And was that ever done, apart from, of course, Dr. Mullen has done it through this process here.

MR. GULLIVER:

A. No.

CHAYTOR, Q.C.:

Q. Okay. And why not? Was anyone opposed to having that done?

MR. GULLIVER:

A. Well, they weren't in favour, so it didn't get done.

CHAYTOR, Q.C.:

Q. And who wasn't in favour of it?

MR. GULLIVER:

A. I don't know if it was both of them or either one of them, but it just--it was something I suggested and it just didn't go anywhere.

CHAYTOR, Q.C.:

Q. Okay. And did they say why? Were you told why they didn't think that would be a worthwhile exercise?

MR. GULLIVER:

A. I don't know if they said it wouldn't be

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worthwhile. I think we're in the crux of all this here, we're spending thousands of hours between all of us, identifying patients, packing up blocks, pulling blocks, pulling slides, re-reading the original H&Es that are being sent off. I think again it was just something else that would have been very time consuming to organize, at that point in time.

CHAYTOR, Q.C.:

Q. So, was that the reason given to you for not having the slides reviewed?

MR. GULLIVER:

A. That was my understanding, yes.

CHAYTOR, Q.C.:

Q. That's what you were told at the time, yes.

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. Okay. And why did you want it done? What benefit did you think that would have been, to have the slides re-read?

MR. GULLIVER:

A. Well, again, you know, this is--we're talking about August/September '05, while we're heavily in the retesting process of

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identifying patients and trying to get patients sent away as quickly as possible, we're not performing the tests currently in the lab. We had stopped the Ventana system until we thought we'd get Ventana in to review it. We knew that we had two outside reviewers coming in to the laboratory. I felt it would be important information to--we have the original slides, why not have an outside pathologist come in and sit down and review the original slides. I think that person could have given us a lot of insight and they could have said, well, you know, in this particular year, I reviewed your slides, the staining quality seems to be fine, there doesn't seem to be something at issue with this or this. Or they might have said, as you know, Dr. Banerjee had looked at stuff, you know, internal controls weren't staining, but yet, reported. I just felt that we could have got a lot of useful information from that exercise.

CHAYTOR, Q.C.:

Q. And were you aware that up to, by August 1st, 2005, Dr. Carter had reviewed the original

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slides of approximately 80 or 90 patients?

MR. GULLIVER:

A. I was aware that she was reviewing 2002 cases.

CHAYTOR, Q.C.:

Q. Okay. So, and including the slides, were you aware that she had already started a process which included reviewing original slides?

MR. GULLIVER:

A. I think from 2002.

CHAYTOR, Q.C.:

Q. Yes, okay. In going through, perhaps we could just bring up--and I'm not going to take you through all of your spreadsheets because time is of the essence.

MR. GULLIVER:

A. Yes, I know, but I can assure you that the same process was done every single year.

CHAYTOR, Q.C.:

Q. Was done for each year. And so there's nothing in particular that you want to point on any of the years?

MR. GULLIVER:

A. I don't think so, no. And I did these searches originally, Ms. Chaytor, and when Barry came back to work, you know, I kind of

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said to Barry, you go in and do searches now and see if we can get similar numbers for each year, which he did, just to kind of cross-reference that my searching was similar to him.

CHAYTOR, Q.C.:

Q. So, he went back over what you had already done?

MR. GULLIVER:

A. Yes.

CHAYTOR, Q.C.:

Q. Okay. And in doing that--well, let's look at 2373, I think, or 74, might be the year before, 2001, or let's try--no, sorry, let's try 73, 2373. So, this is just another, your spreadsheet this time is 2000. And the reason I look at 2000 is because in this time period then you'd be at the 30 or below mark, right? And so then on your first page here, and then this is your writing, I take it, is it?

MR. GULLIVER:

A. No, that's Barry's -

CHAYTOR, Q.C.:

Q. Oh, sorry, Barry's, right. And this is your writing up in the corners.

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MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. Okay. And similar then, he's got the negative/negatives.
MR. GULLIVER:
A. And then the next group would be the ones that had a positive, certain positivity, and even see one there--go back.
CHAYTOR, Q.C.:
Q. Sorry.
MR. GULLIVER:
A. And if the report said positive, weak positive, that we see here.
CHAYTOR, Q.C.:
Q. So, if you just said positive -
MR. GULLIVER:
A. We just wrote down positive and we--that's exactly what was written in the report.
CHAYTOR, Q.C.:
Q. And I took Mr. Dyer through some of this in some detail. This person here is crossed off and DCIS is written there, what were you told to do in terms of DCIS patients?
MR. GULLIVER:

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A. They weren't sent for retesting. And again, this will be somebody who Dr. Cook will say to us on review, this was a confirmed DCIS, so we haven't got to send that person for retesting.
CHAYTOR, Q.C.:
Q. And who told you to also limit the test review to primary breast patients?
MR. GULLIVER:
A. Oh, that was right from the beginning with the oncologists, who would review? And they said, well, it's primary breast patients who would be getting the hormone therapy, so that's the ones we're trying to identify.
CHAYTOR, Q.C.:
Q. Okay. So, when you went in and found ER/PR tests run for -
MR. GULLIVER:
A. Metastatic, for example. If we see an ER/PR result that it said, and it was a liver specimen -
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. - and the question mark was, but is it metastatic from breast cancer, and those ones

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were still--that's the other categories you'll see in the files.
CHAYTOR, Q.C.:
Q. Yes. So, you actually--in order to be able to determine that, you had to actually print off the pathology reports.
MR. GULLIVER:
A. Oh, I had to read every one of them, thousands and thousands -
CHAYTOR, Q.C.:
Q. And you had to read through them?
MR. GULLIVER:
A. - and thousands and thousands and thousands of pages.
CHAYTOR, Q.C.:
Q. So it was more than 2800. 2800 comes down to primary breast?
MR. GULLIVER:
A. Right.
CHAYTOR, Q.C.:
Q. Right. And then you -
MR. GULLIVER:
A. There might have been over 3000 in--understand, each year there might be 10, 15, 20 ER/PRs done per year that are done looking

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for metastatic disease to another organ.
CHAYTOR, Q.C.:
Q. Right.
MR. GULLIVER:
A. That primary cancer was the breast.
CHAYTOR, Q.C.:
Q. Okay. And so and so you would have reviewed pathology reports where they were looking at liver, lung -
MR. GULLIVER:
A. Lung, brain.
CHAYTOR, Q.C.:
Q. - brain. And -
MR. GULLIVER:
A. Mostly lung, brain, liver for most of them.
CHAYTOR, Q.C.:
Q. Okay. And do you know about how many of those tests then got put to one side and -
MR. GULLIVER:
A. All of them, all of them went to -
CHAYTOR, Q.C.:
Q. They all got put to one side?
MR. GULLIVER:
A. They weren't sent for retesting.
CHAYTOR, Q.C.:

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Q. But do you know how many there would be, would it be over 100, over 1000.
MR. GULLIVER:
A. Oh, no, not 1000. I would think on average like 10 to 15 reports per year, so there might be 100 in total.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. And I think remember I said to you earlier I thought the total number was like 2860 in total and it came down to like 27 something for primary breasts.
CHAYTOR, Q.C.:
Q. Okay. So that the number comes down to about 2700, so it's about 160 or so?
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. And those are just St. John's, I take it, though?
MR. GULLIVER:
A. Yes.
CHAYTOR, Q.C.:
Q. Are they? Because that's all you would have

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pathology reports for?
MR. GULLIVER:
A. Yes. And out of town would have less. We went through this here with NLCHI. There'd be less non-breast specimens coming in from out of town just because of the kinds of patients. Those patients would have been in St. John's for their tertiary care.
CHAYTOR, Q.C.:
Q. Okay.
THE COMMISSIONER:
Q. Ms. Chaytor, it's five so wherever you can find a convenient spot we'll break for the day.
MR. GULLIVER:
A. I was going to--before you leave the spreadsheets.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. I was going to ask could you pull up 1997?
CHAYTOR, Q.C.:
Q. Sure.
MR. GULLIVER:
A. Because you asked me just then is there

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something else I'd like to -
CHAYTOR, Q.C.:
Q. 2370, I think.
MR. GULLIVER:
A. - point out before you move on.
CHAYTOR, Q.C.:
Q. Yes, 2370, I believe.
MR. GULLIVER:
A. Now, 1997 -
CHAYTOR, Q.C.:
Q. Now, this might--yeah, this is yours, is it?
MR. GULLIVER:
A. So I mean, and I did these here kind of working backwards, you know. And by this time I'm weeks, you know, reading reports and documenting, writing up sheets and stuff. And I guess I just want to show you this sheet for '97. When you look what's filled in here reading the pathology reports, to read there the controls on original. That means if the pathologist documented in their written report I read the positive external control was in there. And go to the far left if I had seen any other comments where it says there "positive internal control."

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CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. And if we went to the next page and next page.
CHAYTOR, Q.C.:
Q. Yes, you can't see there. Yeah, here we go.
MR. GULLIVER:
A. And again -
CHAYTOR, Q.C.:
Q. This is when Dr. Khalifa is -
MR. GULLIVER:
A. This is to show you this is what Dr. Khalifa did.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. So most of the time he documented he read the positive external control and/or the patient's internal control.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. Because I was struck by it after doing, like, 2004, 2003, 2002, 2001, 2000, '99, '98 and then -

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CHAYTOR, Q.C.:
Q. You went back and -
MR. GULLIVER:
A. - '97 we had more complete information to put on the sheets.
CHAYTOR, Q.C.:
Q. Right, okay. Yeah, that is an interesting observation. And so then also in that--so if we look, for example, then in this 2372, for example. And I think that'll be 1999. So the controls on original there's nothing filled in?
MR. GULLIVER:
A. It's not very often you see it documented in the report.
CHAYTOR, Q.C.:
Q. Right.
MR. GULLIVER:
A. Some of them, you can see some of them there.
CHAYTOR, Q.C.:
Q. Some here in '99. And a couple there, okay. And no mention of any internal controls in the report for -
MR. GULLIVER:
A. If it was there, I would have written it over

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to the side.
CHAYTOR, Q.C.:
Q. You would have filled it in?
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. Of a patient had HER2/neu done, I would write that to the far comment side.
CHAYTOR, Q.C.:
Q. Mr. Gulliver, in looking through these, for example, this is now 1999, and if we look through, we see a lot of, starting page one is your negative, negatives?
MR. GULLIVER:
A. That's where I start all of them at.
CHAYTOR, Q.C.:
Q. And again, yes, yeah, that seems to be how you would start out. And then we come down estrogen receptor. They're all very low numbers, one, five -
MR. GULLIVER:
A. On the weak, the weak positives -
CHAYTOR, Q.C.:

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Q. - ten -
MR. GULLIVER:
A. - yes.
CHAYTOR, Q.C.:
Q. Okay.
MR. GULLIVER:
A. Again, what's missing is -
CHAYTOR, Q.C.:
Q. I'm seeing a 20 here.
MR. GULLIVER:
A. Right.
CHAYTOR, Q.C.:
Q. I'm seeing a 20. But you would have been checking for anything 30 -
MR. GULLIVER:
A. Anything.
CHAYTOR, Q.C.:
Q. - 30 or below?
MR. GULLIVER:
A. Yeah.
CHAYTOR, Q.C.:
Q. Okay. The number 30 just didn't come up very often, I guess, it was either -
MR. GULLIVER:
A. And again you can see here '99, there's one at

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ten percent for PR and 70 to 80 for PR.
CHAYTOR, Q.C.:
Q. Yes.
MR. GULLIVER:
A. Again, it was put on this sheet to ensure that we rather err on the side of caution than, you know, than not.
CHAYTOR, Q.C.:
Q. Okay, perhaps we could take it up again another day, thank you, Commissioner.
THE COMMISSIONER:
Q. All right, then, we'll break until the morning and commence again at 9:30. For those in the room, I want to plan for their next week. I remind you that Tuesday is voting day, as a result we will have to adjourn at 4:30 to enable our staff to have the required amount of time in which to vote. I'm therefore suggesting we start at 9:00, so that we will have the same full day that we would normally have. So, that will be commencing at 9 instead of 9:30 on Tuesday morning, next week. Thank you all, 9:30 tomorrow morning.
Upon conclusion at 5:05 p.m.

CERTIFICATE

I, Judy Moss, hereby certify that the foregoing is a true and correct transcript in the matter of the Commission of Inquiry on Hormone Receptor Testing, heard on the 9th day of October, A.D., 2008 before the Honourable Justice Margaret A. Cameron, Commissioner, at the Commission of Inquiry, St. John's, Newfoundland and Labrador and was transcribed by me to the best of my ability by means of a sound apparatus.

Dated at St. John's, Newfoundland and Labrador this 9th day of October, A.D., 2008

Judy Moss

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