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NO.65/2006

R V ANDRE CHAD PARENZEE

MONDAY, 5 FEBRUARY 2007

RESUMING 10.06 A.M.
MS MCDONALD CALLS
+ELIZABETH MARA DAX AFFIRMED
+EXAMINATION BY MS MCDONALD
A. I'm also known as Taylor, which is my married name.
Q. Are you an Associate Professor.
A. Yes, I am.
Q. Have you provided a report for the court in relation to this matter.
A. I have.
MS MCDONALD: Your Honour the report should have a cover sheet with 'The Statement of Elizabeth Dax' on the front of it.
HIS HONOUR: Thank you. We haven't seen it.

MS MCDONALD: We have a spare copy here.
XN
Q. I'll actually have two documents produced to you, I'll call you Dr Dax if that's all right; Associate Professor is quite a mouthful. The first document has a cover sheet with 'Statement of Elizabeth Dax' on the front of it. That's the report you provided to the court.
A. Yes, it is.
MS MCDONALD: I think I tendered this as P56 through another witness. Sorry about that your Honour.
HIS HONOUR: I see.
XN
Q. The second document I've asked to be produced to you is a copy of your curriculum vitae.
A. Yes.

EXHIBIT #P61 COPY OF CURRICULUM VITAE OF PROFESSOR DAX TENDERED BY MS MCDONALD. ADMITTED.

Q. I don't propose to take you through all the details on your curriculum vitae. We see on the front page your formal qualifications.

A. That's correct, yes.

Q. Under that a heading 'Professional experience'.

A. Yes.

Q. Then you listed a number of positions that you currently hold.

A. Yes, that's correct.

Q. Could you just take us through those positions and explain what they involve, starting with, first, Director, National Serology Reference Laboratory.

A. Yes, my present primary position is the Director of the National Serology Reference Laboratory. That is an institution that is responsible for the quality of HIV, hepatitis and blood-borne viral testing in Australia, so we are responsible for making sure the correct tests are used in the correct way. We are also a WHO collaborating centre. We do a lot of international work helping to develop laboratories in resource-poor areas.

Q. I'm struggling to hear you at the moment. Perhaps you can speak into the microphone.

A. Yes, I can do that. Do you want me to go over that again?

Q. No.

A. My appointment is with the University of Melbourne, Department of Microbiology and Immunology. I have a part-time position there which enables me to teach students. The NRL is situated within St Vincent's Institute and Research and so I have a position there which is essentially an honorary position and those are, I think, the relevant appointments at present.

Q. You've said that the National Serology Reference Laboratory is responsible for ensuring the correct tests are conducted in the correct way.

A. That's a shorthand way of expressing it, yes.

Q. How is that actually achieved.

A. Okay; the quality of blood-borne viruses - virus testing was decided in 1985, when no-one knew how the tests should be interpreted or which tests to use, that there would be a national reference laboratory that would help to work that out, and so the government developed the National Serology Reference Laboratory which, in those days, was called the National Reference HIV Laboratory, to collect a sample against which the tests could be pitched to ensure their quality, their evaluations. So way back then the NRH - and I wasn't associated with it at that time I might add - collected sample banks from people who displayed the signs or symptoms of having HIV or, later who were picked up with the tests, and developed this sample bank against which the tests would be evaluated and, over the years, that sample bank has changed and become more refined, and we now have a sample bank in Melbourne of some thousands of samples against which we evaluate any new test that comes into the country before it is approved for marketing. So these tests, if they are going to be used for blood screening for example, which we consider the most critical use, would be evaluated in up to 10,000 samples, whereas others would be perhaps evaluated in different ways depending on how long they've been in use. Also, we are under contract to the Therapeutic Goods Administration to follow the performance of those tests and - in a post-marketing monitoring program it's called - and the way we do that is through a national quality assurance program. If laboratories do HIV testing they are required to have a liaison with the NRL, so to be sure that the data are captured on an ongoing basis to assure that the specificity of the tests are monitored and, in some cases, the sensitivity too, and we also from time to time conduct quality assurance programs to ensure that in each laboratory the process is operating, and we do that by sending out

particular samples and making sure, if you like, they get the 'Right answer'.

Q. You talked about the sample bank; samples of what.

A. Okay; those samples have been collected in an ongoing way and those samples may be negative samples, they may be previously shown to be HIV positive in a range of different tests, not at one test. They may be samples that have been shown to be cross-reactive; that is, they actually cross-react with the tests, although the people are not shown to have HIV or been exposed to HIV. So those samples are collected from all over the world too to ensure that if someone acquires HIV from outside Australia the viral types are represented in that sample bank, and so that's how we make sure that the test recognises the negative and positive populations of samples, and also assesses its specificity against samples that might cause cross-reactivity and different sub-types and so on. And each test is looked at very thoroughly I can assure you - more thoroughly than perhaps most countries in the world.

Q. You've also referred to the Therapeutic Goods Administration.

A. Yes.

Q. Does that organisation have a role to play in relation to tests for HIV.

A. Yes, it does. The Therapeutic Goods Administration is responsible for the efficacy, safety and quality of medicinal products that are sold in Australia and that includes medical devices and in-vitro diagnostics, which HIV tests come under. The manufacturers or sponsors are required to submit dossiers to the TGA giving all the information about their production, how it's determined that they are - their performance is evaluated and how the manufacturers are qualified to meet quality management systems that are acceptable to the TGA, and the TGA reviews part of that information about the quality of the production, about the labelling of the boxes that the kits come in, and the bottles that are in

the boxes and so on, whereas the NRL, they pass on the performance evaluation to the NRL because we are set up to do those evaluations.

Q. So you work hand in hand.

A. We do, but we do work on contract to them, so that's an independent - the idea is that the performance is assessed independently.

Q. Just going back to your curriculum vitae, you've taken us through your current positions.

A. Yes.

Q. I just want to ask you about a couple of them in particular, over on p.2. There is reference to a position of Principal Fellow at the St Vincent's Institute of Medical Research.

A. Yes.

Q. Could you explain that one for us.

A. That is as I said earlier - the NRL is not a legal entity per se; it is encompassed within another group, the St Vincent's Institute, and that's hour host institution. We operate under their ABN so it's a legal thing, but, on the other hand, they see us as part of their group and our scientific publications and so on are subject to the same scrutiny that the institute is and, as one of the more highly qualified people, I was given the title of Principal Fellow.

Q. Over the page you list your memberships and awards.

A. Yes.

Q. Again I won't take you through all of them but just focussing on a couple, the second entry 'Member of Executive Committee of AIDS Society of Asia and the Pacific'.

A. Yes; the Aids Society of Asia and Pacific is a group of organisations that have the aim of stemming the HIV epidemic in Asia and the Pacific particularly. It is a group that is concerned with utilising civil actions to promote that rather than scientific, so it's a very important group, bringing lots of different organisations with lots of different perspectives

together, and that includes business coalitions, scientific groups, the Australasian Society of HIV and Medicine, just to name a few.

Q. You've just mentioned the epidemic in the Asia Pacific.

A. Yes.

Q. Do you have any doubt there is an epidemic in the Asia Pacific.

A. No, there is no doubt. I read testimony of another witness, Martyn French, who went to Kampala in Uganda and realised what it was like in the hospitals there. I've been in the hospitals in Asia and it's terrible; it's terrible. There are people there who have been infected for periods of time. They are occupying hospital beds, there is no hope for them, there is no help for them, because they don't have access to anti-retrovirals and these hospitals can be quite full of people who are infected and have progressed. And we know very well that when people are sick there is a lot of people who are not sick with this infection, because it's only when they become sick and immuno suppressed that - when they're really immuno suppressed that they actually become sick - sorry, I've got that round the wrong way - but it's very important to realise that, where you have sick people, there are a lot of other people who are infected, and there is no doubt that these people are infected with an infection that is going to progress.

Q. You also have described being in a working group on the development of the national HCV testing policy in 2005.

A. That's correct. The way the Commonwealth puts together policies is they call together committees of people who are involved in whatever their objective is, and those committees discuss ways to best put together the policies, so we met as a group. The head of the group was Frank - Professor Frank Bowen, who is an excellent chair, and we discussed all those aspects of HIV testing, we put together a document which rested of course on the science of the whole testing and

epidemiology etc., and then we put that out for discussion; where it is right now, it's out for discussion and the final document becomes the policy, so I was a member for that committee as I was a member for the HIV testing policy and the in-vitro diagnostics policy that's being released sometime this year.

CONTINUED

Q. What is that last policy.

A. That's to do with how invitro diagnostics are assessed and used within Australia.

Q. You refer to being part of an NPPAC Working Group.

A. Yes.

Q. On standards for performing HIV and SCT testing, 2005.

A. Yes.

Q. What did that involve.

A. That group is a pathology group which is translating the policy into use, so it's telling the pathologist actually how to use the tests, in a court, with the international regulations that laboratories operate under and in accord with national policy. So it's a binding - it's a document that brings those different guidances together if you like.

Q. You refer to being an associate member of a Medical Devices Evaluation Committee.

A. Yes. That's a committee that evaluates the efficacy, safety and performance of medical devices. I'm an associate member which means that I'm called in if there's a particular issue to do with invitro diagnostics test kits. I don't sit on every committee meeting because many of them are medical devices like pacemakers and things so.

Q. The next probably doesn't require much explanation, you were awarded a Member of the Order of Australia.

A. Yes, that was in 2001 and I'm like David Cooper I'm very proud of that, particularly as a lot of the citation related to my work in the US rather than Australia. I've been working in the area now for nearly 20 years, I started working in HIV in 1986. And I think it's a wonderful recognition.

Q. Further down at the page you describe some of your involvement on the international stage.

A. Yes.

Q. Consultant to the Department of Medical Sciences Thailand and NIH Thailand.

A. Yes, that's a consultation that's now gone on for as

many years as you can see, started in 1992, 1993 and it's been a great development in Thailand. They now use HIV tests in many ways in the ways that we do in Australia. They have a national laborstory that's moulded on the NRL in Australia. It's run by an extraordinarily meticulous and clever woman who understands HIV testing as well as anyone else in the world and has put together some incredible ways to look at HIV test kits and evaluate them thoroughly and she has the opportunity to do that in Thailand with Thai samples and that yields some very solid and interesting information about HIV test kits.

Q. You've also referred to being a temporary advisor to WHO Geneva.

A. Yes.

Q. What's that about.

A. There are numbers of ways that I have been a consultant or an advisor in Geneva. WHO seek information from people all over the world on how to put together the ways they go about things, so for many years there was a diagnostics committee. It faded away because we thought at one stage we knew all about diagnostics but it's now being resurrected because there are so many new things and different things coming to light. So that's one of the areas but I've also been an advisor on how to best interpret Western Blots, how to best interpret the tests and put them together in testing strategies, how to mesh the tests with practice, clinical practice and also some regulatory issues that I have formed committees. I hope you don't think I do it by myself, it's a committee.

Q. I notice you managed there to have the time to have four children as well.

A. I did, I'm very proud of them. I didn't do that by myself either.

Q. You've listed the various grants you've received over the years, and some of them are for very large sums of money.

A. That's correct.

Q. It would be fair to say in the scientific world the receiving of a financial grant for study is a matter of some prestige.

A. Yes, I think that's true. I think that people don't give you the support and the money unless they believe in what you're doing and of course every grant is peer reviewed, it's reviewed very carefully against a lot of other information. So the idea that you might be awarded a grant it's not plucked out of the air, you have to submit a huge amount of information and supporting evidence.

Q. Are any of the grants that you've listed there particularly relevant to this issue of testing for HIV. I'm inviting you to flag any that are of any particular relevance.

A. Well I think the one with Centre For Disease Control in the USA 'Characterisation of the Humoral Response to HIV Infection by Surface Plasmon Resonance' it's comparative validation and development assays. That one was particularly relevant because instead of just looking at - what we were trying to do is describe the immune response in very early infection and this is very important. I'm sorry, shall I go on?

Q. Yes.

A. It's a little convoluted. In terms of the epidemiology, that is the study of HIV or any other infection, in populations, there are two principal means of following an epidemic. One is looking at the prevalence, that is how many people are infected at any one time. The other is the incidence and I'm sure Dr Kaldor will talk about this later, and that's how many people become infected per unit time. So that tracks how quickly people are becoming infected or the speed at which they are becoming infected but also it means that you can follow the epidemic so that if you take on an intervention such as needle exchange programs or a big campaign then you can look at the incidence. And CDC had put out this call for people who were prepared to look at the

possibility of developing tests that could measure incidence and the NRL answered that and we did develop a test - it's presently being commercialised - that can distinguish early infection from later infection. But we wanted a way to look at that in such a way that we could characterise the binding of the actual antibodies in early infection to antigens - I don't need to explain that, right?

Q. No, you don't.

A. - to antigens so that we could look at the actual characteristics, the binding and then compare them with how the tests operated and that was a very novel approach and has been carried out - the grant's finished now - but it was a novel approach and we did develop the tests that does distinguish early from late infection and that is based on a particular type or a particular class of antibody called IGE and - sorry it's IGG - never mind, it doesn't matter. It's a particular class of antibody that appears very early in infection and then falls away.

Q. So when that test is eventually used, does that mean -

A. It's an IGG3 based test, for what it's worth.

Q. When that's eventually used you'd be able to determine whether someone has had the virus for some time or it's been a recent infection.

A. That's correct.

Q. That's the extent the test has got to now.

A. It's very intricate these days, it really is. It's brilliant.

Q. One other grant that I'll just take you to. The second from the bottom AusAID, maintaining the accuracy and quality of HIV testing by implementing sustainable national quality control programs. Do you see that one.

A. Yes.

Q. Grant $420,000.

A. Yes, sorry it's not the bottom of my page, yes. Now that's quite some time ago but we have maintained that program one way and another over the years and we send

out quality assurance programs to laboratories all over the world, particularly in Asia and AusAID at one time supported that because we didn't have WHO support, usually we have some WHO support for that and over the last three years AusAID has taken that up again and it's supporting us again in this endeavour to help laboratories in the developing world elevate their performance and so that the laboratories are operating in a satisfactory manner to deliver the correct diagnoses.

Q. And you finish off your CV by listing the many publications that you've been involved in, and I won't take you to those. You told us that your involvement in relation to HIV started in about 1996.

A. That's correct.

Q. How did it start.

A. I started a job at the National Institute on Drug Abuse in the US and that's the National Institute of Health, that's the peak science body. I started with that particular institute as a lab chief and I was brought in because in 1986 the epidemiology looked as though drugs of addiction might have had an affect on the course of HIV. It looked as though perhaps that people were getting sick quicker and so my job was to start a laboratory that had two different tasks, one was to monitor our clinical subjects and make sure that while they were doing clinical trials or trials for us that they weren't taking drugs and the other was to supply HIV testing for a national survey of HIV injection drug users in the US. And so that lab was set up. And in 1986 you will realise that that was very early in the course of HIV testing because the test only became available in - the first tests only became available in 1985. So there was lots to learn at that time about HIV testing and we had to learn and discover what was the correct way to use the tests, what was the correct way to interpret the tests and so that was part of my job. The other job was actually acting as a physician, in

those days I used to practice as a physician and look after the clinical side, make sure that the subjects for the clinical were okay, because we used to do all sorts of tests on them.

Q. Just talk us through your involvement with HIV since that first position.

A. Well, over the four years that I was at NIH - I had been at NIH earlier than that I was actually there 13 years - but over that time we did develop tests, we did a lot of evaluation of tests for the manufacturers and trying to work out how to use Western Blots with high specificity. Your Honour, at that time 30% of our subjects were HIV infected, so it was a tragic story for these people. And I might add there was no therapy available so many of our subjects in fact died. But we used the samples that they gave us, with permission, of course, to study the tests as they became available, to refine the tests. We talked about the testing with the manufacturers and when we decided to come back to Australia in 1990 I was offered this job with the NRL and I found that a particularly enlightening part of my work, you mentioned I had quite a family, so I took that job and stopped medical practice at that point in time because it suited me but I have worked full-time in this area since and as I have said to you we have now collected a sample bank at the NRL that we can look at tests in many different ways. I think our evaluations of the test kits are probably well recognised throughout the world. The manufacturers certainly recognise us as a point for valuable information about their tests and how they might be used and we also over that time because we were asked to in terms of our contract, develop post-market monitoring mechanisms. So we have a very unusual situation where we can actually follow these tests as they're used over time, and that is a unique position in the detail that we do it in the world. And as I said, my job also has encompassed quite numbers of areas and I think it's fair to say the NRL is recognised

internationally far better than nationally isn't the word, but we are very well recognised internationally for the value of our work.

Q. I move on to ask you some questions about how these tests actually work and how reliable they are. Given your extensive experience in HIV I just want to ask you a couple of general questions about HIV. You have heard the suggestion it's never been proved to exist.

A. I have, yes.

Q. Your comment on that.

A. I think I mentioned to some of my colleagues that if you want to you can prove the world is flat. If you look through a tight enough telescope and get information that is selective enough you can prove it's flat, but if you take a wider look and use different instruments you can in fact seat horizons, curve, or you can take a spaceship and you can go and you can actually take a picture of the world, and you can deny the space ship exists and so you are still looking through that telescope and I think that what we have been subject to in much of this is a telescope about HIV. There is no doubt to me that HIV exists and I think it's a travesty, quite frankly, to say it doesn't. I think people have opportunities now to be able to access therapy and there is a lot of work going on throughout the world to do that. So there's many ways you can see that the virus exists, there's many mechanisms that occur, there's many instruments that can be used, so there is no doubt in my mind that HIV exists.

Q. I believe you have also been made aware of the suggestion that there's never been a photograph or a electron micrograph of the virus.

A. I think Martin French acknowledged that that was actually not true that there's many many photographs of the virus. There's photographs of the virus within the cell as it buds from the cell, taken from cultures, taken from plasma, I mean - I'm sorry but I just cannot reconcile that statement.

Q. For that reason have you brought along for his Honour some examples of the types of photographs there are in existence.

A. I did and the photographs weren't simple electron micrographs, they are photographs that are taken by different mechanisms, so that it's like, you know, looking if the world's curved, if you look at it from several different ways and with different instruments you begin to form an idea that in fact the world is curved not straight, flat. And so I've chosen some pictures that are obtained by different mechanisms and all pretty much show the same conclusion.

CONTINUED

Q. We'll go through them; the series of images marked 1.1 through to 1.4.

A. I believe they are a thin section of the electromicrographs. I don't pretend to know how to do electromicroscopy, and I'm not an expert on electromicroscopy at all, but I chose these ones because they are done - when the tissue is embedded, they're done in thin sections and they show, in different magnifications, the virus as it is looked at more and more closely and, finally, represents the virus, as we know it - an envelope virus with a central core.

MS MCDONALD: I tender that.

MR BORICK: I think it should be identified where it comes from.

HIS HONOUR

Q. Can you tell us where those photos come from.

A. No, I can't tell you exactly what the source is. I can go back to the Internet and find any number of those. These are not from my lab, we don't know electromicroscopy - similarly with the others that have been tendered. I can go back to the original site. If you would like me to send that information, I can. I took the photographs off the Internet.

MR BORICK: I object to the tender.

HIS HONOUR: I will allow them in. Dr Dax says she will give us the source of them and I propose to allow them.

EXHIBIT #P62 FOUR SLIDES TITLED 'E.M. DAX ELECTRON MICROGRAPH THIN SECTION' TENDERED BY MS MCDONALD. ADMITTED.

XN

Q. To make it clear, what you have produced to us as P62 is just an example of the sorts of images that you have seen many, many times over your career.

A. That's correct. I mentioned that these are commonplace, these types of electron micrographs and, again, I emphasise that that is not my field but I can find them

very easily. We can find them in papers, in any virology textbook - as I think Martyn French said - you can pick up images such as these.

Q. Could you just talk us through, starting with 1.1, what it is that we see in each of those electron micrographs.

A. With the proviso that, of course, an electromicroscopist might explain it a little differently but I will do my best. In 1.1 you can see the outline of a cell and perhaps the edge of another cell towards the top right. What you can see is the virons budding out against that cell membrane.

MR BORICK: I am having difficulty with this because I don't know what the doctor is referring to. I'm not sufficiently skilled to understand. Could we do it by way of markers at each point?

HIS HONOUR

Q. Perhaps it is easier to mark the photostat than the original, so I will give you the photostat. Could you just mark the areas that you're speaking of and we can show them to Mr Borick.

WITNESS MARKS PLAN

EXHIBIT #P62A PHOTOSTAT OF P62 TENDERED BY MS MCDONALD. ADMITTED.

A. You might like to confirm my marking with Dr Dwyer.

Q. In due course, Ms McDonald will be calling him.

A. The electromicrographs are only one way to identify the virus and there is many other ways.

MR BORICK: With the cell, it is hard to see where the line ends, what the witness is actually pointing to.

A. It is the whole of this area in the bottom left-hand corner and you can define the cell membrane. Each cell has a membrane and that is defined by the slightly darker border.

MR BORICK

Q. There's the bit that looks like a finger point; exclude all that.

A. That is part of another cell. When these cells are

prepared, they are embedded in a block and sometimes they get a bit squashed, but I think that is a pretty clear picture.

HIS HONOUR: I am allowing you a little bit of latitude, Ms McDonald. It might help explain it.

XN

Q. Going back to the document, now we know what you are referring to as virus particles in the cell, 1.2 is a closer view of part of what we see in 1.1.

A. Correct.

Q. What about 1.3.

A. 1.3, in the top panel you see the actual virus budding out of a cell wall and that is that Hamlight projection. Then in the next view, the lower panel of 1.3, you can again see the cell on the left with its membrane and a high magnification view of the viron, which is illustrative of how we know the structure of the virus to be, through numbers of different ways to look at it.

Q. 1.4, is that a diagram you have included to illustrate what it is that we're seeing in the pictures.

A. That is correct. It shows a schematic of the life cycle of the human immuno deficiency virus, HIV, and how it makes passage through into the cell, replicates and, finally, buds the components of the virus are synthesized within the cell and bud out, taking with them certain parts of the membrane.

Q. You mentioned that the sort of image that we see in that last exhibit, P62, is just an example of the sort of pictures you see many times. Looking at Exhibit P16, that is an article by Gelderblom and others.

A. Yes.

Q. If you flick through that article, particularly getting to pp.50-51 -

A. I note, first of all, it is received in 1987.

Q. - 50-51, are they more pictures of the sort of things that we were just looking at in P62.

A. It would appear similar, yes, certainly.

Q. That was back in 1987, there were these pictures being

published in articles.

A. Yes, and these certainly do look very much like the pictures we were just looking at in the previous exhibit. Again, you see the morphology of the virus under electromicroscopy looking very similar to the morphology we understand to be HIV, with an outer envelope and inner core and, I think other people can tell you that the electron micrograph, in appearance of particular viruses, are quite characteristic.

Q. I want to produce to you another electron micrograph you have produced to the court. In this exhibit you have produced one electromicrograph and two excerpts from articles.

A. Yes. This is from the same group.

EXHIBIT #P63 DOCUMENT CONTAINING SOME COMMENTARIES, THE FIRST OF WHICH IS IN 1988, WITH A TITLE 'THE ORGANISATION OF THE ENVELOPE PROJECTIONS ON THE SURFACE OF HIV' AND AN EXTRACT FROM A FURTHER ARTICLE IN 1989 'MORPHOGENESIS AND MORPHOLOGY OF HIV. STRUCTURE FUNCTION RELATIONS' TENDERED BY MS MCDONALD. ADMITTED.

Q. You have included those two excerpts; 4.1 and 4.2.

A. Yes.

Q. Why have you included those.

A. These are what is called scientific abstracts. Any paper in a peer-review journal is expected to summarise its information in a short so-called abstract, so I have included these abstracts to tell you exactly what this group was talking about in that time and explained what they were doing, in context with the types of photos they were generating of the HIV at that time. I also included it because it was a slightly different technique of the different instrument to develop the photograph and it is called a section electron microscopy and that basically looks at thicker type sections. I emphasise, again, I am no expert on this, just that I was looking for different techniques that developed similar morphology, pictures of morphology.

Q. Looking at 4.3, the dark circular object we see there, that is the virus.

A. That is the virus but in from a cell membrane. Again, you see the bottom of the panel, the cell with a stretched membrane, the virus budding out, that's how it escapes the cell and probably on the left of the budding virus, we see another virus, but I'm no expert on this.

HIS HONOUR

Q. Just so I'm clear in my mind, you say you're no expert at these. Are you in a position a physician might be in when he gets an x-ray from a radiographer who interprets the x-ray and the physician can look at the x-ray and still interpret it and understand the x-ray but doesn't understand the detail that the radiologist would understand when taking the picture and looking at the picture.

A. I think that is a very adequate way to put it. In medical practice we do a lot of those things. We couldn't actually take the x-ray. We have enough experience in looking at those x-rays to know what is on the picture, if you like.

Q. Ultimately, in that situation, it is the physician who has to make the decision and give the advice to the patient.

A. That's correct. I might just add to that, if I went back into medical practice now, the type of x-rays that I would have seen 15 years ago when I was caring for patients would be quite different from the types of x-rays that are available to me now - as it is with HIV testing, for example. The types of tests that have been cited in evidence here are really dinosaurs, in lots of ways.

Q. You're talking about the evidence of the two witnesses: Dr Turner and Ms Eleopulos.

A. Yes, I am. I think that things have moved on so entirely from the types of tests that have been quoted, that we really need to look at these things in rather a different way. It is what I was trying -

Q. A blinkered view of the world.

A. Exactly.

XN

Q. Finally, on that diagram 4.3, there's been a lot of talk about knobs on HIV particles. Can we see some of those knobs there.

A. Yes, I believe you can. I would think that if you look very carefully around the outer budding virus that you can see, the morphology indicates there are knobs.

MR BORICK: Could we have those indicated again, I don't know what the doctor is looking at.

HIS HONOUR: I can see them on this photograph but perhaps you might want to look at the original.

MR BORICK: I don't know what your Honour is looking at and I don't know what Dr Dax is looking at.

HIS HONOUR

Q. Dr Dax, you might like to point them out for Mr Borick.

A. Can I please write on this photocopy?

Q. Yes.

A. What I am doing for you, Mr Borick, is outlining those, so you will get - even if you need a new pair of glasses you should be able to see the outlines here.

Q. You have actually drawn semicircles around them.

A. Yes, I have tried to not write on them.

Q. No, you have drawn semicircles around them.

HIS HONOUR: I will give Mr Borick the original and the photostat, so he can have a look at them.

CONTINUED

MR BORICK: Thank you, your Honour.

EXHIBIT #P63A PHOTOSTAT COPY OF EXHIBIT P63 TENDERED BY MS MCDONALD. ADMITTED.

XN

Q. One last image of the virus you produced for us, you've headed 'Fluorescence Microscopy'.

A. Yes. I think this one is going to be quite difficult to explain. It's quite a complicated image, but I'll do my best. It's a very pretty picture, in colour, that shows a cell -

HIS HONOUR: Mr Borick, have you got a copy of this?

MR BORICK: Yes.

A. This is a very pretty picture of a dendritic cell which is one of the cells which I think has been talked about in this court today, and I think it's a white cell underneath it. I see a 4T cell which is shown in purple, and if we stain the virus in such a way that the indicator is marked with a fluorescent compound we can shine a particular type of light and that will light up, so, for example, you may have antibodies to the virus that are labelled with a fluorescent dye and then you will shine the particular light through the microscope and they will light up, so you can see here in this image the green dots which are the fluorescently labelled virus.

XN

Q. So perhaps we'll do it by colour coding.

HIS HONOUR: Are you tendering this?

MS MCDONALD: Yes.

EXHIBIT #P64 DOCUMENT SHOWING PHOTOGRAPH ENTITLED 'DENDRITIC CELL ENHANCEMENT OF HIV INFECTIVITY' FROM THE SOURCE STEBBING ET AL NEJM 2004 TENDERED BY MS MCDONALD. ADMITTED.

XN

Q. Just remind us what is a dendritic cell.

A. A dendritic cell is a cell that is present particularly in a genital tract, that is a protecting type of cell

and HIV binds readily to dendritic cells. Dr Dwyer might fill you in a little bit more than that. He might have a better description than that, but basically it's a cell that HIV binds to readily, and they are surface cells on the immucosal membranes which are lining the genital tract, for example, and I think here they've been talked about in the penile foreskin, I think somebody else was giving evidence about that.

Q. The little green dots that we see on that image, that's the virus.

A. That is the virus being lit up with an indicator mollecule on it that fluorescents in particular light, yes.

Q. The purply coloured circle towards the bottom, what is that.

A. I believe that's a CD4 T cell and the blue in this particular - again I'm not familiar with the actual microscopic techniques here, but the blue indicates DNA of the cell and that's a CD4 cell at the bottom.

Q. That's all I want to ask you about that for the moment.

A. Thank you.

Q. Before we move on to the defence, just a couple more general questions about HIV; what do you say to the suggestion that it's never been isolated.

A. Well, I think that that's absolutely incorrect, as other witnesses have said. The ways that HIV has been isolated are in number, and -

Q. Can you take us through some.

A. Some of them have already been cited, such as if you take somebody who has been infected with HIV and you co-culture, you grow together with non-infected cells you can see those cells becoming infected. You can then isolate the virus from that germish, that culture germish, if you like, but you can pellet the virus by spinning it fast, purify it, you can collect the virus by collecting antibodies, putting it through column - the plasma or the isolate through columns that grabs the virus and then wash it off so that you are then seeing a

purified virus. There are ways to purify it from tissues which are pretty much variations on that, and so those are the types of ways that are used to purify viruses. There is a whole microbiology on the purification of viruses that we could go to.

Q. What do you mean there is a whole microbiology.

A. A whole literature of purification of viruses, including HIV that we could go to.

Q. One final general proposition; what do you say to the suggestion that has been made in this court that it hasn't been proved that HIV is sexually transmitted.

A. Well, I don't know what we're doing handing out all those condoms if it hasn't been proven. And, if people use condoms in sexual relationships, whether they are discordant couples or cordant, we have individual evidence, we have population evidence, we have medical evidence, we have all sorts of other evidence that, in fact, HIV is sexually transmitted. There is no question in my mind that HIV is sexually transmitted.

Q. Have you produced to assist his Honour in following your evidence about how this testing works, two diagrams, one that you've marked 2.1 and the other one marked 2.2.

A. Yes, I thought that might help not only in explaining the electromicrographs but I also thought it might help with some of the areas that haven't been covered in the testimony as far as I see, as to the accurate representation of what happens when HIV gets into the body, the accurate representation of a particle and what it consists of, and talking about the various parts of the virion that are represented in developing tests and testing, so I thought that might assist your Honour in explaining some of that.

HIS HONOUR: Mr Borick, any objection - have you seen this?

MR BORICK: I've just seen it for the first time, but one is headed 'R Wyatt 2002' and the other one is not. Again can we have some indication of where these come from?

A. I can't tell you immediately but I can certainly let you know. I have no problem with that.

HIS HONOUR

Q. But you yourself were able to interpret them.

A. I believe so, yes.

EXHIBIT #P65 TWO DOCUMENTS MARKED 2.1 AND 2.2, ONE WITH THE NAME 'R. WYATT 2002' AT THE FOOT AND THE OTHER HEADED 'HIV-1 VIRUS PARTICLE MAKEUP' TENDERED BY MS MCDONALD. ADMITTED.

MR BORICK: I haven't really been heard on that. Dr Dax has said she believes she can interpret them. A little while ago there was discussion about the interpretation of the EM photographs and your Honour stated that the interpretation of X-rays is a completely different thing. I'm not sure in relation whether in relation to the electron micrographs and so on Dr Dax has said specifically 'Yes, I can interpret them'.

HIS HONOUR: You can examine her about that.

MR BORICK: Can I find out where they come from?

HIS HONOUR: Dr Dax said she can provide that information.

XN

Q. Are these sorts of diagrams that are used every day for teaching in this area.

A. Absolutely; you wouldn't go to a medical meeting on HIV or a scientific meeting on HIV and not be shown diagrams similar to these for all sorts of different reasons. Anyone who has been to a meeting on HIV would have seen diagrams similar to these ones.

Q. If you went to a DNA conference you always get pictures of chromosomes and the like.

A. Yes.

Q. I want you to talk us through each of these two diagrams and you can start with whichever one you think is better to deal with chronologically.

A. The Exhibit 2.1 I actually brought because I thought it might help people who had not seen electron micrographs before. I thought it might explain what was happening

in the electron micrographs, that virions may, first of all on the left, bind to the cell membrane, which is shown as the grey line, to the cell and this is supposed to be a sort of cycle of binding, that they may bind to the cell in collaboration with other proteins that might exist on the cell surface, and the virion binds to the membrane, the DNA is injected in, and that's how it gets into the cell. I thought that might be a bit of an explanation of how complex the structure function is and how difficult it might be to explain in absolute detail, but you can see that virions are very well cell associated, and this is slightly different to the ones that I showed you in the electron micrographs because that was more budding out. This is what goes in.

Q. Just to take it right back to basics, obviously the circle we see to the left with a cone shaped core, that's the HIV.

A. That's a representation of the HIV, yes.

Q. The things that look like they have wings on them around the edge.

A. Yes, little butterflies; they are representing the knobs which have received a lot of attention in this court, and then the tooth shaped darker area in the centre represents the core, and I really brought it to show the morphology of how people construct the morphology rather than anything else.

Q. What about the series of four circles that join the HIV particle to the cell.

A. They are proteins that exist on the surface of the cell that assist in the virion binding to the cell membrane.

Q. If we go to the right, what are we seeing in the right image there.

A. I'm not sure that it's terribly relevant to get this all in, but what it's depicting is the virion binding to the cell membrane and actually injecting its genetic material into the cell. That's the schematic of that.

Q. Turning then to the diagram that you've numbered 2.2.

A. Yes.

Q. Just tell us about that one.

A. All right, this is also a depiction of the virus and it shows you that the virus contains a number of proteins and, when we break the virion up, those proteins tend to break up in a similar sort of way. No matter what viral preparation you break up, it tends to break up in a certain way to represent the different parts of the virus. I know you've talked about when you run those proteins, that broken up virus on a gel, you get proteins that run at different speeds under an electric current, under electrophoresis, and that runs very uniformly, if the method used is pretty much the same. So, if you put broken up virus preparation on a gel and you run those gels under the same condition you get pretty much the same picture, and you can identify these parts of the virus that are listed on the left, and this is an important part of HIV testing as I think everyone in the court will realise.

Q. There are two headings in the legend.

A. Yes.

Q. 'Virion Proteins' and 'Host Cell Proteins'.

A. Yes.

Q. Can you explain the difference to us.

A. Yes; when the virus buds out of the cell after it's produced within the cell, it carries with it part of the membrane or part of the host proteins, and this is just showing that the virus in fact can pick up host proteins and that is exactly one of its clever ways of escaping the immune response that is mounted by the host. Usually what happens, if somebody gets infected with an infectious material, the body creates antibodies and that eliminates the infection, but also helps protect from future infections, so, for example, it's uncommon to get measles twice because that immune response persists throughout life. But the HIV is a very clever virus; it moves and changes all the time and one of its ways to avoid the host's immunological response to get rid of it is to, in fact, pick up these human proteins

that are not recognised as foreign.

Q. What do you say to the suggestion that because this is what the virus does, it picks up some of these cellular proteins, that means because you cannot get rid of the cellular proteins you can't say the virus is isolated there. What do you say to that proportion.

A. I can't understand why that makes a difference, quite frankly. The virus is there. It can be shown to be there by numbers of different methods and it depends how thoroughly you wanted to disperse the virus from its environment, but you can certainly isolate the virus. You can work out ways to make it more and more pure, but, just because there is some proteins from the environment in it, it doesn't mean the virus isn't isolated. It certainly is isolated; you can demonstrate the isolated virus, you can measure it, you can photograph it, you can identify it by immunological methods. You can identify it by molecular methods. There is many different ways you can say that preparation contains that virus, whereas as a cellular preparation without HIV does not contain the virus.

Q. One of the things you can also do is transfer it from one culture to another.

A. One culture to another; one person to another.

HIS HONOUR

Q. Have you read Dr Turner's evidence.

A. Yes; I think I've read most or all of it.

Q. He talks about the gold standard. Firstly, what did you understand him to be talking about and, secondly, what would you say to his evidence on that topic.

A. I find that I think I understand what Dr Turner means by a gold standard, in that it's really a very physical concept that he has, that you want something that is there, that you can always punch at or - but I don't understand why he can't see that the virus is there if you look at electron micrographs, if you look at immunology, if you look at virus isolation, if you look at molecular methods, so we can actually take virus

preparations and quantify them these days. That's not difficult, and we can quantify them by numbers of different methods and numbers of different molecular methods, but I think what it ignores too is the way we know that people have HIV antibody or they don't, goes back historically. So that people who got sick with HIV had that HIV syndrome - and not necessarily AIDS - but had that HIV syndrome, developed antibodies; those people that transmitted HIV through blood transfusion had those antibodies.

CONTINUED

There are cohorts where the transmission took place, for example, in Ireland, a group of women got Anti-D for RH babies, treating that, and got contaminated preparations and the virus was passed on. So there's a lot of ways you could say there's a gold standard. Now I'm not quite sure and I suspect that this gold standard again is looking at it in such a way that it shows no latitude to what that standard - what you're really looking at.

Q. He tried to describe it, well, not tried, he did describe it to me in terms of a paternity suit. I don't know if you remember his evidence about that. Basically he was saying if you don't know who the father is or if you haven't got an identified father you've got nothing to compare your sample with so you never know who the father is.

A. Yes, I find that an extraordinary sort of concept in this day and age because there's always sorts of paternity suits out there and we know even though you have a basic human DNA with lots and lots of sections of that DNA, that if two people are closely related they have some very similar sections of their DNA, which unrelated people don't. I mean paternity suits rest on this type of evidence. And, similarly, with viruses, we know about their composition, their molecular composition and we - I think that it was presented, the evidence was presented or it will be presented about the different types of viruses and mapping them and showing that you can follow where viruses go by their molecular structure, and so I find that little - I find that rather a difficult explanation to accept.

XN

Q. Are we now able to identify the whole genome of the virus.

A. Yes, yes, but I think also - I don't want to complicate things too much but I think it's naive to talk about 'virus', even a single person who is infected with HIV there will be different forms of the virus. The virus is very clever at mutating, it changes its structure a

little bit all the time, so that's another mechanism it uses to escape the immune response. But there is a basic structure, it's called the conserve structure that makes it HIV, that's that particular DNA sequences, or RNA sequences in this case, that is characteristic of that virus or that organism and those are the characteristic structures of the organism that make sure that, you know, the DNA makes a human rather than a monkey. And, for example, the difference between a monkey and a human genome is really not very large or even the human and the mouse but there's enough conserve to change that DNA to produce humans versus a mouse. And similarly, the virus changes all the time but there is a conserved part that makes it an HIV 1 or an HIV 2.

HIS HONOUR

Q. And identifiable.

A. Absolutely identifiable.

XN

Q. And that is absolutely unique to HIV that conserved part.

A. Yes, of course, that's what makes it HIV, it's the fundamental building blocks of the virus. So yes, and even though things change around that basic structure but the fundamental HIV structure is there and that's what makes it loop around and create something that has characteristic morphology, characteristic immunology, characteristic clinical patterns, characteristic transmission, and so on.

ADJOURNED 11.29 A.M.

RESUMING 11.45 A.M.

Q. I want to move on to tests for HIV. This is really your area of expertise, isn't it.

A. Yes, it is, unqualified.

Q. Starting off with a general proposition, would it be fair to say there have been huge developments and improvements in the testing that's used in Australia for HIV.

A. Yes, absolutely.

Q. Can you try and give his Honour an overview as to what's happened over the years.

A. Yes. An antibody test rests on identifying the interaction between an antigen and an antibody. There are many tests that use that principle and that is the principle behind HIV testing, whether it be antibody ELISA, and very few ELISA's are used in Australia any more, a microparticle immuno assay, a chemiluminescent or a Western Blot, or a P24 antigen where the capture is the antibody and it captures the antigen. So the principle is the same for all these antibody tests, it's a question of how you put those tests together as to how they operate, what their performance is. At first, in 1985, the antigen was made from cellular preparations of HIV. So when the tests were put together and the antigen was put on the plate to capture the antibody in the blood there were a lot of other proteins involved, cellular proteins because the virus was not isolated at that time, it was made from these cultures. So, in the first instance you did get much more cross-reactivity. At that time the cross-reactivity was perhaps 4 or 5%, but very quickly, as science evolved, those viral preparations were purified more thoroughly, the human proteins were taken out of the antigen preparations so the tests very quickly became more specific. Those tests were called the first generation tests, they were viral preparations made from cells. And the next generation tests, the second generation tests then used preparations of proteins that were either recombinant or synthesised. Recombinant means that you grow the protein in a cellular mellor and you get the cells by various tricks to grow the protein for you, so the protein comes out of the cell, can be purified from the cell as a particular protein that is related to HIV by its genetic sequence - by its sequence. That's recombinant and synthetic means you know the sequence of the aminoacids in the proteins so you put them together in a sequencer, a special machine, and grow that

protein. So once they were grown without cells those tests became more specific again, in fact their specificity was then around 99%. When HIV 2 was isolated it became clear from the blood transfusion services that it was not acceptable not only to block the transmission of HIV 1 but HIV 2, so HIV 2 proteins were included on the plates, that's the third generation. The fourth generation employs synthesised or recombinant antigens on the plate, this is antibody tests, and they are applied in such a way that there's a series of steps before you get the signal to denote. And this series of steps makes this test more specific, more sensitive than any other test, antibody test in history. So that's the antibody tests and they have done four generations, they are highly specific, they are highly sensitive. Now I can read the transcript and say how do you know, I mean somebody is going to ask me how do I know they are highly sensitive and highly specific, that is because over the years we have collected serum or plasma from people who have been infected who have transmitted through blood transfusions, who have had infection and become ill and those people demonstrate the presence of antibodies, the presence of nucleic acid, RNA, within their cells, they demonstrate the HIV DNA and they also can be shown to have virus in their blood or in their tissues that can be purified, and sequenced. So we take those samples and we compare the performance of the tests in those samples that are negative and those samples that are positive and I have also alluded to when we evaluate the kit we look at other characteristics of the kit to make sure the integrity is there, it's robust. So a lot of work goes into evaluating a kit before it goes on the market. In Australia, only fourth generation tests are used, consistently, in the laboratories. There are some third generation tests that are on the market. Those tests that are used all recognise HIV 1, HIV 2 and the major outlier types which are a type of HIV that's seen

in Western Africa that at first didn't react in the tests as they were being presented early on but appropriate antigens were added so now those tests all recognise this type of HIV called O-outlier. So you can see they are highly sophisticated in terms of what's on the plate and what can be identified.

Q. You've talked about the first generation of tests coming into use in about 1985/1986.

A. 1985.

Q. And out of the four generations those were the most basic sorts of tests.

A. Yes.

Q. And it was in that first generation that you had the much higher incidence of false positives and false negatives.

A. Not so much false negatives because if we talk about false negatives, in my statement I've presented to you a testing strategy, it's figure 1 in my statement. Is it appropriate to look at that now?

Q. Yes, if it assists you explain.

A. It's in appendix 1 on p.7 of my statement. HIV, antibody tests are set up to be highly sensitive and so when we put some sample into an HIV test if it doesn't react, give a reaction we can confidently say that that test is negative.

Q. In this country is the focus of the HIV test to make sure that if there is any chance they are HIV positive they are picked up.

A. The focus of the first test is to exclude anybody who could be infected by grabbing anything that looks like an HIV antibody, whether it be through antibody specific or non-specific. The tests are purposely designed that way.

Q. Because the real concern is you don't want to let someone slip through thinking they are negative when in fact they have the virus.

A. Yes and it's driven largely by the transfusion services, which must have maximum sensitivity to make sure that no

infected person becomes a donor but also, if they are reactive to err on the side of caution; the zero tolerance principle that blood services obey, they will not use that donation either. Now it costs quite a lot to collect blood donations so you can imagine the blood service is not happy if the specificity is low. So there would be no reason why we couldn't still use the first generation tests for catching those donors who were truly infected. But to go back to your question Ms McDonald, those tests were less sensitive in terms of the amount of antibody they could detect or the affinity of the antibody so the window, the so-called window period was longer, around six to eight weeks, whereas the window period of the fourth generation assays is two to three weeks. So it's a marked difference and I think that's what you were getting at with that, so it is a marked difference and that would be the reason why we would now reject the early generations, but I might add, in America where the FDA doesn't have such a neat system as we have in Australia, they do still use some of these old-fashioned tests and it's a quirk and it's important to note that because quite a bit of the literature is still quoting information that comes from the US where the public health laboratories still use tests that are no longer used in Australia and the blood transfusion uses a system that was introduced in Australia in 1996 which is still not introduced in the US. And we have a huge data to show that that test is highly specific, highly sensitive.

Q. I think I have taken you off track. Can you explain to us what appendix one indicates.

A. I think the other thing that I noted from the transcript we talked often about the tests as though they were used in isolation, this is actually not so. Not only are we very careful in Australia about the types of tests that are used and their performance before they go on the market but we are particular about how they are used. So we all adopt the use of testing strategies, those

testing strategies are recommended in the packaging inserts of the kit, in the HIV testing policy, by the impact document and by standards for blood transfusion and diagnostic.

CONTINUED

What those standards suggest is that if you have a sample which you are screening for HIV - if I might digress for a moment - one of the things about the screening with HIV that is different from many other infectious diseases is that HIV may show no clinical symptoms for a period of up to a median of 10 years after infection - something like that. Somebody can be infected and not be aware of it. Those tests are different to other infectious diseases, where you have a clinical syndrome that basically acts as your screening test - your first test - so the physician will suspect that somebody has glandular fever, measles etc., and then do the test, which is confirmation. Here, there is no symptoms in many cases, so we screen and that's our first port of call. Those tests have to be of exemplary performance, very different to others that operate at far lower sensitivities and specificities. The ease of the source of the comparison, except between those tests that are submitted for transfusion infections, the sample is taken and the first test is done - antibody immunoassay. If it is negative, the predictive value, the chance that that is a truly negative result, is close to 100%, only if somebody is in the window period. Very rarely do you see a false negative. The other possibility is a lab error. Lab errors are voided by many different means and I won't go into that. If the test is reactive, there's two possibilities - three actually - it can be a technical problem with the lab, a true reactivity or a false reactivity. What we do is we repeat that test in duplicate - in duplicate samples of the original sample. If two of the three tests that have then been performed are reactive, that is then called repeatedly reactive and we are convinced in the lab that that is either a true positive or a false positive - a true antibody or a false. It can be one of the two at that point. We then go on to supplement testing. There's true and false reactivity. We have to sort that out. We have to be clear if it is a true

antibody or a false and we use supplemental testing. In Australia, we use the Western blot. We have heard a lot about the Western blot. What a misnomer. There are numbers of western blots and they're all prepared in a slightly different manner. They may show slightly different patterns. In Australia, in the general population, the prevalence of HIV is extremely low, as everybody will know and I'm sure Dr Kaldor will tell us a lot more about it. In Australia, our epidemiology is very different to most countries and most of the infections are in men who have sex with men, however, in the general population HIV is very low, therefore, if you do that second test and you have false reactivity, we use the Western blot because it is highly specific when you interpret it in a stringent manner, which we do for Australia. There's so few infections in the general population, you may see a negative pattern - no bands at all - a positive pattern, which we have designated through a lot of experimental evidence as having a glycoprotein and three other bands. The chances of that pattern occurring in somebody who doesn't have true antibody are almost zero. We have not seen it.

Q. It is the pattern you're looking at in the Western blot.

A. It is the pattern. If the prevalence is high, then the chance of the pattern being a positive is much higher than if the prevalence - because the ratio of the true pattern to the false pattern, and that is few, would be quite different. We have to look at probabilities, so we have cut out whole layers of testing that is being presented, I think, in the transcript, as though the tests were just performed de novo. That is not how it is done. It is done very carefully, in a sequence, using tests that are developed with sequences of chemical reactions that read out the non-specifics and so you see very few false reactives and, when you do, there are numbers of ways to sort out that false and true reactivity, including the Western blot, but not only the Western blot.

Q. If we assume for a moment that we have someone who has had an ELISA, that has been reactive, positive, they've gone on to have a Western blot, again positive -

A. Can we talk about reactives, not positives?

Q. Yes.

A. We try not to talk about positives because it is misleading.

Q. A reactive ELISA, a reactive Western blot and that person has gone on to have their viral load measured and there is a significant viral load. Putting those three together, is there any room for error that that person is HIV-positive.

A. Statistically, no. If that's done in a reputable laboratory, with reputable tests, statistically, no.

Q. This testing strategy you have been talking about, are they employed throughout all of Australia.

A. Yes, in fact the TGA requires that anybody changing the package excerpt must declare that and so do the laboratory registration groups - the National Association of Testing Authorities - NATA - they require that all this is used according to the specific testing strategies and in the way that is specified in the package excerpt which is how the test was evaluated.

Q. In terms of the use of the testing strategies, when you referred to it occurring all around Australia, that includes our IMVS in South Australia.

A. Certainly.

Q. Taking you back to appendix 1, because we have yet again gone off on a tangent, could you address us on what appendix 1 shows.

A. Appendix No.1 illustrates a testing strategy. It is the type of testing strategy that is used in Australia. The sample is tested in an immunoassay, and I have said not usually an ELISA these days, we have far more specific and sensitive tests. Tested once, if it is non-reactive, because the chance of it being a false negative being almost negligible, we can say it is negative, if that test is non-reactive. That is the

left side of the strategy. Do you follow that, Mr Borick?

MR BORICK: Yes, I do.

A. On the right side is reactivity where the same immunoassay is used in duplicate. I think that there might have been some confusion earlier on - for instance, Professor Cooper might have said that there was a second test used there, and in some situations there may be and it is perfectly acceptable in this day and age to use two immunoassays there, but in Australia we go on and do the Western blot. The Western blot, if the first immunoassay is reactive - repeatedly reactive - can be non-reactive or negative, in which case you would diagnose the person as being anti-HIV negative, or it can be positive, demonstrating a pattern, as I have suggested to you, which denotes positive antibody profile. There may be bands on there that are not indicative of HIV or may have one band or perhaps two that run in the same position as the HIV proteins. I can get onto that later, if you like. That is called an indeterminate. The laboratory, at that stage, would say in the report 'If you have any indication that this person has been exposed or suspect that they're sero-converting, send us another sample'. If the diagnosis is anti-HIV negative, that is the report. If, for the first time, the diagnosis is anti HIV-positive, the NRL advise the laboratory to request another sample to make sure that that sample gives the same result and, by and large, that is followed throughout Australia. That is the testing strategy and it is based on a large amount of evidence and on probabilities which give you your predictive values and they're population based.

Q. You have mentioned about Professor Cooper's evidence, he also used the phrase 'different platforms' when talking about some of the testing.

A. Yes.

Q. Can you explain what is meant by that phrase.

A. Different platforms means the different ways that might be used to create an immunoassay or the different methods that might be used. I have suggested that there are microparticle immunoassays, chemically luminescent immunoassays, there is Western blots, ELISAs, all of those are different platforms but it can also relate to the antigens that are used, so one test might use the glycoprotein - the GP glycoprotein - another might use a combination of glycoprotein and core protein, for example.

Q. Going back to the first test that occurs, the one that is very sensitive, what do the current studies or what does the data currently available indicate is the rate of false positives with that first test.

A. Yes, I can show you that with absolute accuracy. Certainly, that false positive rate in diagnostic laboratories is around .5% - something like that, and I don't have those current data for the last couple of years. We collect those data in the blood transfusion service on an ongoing basis and the false reactivity rate is .01%. That is of all the donations that are tested, between 1 in 10,000 would show reactivity, repeat reactivity.

Q. Is that with the first test.

A. That is with the first test.

Q. Then moving onto the second test which is more specific.

A. If it is interpreted correctly, yes.

Q. I think you're aware there has been a lot of talk about antibodies being promiscuous and P24 being found elsewhere and so forth. Firstly, P24 simply indicates a molecular weight.

A. That's correct.

Q. It is something that shows at that band.

A. At that position on the gel, correct.

Q. What do you say to the suggestion that a reactive result in a Western blot can be attributed to non-specific proteins.

A. A huge body of work has shown that if you have a

particular group of proteins, visible together on a Western blot, then that particular group denotes that that person has been exposed to the virus and has generated antibodies to each of those different proteins. I think in the testimony it is misleading because it sounds as though, when you get a Western blot, you might get one or two bands often but that is not the case. If somebody is truly infected, by and large they show the full band pattern of HIV and it is not wishy-washy and so on but, in other circumstances, you may get one or two bands and it takes a lot of practice to read those accurately. You have to know which Western blot you're reading frequently and so on and so forth. You would never give a Western blot to a novice to read. You have to practice for years and years and years to be able to read them absolutely accurately when it comes to the very difficult ones. The ones that are quite obvious - I'm sorry, but they're quite obvious and if somebody has been exposed to the virus and generated antibodies against all areas of the virus, it is not as though they throw one band and you're struggling to find one or two or three, they're all there.

Q. Has that been one of the developments in HIV testing - that is the Western blots become a lot cleaner.

A. Yes, they have, because, for the reason I was describing before, at first the virus was grown in cellular cultures and they were human cells, so then when they were squashed up they took their proteins with them but later the virus has been better purified, better fragmented, so that the proteins run more cleanly. There's been ways that I have learnt - what we do is it is called blocking. We put proteins on the gel, that have nothing to do with HIV, that block that non-specific, so we get nice clean bands and the manufacturers, of course, have done a huge amount of this work. You can even get blots where the proteins are painted on, rather than this electrophoretic

preparation. There's a lot of different ways that proteins are now put forward and the Western blot is conducted.

Q. Can you just explain the difference between specific and non-specific proteins in this context.

A. Yes. Specific being that those are proteins that we can identify as part of the HIV. They have a particular sequence. We can take those proteins, we can sequence them, or, alternatively, we can synthesise them, turn it around the other way and we know the sequence, so we can put it in a machine that actually makes the protein and it behaves in the same way immunologically as the native protein. Whereas non-specific reactivity, it may be that there is a protein that the antibody sees, something like an HIV protein or it may be just sticking antibodies, sticking to something. I think Gus Nossal mentioned that early antibodies tend to be less specific and rather sticky, low affinity. If you have a new infection or vaccination, you may get some of the sticky stuff around but it doesn't fall in those nice neat bands.

Q. Have you read the two page document been produced by Gus Nossal.

A. Yes, I have.

Q. That accords with your opinion.

A. Certainly. It was a bit embarrassing to be called the 'World famous scientist' in The Australian before Gus Nossal and David Cooper. I want the court to know that was a completely erroneous order of attributes.

Q. I am going to ask you some questions using the PowerPoint presentation that Dr Turner used. Looking at Exhibit A6, you have seen this set of PowerPoint slides before now.

A. Yes, I have.

Q. I want to take you to some slides that appear at p.6. Does your copy have page numbers.

A. Yes, I have.

Q. Slide 34.

A. Yes.
Q. Middle right.
A. Yes.
Q. That's a table that purports to set out the different standards applied in different jurisdictions and I will come back to that question in a moment. We see there under the heading for Australia a criteria set out. Is the correct criteria applied in Australia.
A. The criteria, I think, say 'any one of the glycoproteins' and then 'any three of the gag or pol'. I think that's not correctly reported. The criteria that we use in Australia are a glycoprotein and three other specific viral bands.
Q. One glycoprotein and three specific viral bands.
A. Yes.
Q. In terms of specific or non-specific proteins, where do those sit.
A. The specific bands relate to the bands on this particular Western blot but they may differ a little bit between Western blots, but the specific bands would be P24, P55, the glycoproteins, GP160, GP120 and GP40 and the gag or the pol bands.
Q. Going back to the criteria that is used here. When you talk about one glycoprotein and three specific, are those all proteins that are specific to HIV.
A. Yes, those are the ones that fall in a pattern. It is not as though they are any old proteins, it is the pattern that they appear in. The chances of a non-specific reactivity showing that particular pattern we have shown over the years is almost zero - well, it is zero. In a low prevalence population, these are highly stringent criteria.
Q. I want you to try and explain that for us. You have referred a number of times to the significance of how high the prevalence of that virus is.
A. Yes.

Q. Why is that significant.

A. It's significant; this is to do with predictive values. Let's say you take a test and this time we're talking about one test, and you examine people in a population, you will get non-specific reactivity in that population and you would select the negative population to do this testing in. You would get maybe at .5% - five people in 1,000. In another negative population that would remain pretty much the same, 5 in a 1,000. If one population now, in the general population, had 10% of people infected - and, your Honour, there are communities not so far from Australia where 10% of people are infected - the chance then of the reactivity being non-specific, that is just sitting in the population of negative people, compared with the specific, is very small, so you can be less stringent about your Western blot criteria. So in Africa where you have a very high prevalence, the chances of having two bands on a Western blot and it's being non-specific are small, or the chances of two EIA's being reactive against, you know, against not being a true reaction, again, are small, because the overwhelming reactivity, 10% in that population, will be reactive and truly reactive; they are infected. If it's 2% then your chance of the pattern being truly reactive is still much higher than the non-specific, but it's less so, so you might want to increase the stringency of your criteria. In Australia, where in the general population the prevalence of HIV is very low, it's likely that you get non-specific reactivity in about the equal rate to specific reactivity in the general population. Therefore, you need to be absolutely sure and you need to invent these stringent criteria which was done through a series of examining specific, non-specific blots in a very large population in the late '80's, and we have stuck with those criteria, although some of the labs now use the criteria that are designated by the test kits rather than these very stringent ones. Does that - I hope it

explains -

Q. So when you say we have very stringent criteria here in Australia -

A. Yes.

Q. - how does that compare to other countries.

A. It's the - it's most stringent. I think the American Red Cross at some time used four bands but then they backed down to three, but when we set the WHO criteria we were less stringent because we wanted to have a universally acceptable system, and we wanted them to be useful in all prevalences and that was a very tall order. It took us three days to come up with our WHO criteria, and we finally agreed that the glycoprotein had to be present plus those two bands.

Q. To try to reduce this to pretty crude lay terms, is it the case that once you've got a reactive to that first test you want your second test to make it absolutely clear that this person in fact is HIV positive.

A. You certainly want to distinguish between true and false reactivity and, by implication, anybody that has true reactivity has been exposed to the virus for many reasons that I've covered, in terms of the knowledge about the virus, how it behaves and how the body behaves in response to it.

Q. So, before you diagnose someone in this country as being HIV positive, the test has to have shown that that very highest most stringent criteria has been satisfied, the four bands.

A. Pretty much. As I say, lately people have relaxed a little bit, using the manufacturer's criteria, but certainly the criteria, as designated, must be followed to a tee, that is part of the laboratory - it's undertaking when it use those tests. Don't forget not too many labs use the Western blot; most of the initially reactive and repeatedly reactive tests are referred on to central laboratories to perform these tests.

Q. What do you mean by central laboratories.

A. The State reference laboratories. Not every laboratory performa Western blot because - there are a number of reasons; first of all you want to keep your epidemiology and reporting straight. You want the experience of the people - it's not a particularly easy test to do and you certainly have to train people to do it. It's not a cheap test so you don't want wasting because kits are sitting there expiring, and so the samples tend to be referred to central labs, reference laboratories.

Q. On a discrete topic, p24.

A. Yes.

Q. There has been a lot of reference to that in the evidence. Is there a p24 that is unique to HIV.

A. If you take a virus from someone who is infected and isolate the p24 - isolate that virus, break it up and find the p24, that will have a unique sequence, yes. And one of the ways that we could find that is run it on a gel, not a Western blot, but a gel, and the molecular weight of p24 or the molecular weight of 24,000 - take that protein out of the gel and sequence it, you would find it was an HIV p24 but, if it were not and there were a protein there, you would have a different sequence.

Q. So there could be another p24 found elsewhere but it would have a different genetic sequence in the HIV p24.

A. Absolutely. It's not so difficult to find a protein with the same molecular weight; there are lots of proteins that have that molecular weight.

Q. When you break it open, if you like, and look at what's inside, the HIV p24 is quite unique.

A. It is unique.

Q. I want to just take you to a couple of aspects of what Dr Turner has told the court, and I just ask you to comment.

MS MCDONALD: At p.90 of the transcript your Honour.

XN

Q. Reading from line 25 - this is in the context of a much -

A. Sorry, can I interrupt you?

Q. Certainly.

A. The last answer is worrying me because we're talking about p24, and a lot of p24's - but on a Western blot you have that gamisch that I talked about before.

MR BORICK: You have the -

A. The mixture of proteins that you put on before you put the electrophoresis across, and that is from an HIV, so that is an HIV protein, okay. There is no doubt that that is an HIV protein on Western blots these days you couldn't sell a Western blot if it weren't an HIV protein, okay. But antibodies that are not necessarily HIV antibodies could react with that protein. It's possible, but it's less and less likely in the person who hasn't been infected with HIV. Almost everyone who has been infected with HIV will react with that protein on that gel, so I just thought that my answer might have been a little confusing there, so I beg your pardon for interrupting.

XN

Q. We come back then to the fact that it needs to be the four bands.

A. It needs to show that pattern; it needs to a show an acceptable pattern within that prevalence but, in Australia, yes, we accept the four bands as the ultimate criteria.

Q. Reading to you something Dr Turner told the court, as I said this is in the context of a much lengthier answer, he said this 'Now the experts claim that by separating out the proteins of the Western blot some of the 1,023 possible band combinations are caused by general HIV antibodies while the rest are not. The question is how do they know that, how do they know which band patterns are specifically due to HIV and which aren't'. I ask you that question.

A. Thank you. That's terrific. Now how do I explain it? It's possible to see all the band patterns that are shown on slide 31. People who are infected with -

MR BORICK: Where is that?

A. P19 on Dr Turner's testimony, documents numbered A6, and the slide is on p.6, and is numbered 31.

MR BORICK: Thank you.

A. It's true many of those bands will exist, okay, or can exist. And, if you apply basic mathematics to how many different permutations and combinations - and I have not done that, but I assume that that's what Turner has done, and has come up with the 1016 is it? But if you look clinically, epidemiologically, in situations of evaluation, many different ways, you will see that that combination that comes up in a very effective way, or the criteria that come up in a very effective way are not sort of a slew of bands. This is what I was saying before; if you've been exposed to HIV by and large you demonstrate the same pattern on Western blot. It's uncommon not to see those crucial bands, the glycoproteins and the gag and pol, it's very unusual not to see that four band pattern. In fact if someone has been exposed to the virus, only in very early times or if they are very early on in the course of infection put on antiretrovirals, will they not demonstrate that four pattern, so yes you can play around talking about if one band were present and two bands and the probability, that's just a simple sort of high school exercise, but, if you take into account the probabilities of those crucial bands appearing in someone who has been exposed to the virus then it's extremely high and, if you look at the non-specific binding, those people who are repeatedly reactive but, in the end, who have not been exposed to the virus, they'll just demonstrate no bands or perhaps one or two of these bands, but not the four pattern, and that's been demonstrated by a huge laboratory practice, matched and coupled with a huge clinical practice under an enormous research background, evaluation backgrounds, in standard serum and so on.

Q. Just going back to slide 34, which is that slide that sets out the different criteria in different countries,

what is the explanation for why, when we look at this superficially, it looks like one country you can be diagnosed as HIV and in the other you would not.

A. It rests on these probabilities of these patterns being true, so, in Africa - let's take it from left to right - in Africa the tests that are now used would be highly specific and they would - so that if you then ran the Western blot which is not recommended in many parts of Africa, it's too expensive and too difficult for many parts of Africa, but if you did, the chances are, with the high prevalences, the two bands will give you a reliable diagnosis. That doesn't mean every time you do a blot you get two bands; it just says that if there are two bands there it's good enough but, most of the time, your Honour, it's really important to realise that, if somebody has been exposed to the virus, the four band pattern is there. It's most uncommon for it not to be.

Q. It's just a different threshold that country applies.

A. Absolutely, and it's to do with the chances of the blot getting through the first test and the second with specific bands belonging to someone who is HIV positive, because the prevalence is so much higher it's a predictive value thing.

Q. You've said that they don't tend to use Western blot in Africa because of expense and it's just too difficult; what sort of test do they use there.

A. Well, we haven't discussed rapid tests at all I think - I don't recall, but now - gosh, how will I be brief? Since the Durbin meeting in 2000 - Dominic was the Durbin meeting 2002? In 2001, where it was realised that HIV therapy, antiretrovirals actually could stem the course of the infection, and protect people from dying, that the world needed to distribute these antiretroviral drugs to many people. That is very difficult. Logistics are very difficult, but not only the logistics of distributing the drugs, but you'd have to test huge numbers of people, larger than laboratories can cope with, so now people are tested in testing sites

in Africa and Asia called Voluntary Testing and Counselling Sites and they use what are called rapid tests; they are immunoassays that are set up so that the test can be done there and then and the person can be informed that they are reactive or non-reactive and in some cases two rapid immunoassays are used together and the person is told that, if they're both reactive, the person, that he or she is actually HIV positive, then and there, and then that person can get on and seek antiretroviral assistance or medical assistance and get on with it, but in other places they may use the rapid tests and the EIA and, still, in the urban areas, like we do, use the EIA and the Western blot. So there is a lot of different ways that we look at HIV infection in those highly endemic areas where we're trying to roll out therapy.

Q. Another question that was posed by Dr Turner - p.116 - was how did the different jurisdictions know that the tests had been set correctly.

A. Actually it's quite difficult because many of the areas don't have their own test evaluation systems so it would be difficult to say how any jurisdiction might select which tests were used, but more and more the manufacturer's are being called upon to deliver a huge amount of evidence as to how their tests perform before they can get on to the market, and I actually know about how big this information is because we have to evaluate the dossiers and they come in multiple volumes which we have to sift through.

CONTINUED

So America is hugely cautious, as I have intimated, and they evaluate the kits for a long time an an experimental situation if you like, before they go onto the market and they are using tests that are no longer used in Australia, for example. In audits, as I said, the manufacturers have to present their dossier and then they're evaluated against many many samples, and that's true of a number of countries also in Europe, there are bodies that actually evaluate these test kisses, Paul Erlich Institute in Germany and so they have their battery samples that are related to their populations that they are testing to make sure that these work absolutely correctly. So if a test is used anywhere where there is a regulatory authority it's usually evaluated in-country, otherwise countries look at the evaluation data of those countries that do have regulatory authorities, or the manufacturers, and I hate to tell you that in many countries the tests that are used are purchased by members of parliament who use those kits as ways to earn money, they are not necessarily good kits, they are kits passed their expiration date and I don't think it's very helpful for those countries to question how reliable these kits are when there is such a huge body of evidence against their being unreliable. I'm not doing those countries a service at all.

Q. Have you organised for a number of Western Blots to be emailed through.

A. Yes, me and Professor McDonald, I believe, and I have not ever seen these Western Blots per se, they are just ones that were faxed through from the lab so I could illustrate how difficult sometimes it is to interpret these. So I hope they illustrate that.

Q. Produced to you is a set of 10 documents. What do those 10 documents appear to be.

A. These Western Blot pictures, are there 10 of them?

Q. Yes.

A. These look to me to be Western Blots. You can see the

molecular markers on the right-hand side with their migration molecular weight shown. I might just say that the ones you are looking at we as the National Reference Laboratory try to run a completely separate Western Blot to those that are run in any other laboratory and the reason that we do that is so that we can use it as a check on the system. So you can see that this Western Blot doesn't look like the ones you've seen in the slides, for example, or in the text books because this particular Western Blot is run so that the molecular weight bands are run off. So that when we look at these Western Blots we have to look for the glycoprotein that's designated GP41 and three other bands. So what you are look at is a little different and I think it's relevant that it is a different Western Blot to those that are made commercially.

HIS HONOUR

Q. Are they slides, would you describe them; pictures of slide -

A. Pictures of the Western Blots that were run in the labs and I see that they are dated and I see that some of them are more definite than others and some are better photographs than others, too.

EXHIBIT #P66 TEN PHOTOGRAPHS OF WESTERN BLOT TESTS CONDUCTED IN THE AUSTRALIAN LABORATORY TENDERED BY MS MCDONALD. ADMITTED.

XN

A. I draw your attention to those blots and you can see where bands are present, there's usually lots of bands present; they are all there, they are all represented. By the way, the ones on the left will be a negative control, a positive control and there should be a dilution, I suspect that it's in the first one, there should also be a dilution that's run as another control and I'm not not quite sure, maybe it doesn't show it on here but certainly the left will be I think - or maybe the left's a dilution. I'm sorry I don't have - if I

were reading them I would want the information exactly which ones were the controls but I suspect that the left is the negative control and the next one's the positive control.

XN

Q. We see that there's a number, I think it's 31, to the left.

A. I see, that would be the negative. The next one probably will be the dilution and number 33 will be the positive control.

MR BORICK: Which one are we looking at? Are we looking at the top photograph?

A. Yes, this one.

XN

Q. What do you mean by 'a dilution'.

A. That means you take the plasma and you add the plasma of the control sample and you add a diluent which will be a negative plasma, one that shows no bands at all so that you can grade the response and make sure that, over time that your Western Blot is demonstrating the same intensity so that you are reading consistently, basically.

HIS HONOUR

Q. Is that early one 31, 32, 33 or 81 -

A. I think it's 30 - it might be 81. Yes, I think you are right, 81, 82, 83.

XN

Q. I'm sorry I thinkity probably misled you there.

A. Yes, I think I probably did too.

Q. Turning back to some other aspects of Dr Turner's evidence, during the course of his evidence - p.131 - Dr Turner referred to a study that he said you were involved in documenting, involving reformed drug addicts - line 13 - he said the following 'In 1991 there was a paper published by Lange. One of the authors was actually Dr Elizabeth Dax from the National Reference Laboratory who reported that a reformed drug addict, HIV positive, on the Western Blot and ELISA lost their HIV

antibodies and reverted to negative when they reformed. There was only a small group. There is only 10 of these individuals but they reported them, because HIV is said to be for life but these addicts lost their antibodies, they regarded their original positive tests as false positives. Nowadays, drug addicts with positive tests who are recorded as true positive are said to be infected for life and in fact are in the second to highest risk group'. Unfortunately he didn't give us a reference to that study or paper other than to say it was in 1991. Does that ring any bells for you.

A. Yes, I think that was a paper that Dr Lang and a group of us published on an old group of sera. I honestly can't remember exactly what that paper was about, and unfortunately I didn't see it before yesterday so I didn't have the opportunity to retrieve it. It might be quite a difficult one to retrieve, actually. But I suspect this is what I was talking about earlier, that what was known about this group of old sera, banked sera, was that in fact on the early tests they were shown to be reactive but on the later, more specific tests they were no longer reactive; you know, showing reactivity in those more specific tests. Now I would have to go back and look at that paper, I haven't even thought about that paper for a very long time and it's not one that I would have brought up in evidence from my side of the - at any time, I think it's long gone. I mean many of these tests have changed so much as I said at the outset, that the the results that we saw many years ago, if they were non-specific we would not consider them of significance and they may not show specificity now.

Q. Is your best memory then of this study, having not seen or gone back and looked, that it related to really a commentary on the weaknesses in the testing that was available back at that time.

A. Well there wouldn't have been - yes, at the time those banked sera were tested, yes, because if the publication

appeared in 1991 they would have been tested with early-on tests and we in America - don't forget I was in America, not Australia - we in America were struggling with the Western Blot, in fact in America they are still struggling with the Western Blot because they have not defined their criteria carefully enough so they don't really know what to do with indeterminates. In Australia we have a system of dealing with indeterminate results, which is not to do with positive results, but in Australia we have a way of doing that and America continues to struggle, so at that time we were really struggling with how to interpret the Western Blot and I'm not - I'll go back and look at that and I'll be happy to submit a little commentary on that paper because I honestly can't remember the focus of it.

Q. In 1991 you were living in America, were you.

A. No, I moved back to Australia in 1990 but the work would have been done when I was in America and when I was running the HIV lab at the institute.

Q. So it would have related to the situation in America.

A. It certainly did, and to a group of people who were tested, way back when, and I don't remember the characteristics of that particular group just off the top of my head. Was some of the work that was done to try to help us get through interpreting the Western Blot correctly.

Q. I want to put to you now some of the alternative explanations that Dr Turner gave for why someone might have a positive reaction to the tests for HIV or be reactive to the tests for HIV. The first one - p.127, at line 18 - 'So one may reasonably ask if they are not retrovirus, where they come from, and there are three possible reasons. The first is that AIDS patients have diseases, such as microbacterial and fungal disease. Tuberculosis, for example, is caused by microbacteria, as is leprosy. They're micro-related bacteria. In fact, microbacterial and fungal diseases constitute a fair proportion of AIDS diagnosis'. Can I invite you to

comment on that.

A. I think Dominic Dwyer this afternoon might be a better person to comment on the clinical outcomes and the tortuousities that are dealt with there. There is a transcription error by the way it's mycobacteria, not micro, but I think it would be better if that were commented upon by Dominic and I stuck to the testing issues.

Q. So you defer to him on that particular topic.

A. I do, thank you.

HIS HONOUR

Q. Can you go through slide 53 on p.6, it's a conclusion that Dr Turner arrived at. Do you see that slide, or see that conclusion.

A. I do.

Q. He gave evidence in accordance with that conclusion. What would you say to his conclusion.

A. Well, obviously I haven't seen Mr Parenzee's results, but if he were tested in an immuno assay which was reactive, and if he were infected with HIV his Western Blot would have shown the band pattern that we expect to call his status as positive and I have no reason to suggest why the IMVS would have called it positive if those band patterns weren't present. So while I don't have that in front of me, I can't, you know - these labs operate under a system of quality management, using tests that are highly evaluated, highly assessed, using strategies that are defined from several different orders and by and large if they have examined the specimen, they have examined them carefully, that is a true result.

XN

Q. What about if you add to that that subsequent to those tests being reactive viral load was measured in Mr Parenzee's blood.

A. If that were true and that were a dedicated sample to avoid contamination, because if you use the same sample you used for the first tests it's possible that you

could get contamination, most unlikely, but if then the blood from a particular person shows a viral load or DNA can be demonstrated in the white blood cells then I have no other conclusion but that that person is infected with HIV.

Q. And if you were shown that there were a number of occasions on which, separate occasions in time, which Mr Parenzee's viral load was measured in his blood, so it was located and measured, then that also would leave no other explanation open.

A. In this day and age with the tests that are used in these laboratories in Australia, with the tests that are available, that have been evaluated, that are monitored, etc., etc., no.

MR BORICK: I just want to take some instructions on these over lunch but I want to be sure just what they are being put in for. I understand they show examples of western blood.

HIS HONOUR: That's all I understood them to have been put in for, Mr Borick.

A. That's correct.

MR BORICK: So there is nothing specific about any of these things that -

HIS HONOUR: No, I didn't understand them to be specific, other than examples.

ADJOURNED 12.59 P.M.

RESUMING 2.19 P.M.

Q. I want to put to you a passage from the evidence of Ms Papadopulos-Eleopulos in relation to electromicrographs of the HIV virus and just ask for your comment. P.272, line 20, I have been asking her about the Gelderblom article we looked at this morning, which had pictures in there. 'Q. During your evidence you have told us many times that HIV has never been photographed. A. No, no, no, no. I never said that HIV has not been photographed. I never said - just saying here - what I meant - let us make it clear now, you can take photographs from the culture. There are numerous photographs, not only by Hans Gelderblom, but by many, including Montagnier and including Gallo. Also, a lawyer found out what Gallo represented as his electromicrograph actually was Montagnier's electromicrograph but let us not go into those details. There are numerous - let us forget what Gallo did. There are numerous photographs of what is called - what is meant to represent HIV particles from the cultures. I can give you hundreds of papers. What we are saying is, as in this document you have given us yesterday -' and it is P4. She then continued 'Is that there are no electromicrographs - what is meant to represent, apart from Best and Ushenko 1997 papers, there are no photographs of the banded material to show that what they are saying is pure HIV actually is pure HIV'. Do you have any idea what Ms Papadopulos-Eleopulos was talking about there.

A. It seems a little difficult to decipher because she's talking about - she would appear to be talking about photographing bands or the material that went to the bands, which is not really terribly sensible because, as I indicated this morning, once the virus is disrupted and run on the gels, there is no longer a virus to photograph. Perhaps she's referring to the material that is isolated and then put on the gels or on the test base, but I read that part earlier, so I am familiar

with the passage that you're quoting but I don't - it is nonsensical, I'm afraid.

Q. Two final questions in relation to the PowerPoint presentation we were looking at, A6, slide 28, shows the front cover of publication 'Retroviral Testing and Quality Assurance' of which you are the co-author.

A. That's correct.

Q. Then there is a passage cited from that publication, at slide 29. Do you have that in front of you.

A. I'm sorry I have put them down and forgotten to pick them up. They're sticking out the top of my bag. The ones that are sticking up vertically. Yes, I am familiar with the slide.

Q. Firstly, you were involved with this publication.

A. Yes, I was.

Q. To what extent.

A. I am a full co-author on that publication, however, the parts of the book that we each wrote were quite separate. So my contribution to the book was that 10 or so chapters on the quality assurance. That is my level of expertise and I didn't chose to write about the virology, however, I think it is worth noting that my co-author resides, lives and works in America and much of his writing I kept on being critical of because it was very Americocentric. As I have told you, it is a very different approach to testing in the US and we wanted to make this more general, so that was my criticism of his work.

Q. What about the passage that is cited at slide 29; do you have any comment to make in relation to that.

A. Yes. Again, I have trouble in interpreting what is meant by this slide. Just because you have a precursor that is split, I don't see that that makes it any less authentic than having a precursor that is not split, if you see what I mean? I just really don't understand what the point is, I'm sorry, I don't understand the point.

Q. The final slide I want to take you to is slide 38, on

p.7, again you are cited here this time in an article, I think.

A. Yes.

Q. Do you have any comment or observation to make in relation to that passage.

A. Only to refer you to the comment I made earlier on, that interpretation criteria are based on a large amount of information that is put together, the probabilities are weighed up and that different blots behave in different ways because they have different protein preparations that are used in their manufacture and the French would say, for example, it would be fine just to have the glycoprotein bands. They have used that as a diagnostic criterium for quite some time and, as I have explained, our criteria that was set at the end of 1990 weigh against what was seen in the Australian population - the general population - and how often extra viral bands were seen and we wanted to make absolutely sure, based on the evidence, that those criteria were valid within that low prevalence population. Again, gene labs, blots have been created later, they're more specific proteins and, again, have been worked up, as I have mentioned, evaluated extensively by each manufacturer to fulfil their blood manufacturing practice and so on.

+CROSS-EXAMINATION BY MR BORICK

Q. Looking at P66, as I understood it there were 10 separate examples given to us.

A. I think I have 10, yes.

Q. Looking at them, you'll see that the first two are identical, the next two are identical and then there are four of the same and then there are three of the same; do you see that.

HIS HONOUR: That makes 11, Mr Borick.

A. Yes, I think that is 11 and I'm not sure -

HIS HONOUR: 11 and there are only 10.

XXN

Q. We have got two of batch 301751, correct.

A. Yes, I see we're talking about batches, are we? That

helps, yes. That is four of the batch 301751. These all appear to be the same batch.

Q. The photograph shown in the first two in the pile are clearly the same photographs; are they.

A. The same photographs?

Q. Yes, showing the same thing.

A. Yes, they all show the same thing. These ones?

Q. The first two, they show the same thing. They're the same photograph.

A. I don't believe so. If you look down the bottom, the blots are labelled differently and so they're not the same strips - what we call strips. On the first one the strip number is indistinct, I acknowledge, but I think they range from 81, I think we established this morning, through to perhaps 100, I think, whereas, on the second, they go from 1-14.

HIS HONOUR: They have all got the same - they are all the same, except they're different strips.

MR BORICK: The first two in the group, HIV-1 WB batch: 301751, that is identical on the next one I'm holding.

A. That refers to the batch of manufacture -

MR BORICK: Hang on. Down the side, they are the same numbers -

HIS HONOUR: They are all that on every copy.

MR BORICK: But the photographs are the same. If you look at the third one they're clearly different.

MS MCDONALD: The confusion might be creeping in because these weren't stapled, they were loose. Mr Borick is right that there does appear to be two copies of the same thing but it doesn't necessarily follow that his are in the correct order now, in the same order as everyone else's.

HIS HONOUR: I'm not sure what you're talking about. Have a look at the actual exhibits. If you look at the actual exhibit, every picture specifies them and the other proteins are all the same. The only difference I can see is in the strip numbers.

MR BORICK: You're missing my point.

HIS HONOUR: I think the witness is too.

MR BORICK: It is my fault. I will try and get it right.

XXN

Q. Looking at this one I am holding, you can see it from here. I will hold up another one with this hand. Forget all the numbers and look at the photo. They're different, aren't they? That photo is different to that photo.

A. Yes, they're different bands, different day, a different run, yes.

Q. In my same hand, if I just show you now that photo, that is the same as the one underneath now, isn't it; same photograph.

A. I would have to look at the strip numbers. It may have been sent twice.

Q. That is what I was trying to find out. Some have been sent twice and some have been sent four times.

A. Yes, they are the same, I agree with you.

HIS HONOUR

Q. Looking at the exhibit that I hand to you, could you just tell me if there are any duplicates in the actual exhibit of the 10 pictures that we have got. It might be easier if we just staple them and number the pages, so we can identify exactly what we're talking about.

A. Yes, I believe this one is duplicated.

Q. I will get my associate to staple it and number the pages so you can tell us what pages are duplicated.

A. I haven't seen these pictures before today.

Q. You said that when you gave your evidence. It is not a criticism, I just want to get it identified.

DOCUMENT SHOWN TO COUNSEL

MR BORICK: They are not in the order of the duplication.

HIS HONOUR: I will get the witness to indicate to the court which, on the exhibit, are duplicates and you can work off the exhibit itself, if you want to.

MR BORICK: If we could tidy this up.

HIS HONOUR: Let the witness tell us which are duplicates, just so we can get that on the record and you can go on.

A. In the lab, we wouldn't be allowed to do this, we would have to have a proper checker. I don't have my checker with me.

HIS HONOUR

Q. Could you tell us what pages have been duplicated.

A. 1 and 8 are duplicated, 4 and 7 are duplicates of the same blots, 2, 5 and 10 are all the same and 3, 6 and 9 are the same. There are, in fact, only four different blots there and I apologise that I didn't know that but I just asked the lab to send pictures, so I didn't have any idea. There are actually four different pictures there.

XXN

Q. They have all got the same batch number on them, if that is right. What does the batch number refer to.

A. That refers to the production of the gel. The batch will be when the gels were all made together.

Q. There is a reference to a run number.

A. Yes.

Q. What does that mean.

A. The run number will be the date that the gel was run or, if there was more than one run, that would refer to the run but you can see the dates are on here: 10/1/07, 23/11/06 and so on.

Q. The run of numbers on this one, along the bottom, looks like it ranges from 81 and goes through to 100.

A. I believe that is correct.

Q. What do those numbers refer to.

A. That is the strip number so we can keep track of which strips run in order. During the process of running the Western blot, the strips are in fact incubated in a buffer bath and then they are lifted out again, so they have to be numbered so that they can be correctly placed in order.

Q. By using those numbers on the bottom row and still in the same one I'm looking at, could you tell me which are the controls that you spoke about, there was a positive control and a negative control.

A. I can't tell you absolutely because they are not numbered as such. I would have to go back to the work sheet to be able tell you that correctly, but I am anticipating that if you look at sheet No.1, the date it's run is 10/1/07, is that correct?

Q. Yes.

A. I anticipate that strip 31 is a negative control because you can't see that.

Q. Strip 81.

A. 81, I beg your pardon, or it could be strip 84. Neither of those show bands. I anticipate that strip 82 is the diluted control and strip 83 is the positive control or the ones on the right, No.99 is the negative control and 100 is the positive control, but I cannot tell you without the work sheet because every time we run a western blot, those strip numbers are detailed on the work sheet with the identification, the bar codes of the samples and so on, and everything is double-checked by a second technician so that we don't get them mixed up. Is that where you were going towards?

Q. Yes. I just wanted to understand what I've been given. What was your purpose in producing these photographs.

A. Because I thought that that might be helpful to people in the court because there had been so many diagrams of western blots showing that they were very rigid and I want people to understand that these western blots are not necessarily rigid. They are not easy all the time to read, that's why they are conducted in specialised laboratories and there's no 'the' western blot. This happens to be an example of a western blot, and that means a generic type western blot.

Q. You have referred in your evidence to patterns which emerge from the western blot test. By using the first photograph can you explain why you mean by a pattern.

A. Well, most of these are western blot positive examples, but if you look at strip No.82, if you look very carefully, and I would not want to be held to this because these are not western blots per se but pictures of them quite obviously, but if you look very carefully with an experienced eye, you can see a plus minus band at P18, one plus band at P24, a plus minus GP41 and perhaps there's another band that's non-specific just above the P68 band. Those are non-specific bands except for the P24. If only the P24 were present, we would not say that were a positive blot, even though we know that reactivity at that point in the band is characteristic or can be characteristic of HIV infection in combination with other bands; in combination with other bands. In Australia we say that if we want to be absolutely sure that someone is HIV positive, that combination of bands must be the glycoproteins and on this particular western blot the only glycoprotein that is shown is the GP41 so you would have to have that GP41 present plus other bands. Let's look at strip No.87. That's right above the N on the run. You can see that in this particular gel 87, I will classify that for you according to the picture, at P18 there's a plus one, at P24 there is a plus 3, at P31 there is a plus minus, at P34 there's plus, probably plus 23 to 3. GP you can see is a spread band and we know that because the glycoproteins don't run in the gel exactly as a band. That is a plus 3 I would think on this gel. P53 is present at plus 2, P68 would be a plus 2 and the bands above, I can't tell you exactly which bands but that band is also present. So if I were reading band No.87, I would say we had a glycoprotein clearly present, glycoprotein band plus three other specific bands, P68, P53, P34 and also P24, so there's five bands - four, but it meets the criteria that we have set out for a positive in that there's a glycoprotein band and three others.

Q. I understand the numbers, but I'm uncertain still what you mean by 'pattern'.

A. What I mean by 'pattern' is if you were reading these and you were looking at the bands, you would see a pattern that you get used to, and I would suggest to the court that if you were looking at those blots, you would see that there is a pattern involved that the glycoproteins are present in those that are positive, plus other bands, and it becomes a pattern, but the criteria themselves, they must meet that pattern, or that group you could say, a grouping of bands, to be called positive.

Q. Does it mean that each time you want to label a WB test as positive, you should be looking at the same positive person.

A. No. It means that if you were to diagnose a western blot as a positive pattern, you would have to have a glycoprotein band present on the gel plus three other viral specific bands. One of the reasons I was showing you this was because usually when a person has been exposed to the virus and mounted an antibody response, they will deliver a pattern on the gel or bands on the gel that, in fact, show all the bands being present. It's very uncommon for you not to show a full complement of bands except early in infection before the antibody responses develop. On the other hand, I might just add that when someone is very ill, and the immune system is decaying, sometimes it's possible for the P24 to decrease, so it's possible if somebody is very ill that you will have glycoprotein bands and the core bands will decrease, and the earlier less sensitive blots, in fact those P24 bands could be absent, but that's not so in the more sensitive bands that are available today.

Q. In the report that you have provided to the court you opened it by saying 'The evidence presented by Mrs Papadopulos-Eleopulos and Dr Val Turner possibly is true for some particular points, but was widely out of context and often incomplete'. I am wondering if we could try and find some common ground. Could you indicate what you say about the evidence which is

possibly true for some particular points. I put it badly. You say 'possibly is true for some particular points'.

A. I think if we went through the entire transcript we could come to points that they have delivered, but I find a lot of the delivery of the points that they make sort of half truths, quite frankly, so they don't deliver the full picture. It's like what I was talking about the world is flat this morning; that information is incomplete, so some of the information in the transcript that I have read starts off to be true, if you like, but then is cordoned off from the vast amount of information and evidence that's available, scientific evidence, not court evidence, it's cordoned off so you don't get the whole truth so, yes, they start off from something that may have been true, but they don't develop it. I would think we would be here for the rest of the day if we went through the transcript and chose little bits of those sort of examples.

Q. I really wanted you to think of some bigger issues. One big issue in this case is whether the HIV virus was ever isolated.

A. I don't think that is correct, no. I think that's one where the witnesses are frankly incorrect.

Q. So that's not something that could possibly be true, it's just plainly wrong.

A. It is wrong.

Q. You know they have held that view ever since 1983.

A. Yes. Unfortunately, it may have been true in part in 1983 but they have not moved on. It was very difficult in the beginning when the virus was isolated to be absolutely sure because we didn't have all the tools available, we didn't have the information -

Q. I think -

OBJECTION: MS MCDONALD OBJECTS

HIS HONOUR

Q. Please finish your answer.

A. When we didn't have all the tools available etc there

may have been areas where it was difficult to have a complete picture, if you like, but we have moved on. I think we should all move on.

XXN

Q. In the context of talking about transmission by blood you say 'Thus on this evidence alone scientific media and public opinion is overwhelmingly in favour that HIV testing defines the presence of the HIV'.

A. I believe that to be true.

Q. Do you understand from our point of view, the defence point of view, we are not interested in media opinion or public opinion, we are interested in scientific opinion; you appreciate that.

A. Yes, of course, I absolutely appreciate it.

Q. I take it we've got some common ground.

A. Yes, I think we do.

Q. We are not going to talk about he's silly or not silly, we are talking about science; you comfortable with that.

A. Absolutely, go right ahead.

Q. Let's go back to the starting point. What is a virus, define a virus for me.

A. Again, I'm not a virologist so this might not be a virologist's true definition, but I see a virus as an infectious particle that can be defined, isolated and tracked one way or another. It doesn't have to be one specific way. There are many techniques available to define virus existence, so it would be something like that.

Q. Firstly, you agree that it's a particle.

A. Yes, viruses are, if you like, particles. It depends how you define a particle but yes, they are an infectious particle.

Q. It is not merely a protein or a piece of RNA or DNA and it's an antibody, it's a particle.

A. Sorry, it's not?

Q. It is not merely a protein or piece of RNA or piece of DNA and it is an antibody, it is a particle.

A. It's a combination of those things, except the antibody.

A virus has to have a way to propagate so it would have to have some genetic material, and how it's packaged varies from virus to virus. There's lots of different ways viral particles are packaged and each of their proteins is different and each of their genetic makeup differs between viruses.

Q. How does a scientist prove the existence of a virus.

A. Well, again, as I said before, there are a number of ways. For example, the hepatitis C virus has not until very recently been seen. It was defined by isolating genetic material in the blood because it was clear that there was an agent causing hepatitis. That sequence was known before the virus was ever purified or seen, but there's very good evidence that HIV exists because the non-A non-B hepatitis that used to be transmitted by blood transfusion once hepatitis C testing was introduced was no longer seen. On the other hand, it may be the virus was seen down the microscope somehow in a situation where people were looking at tissues or cultures. It may be that the virus is isolated because there is a disease that has previously been not seen, for instance, the HIV 1 flu which we know to be flu but we had to then cone down and fine down the specific virus so that was done microbiologically I believe, so there's numbers of ways that it - there's many ways. I think we covered that this morning.

Q. That's a fairly long answer but could you define what you mean by 'virus isolation'.

A. I'm not sure that I mean anything particularly by 'virus isolation'. I mean that you can see in a preparation, whatever that might be, a virus particle that fulfills the criteria that you have suggested that has particular protein composition, that perhaps can be seen by electron microscope, that perhaps can be cultured, that perhaps can be taken from that preparation and propagated in a culture, all those things listed by Professor Cooper last week.

Q. So when I ask you if you could tell me in your opinion

what is meant by the expression 'virus isolation', you would defer to Professor Cooper or Dr Dwyer, would you.

A. As I said before, I'm not actually a virologist, but if I were to purify a virus, I would go about it through using the myriad series of methods that are available to put a virus into a place where you could see it; you could propagate it, you could characterise it morphologically and genetically. I am not sure what you're getting at, I'm sorry. Are you asking me what experiments I would have performed?

Q. I am going to put to you that the virus has never been isolated; that's our case.

A. I'm sorry that that's your case.

Q. You don't have to be sorry about anything. I just want to be sure that when you use the term 'virus isolation' and when I use it we are hopefully talking about the same thing, so I'm asking you to tell me what in your opinion is meant by the expression 'virus isolation', and if you prefer not to give an opinion because you are not a virologist, I accept that.

A. If I as a scientist and a medico were asked has the HIV been purified, I would say from the literature you can clearly see that you can grow this virus in tissue culture, you then take the particle cells, you can electro -

Q. I'm sorry to interrupt you, I want you to answer the question.

OBJECTION: MS MCDONALD OBJECTS

HIS HONOUR: I will let Dr Dax complete her answer. Mr Borick, I think the best thing is let Dr Dax complete her answer. If you say her answer is not acceptable to the question, then you can ask her again.

Q. So, Dr Dax, would you complete your answer.

A. Yes.

XXN

Q. Would you like me to refresh your memory.

A. Yes.

Q. I will put it very precisely. What in your opinion,

underlying your opinion, is meant by the expression 'virus isolation'. I am not talking about any specific virus.

A. In my opinion, it means that you can take a virus and you can recognise it as an entity, a particulate viral entity. Is that what you want me to say?

HIS HONOUR

Q. You just give your answer. If Mr Borick wants you to expand on it or he's not satisfied with it or I would like to understand it, we'll ask the next question.

A. Thank you.

Q. Witnesses, if they try and second-guess counsel, get terribly confused because sometimes counsel don't know what they are asking.

A. I am finding it difficult to define where we are going.

Q. Don't worry about where we are going. Let counsel worry about where we are going. Eventually I have to worry about where we are going.

XXN

Q. How do you recognise it. You have defined it as something you can recognise; how do you recognise it.

A. There might be - as I said before, there's numbers of ways to recognise that particular virus. First of all, you might take somebody - if you think that a person or an animal were infected with that virus, you might draw blood and look for antibodies, for example.

CONTINUED

You may take that virus, treat it and sequence it, and that will be the most highly accepted way of identifying a sequence that was unique, new, different, if we are talking about a different virus. We would compare that virus with sequences of other viruses that have been banked in data bases to see if it related to other viruses, we would perhaps do the morphology so you could see them. I mean I think we - I sort of feel we are getting circular here.

Q. Well, you can recognise a virus by having a photograph of it; that's right.

A. You may be able to, yes, and I've said, again I'm not a virologist, nor am I a morphologist so it would be very difficult for me to recognise a new virus on electron micrograph just because it was supposedly isolated, without any other information. I suppose if I were a virologist I would not take a single criterion for establishing a new virus, I would take a multiple look at it, I think most virologists would.

Q. So from the point of view of a virologist, morphologist, you'd want to see a photograph of it if you could, you'd like to measure it, all those things.

A. I guess so, yes.

Q. Anything else you can think of.

A. Well, I mean sequencing is certainly the most important these days but I think you would look at - it would depend on the virus that you were looking at, you know where would you be going with it, what would be its epidemiology, what disease patterns were caused by it, what clinical associations might it have.

Q. In a paper you published in December 2004, Advances in Laboratory Testing for HIV, you say that 'The ELISA antibody tests were developed and first implemented soon after the discovery of HIV as the aetiological factor for the development of the acquired immune deficiency syndrome; in other words, AIDS' dropping there for a minute. You agree that that's what you wrote.

A. Yes, I suspect you are reading out of a paper I don't

have in front of me.

HIS HONOUR: It might be desirable to give the witness the paper or at least put the paper in front of the witness Mr Borick.

XXN

Q. Yes, I will hand you a copy of the paper.

HIS HONOUR: Can you just identify it for me please?

A. Does it have a submission identified? Mine just says 'Defence copy slide 38 antibody'. It's a review article.

XXN

Q. I'm sorry have you found the passage.

A. Yes, thank you, it's marked, it says 'Anti HIV. Immunoassays - not a licence - were developed and first implemented in HIV soon after the discovery of the HIV as the aetiological factor for the development of acquired immunodeficiency syndrome, AIDS', yes.

Q. Would you agree that you cited Montagnier's 1983 paper in support of that claim.

A. If that's what reference No.6 says, yes. Yes, that's the science paper in 1983, yes.

Q. What evidence in the Montagnier paper, which you have cited, convinced you that Montagnier had proved that HIV is the cause of AIDS.

A. Well, this is the accepted reference, this is the accepted seminal reference for the isolation of HIV and it refers to the isolation of a virus, 'the virus', that is associated with people who had acquired immunodeficiency disease. So I think that that's an accepted reference as the basic isolation. I could have cited many others but when you produce a scientific paper you try and go back to the fundamental reference and this is the accepted fundamental reference.

Q. What I was really asking you was if you let us know what evidence did Montagnier produce which convinced you, you Dr Dax, that Montagnier proved HIV as a cause of AIDS.

A. Well I can't tell you exactly what's in that paper that convinced me, it's an accepted reference, it's the

accepted seminal reference and there's many other references that could have been quoted subsequently, including the Gallo papers and onward. So, I mean, the methodology is standard.

Q. What evidence in the Montagnier paper you cited convinced you that Montagnier had proved the existence of HIV.

A. Well I think that, as I said, they are using methods, accepted methods for that and it was the most probable reference at that time and it was proven to be right and as I say, we went back and that's the seminal reference that's quoted.

Q. In the report which you provided to the court you had some general comments and then you came to a heading 'Synopsis of HIV testing'; have you got your report there.

A. No, I don't.

HIS HONOUR: What page Mr Borick?

MR BORICK: First page.

XXN

Q. See the heading 'Synopsis of HIV testing'.

HIS HONOUR: P.1, the bottom of the page.

A. Yes.

XXN

Q. You say there that 'Since the HIV was isolated in 1983, and subsequently immunological tests were developed by 1985, use of immunology for diagnosis and screening has been widely accepted'.

A. That's correct.

Q. There can be no doubt about the opening words of that sentence 'Since HIV was isolated in 1983' I take it you meant what you said by that.

A. Certainly.

Q. In your evidence this morning when you were asked about HIV isolation, I don't have the exact transcript so I can't give the exact words to you - this is what you said and I'm reading from p.856. I will start with line 13 'At first in 1985 the antigen was made from cellular

preparations of HIV. So when the tests were put together and the antibody was put on the plate to capture the antibody in the blood, there were a lot of other proteins involved, cellular proteins, because the virus was not isolated at that time, it was made from these cultures'. Accept what you said this morning.

A. I accept what I said if that's in the transcript, absolutely, but I think you read into it something that I didn't mean. What I meant was that the virus was not purified each time when it went onto the test preparations, it was not recognised how important it was to split up those cellular proteins and this was a very early time, it was very new but it became very clear very quickly that we had to do better in terms of purifying the virus to use as the basic protein. I think what you're reading into that is confusing the issue of viral isolation, such as you're talking about, and preparation of virus to place on the tests and I think that's a confusing issue and it's probably slightly looser language than I would have attributed to that statement.

Q. I was careful in my question as to use the expression 'isolation' I did not use the word 'purification' at all. It was in the context of virus isolation that I put the report to you and I put your evidence to you. My question to you, is not the statement in the report 'Since HIV was isolated in 1983' inconsistent with the evidence you gave to the court this morning that HIV was still not isolated in 1985.

A. No, it's not, and the reason is because in 1983 the virus was isolated in such a way as I've been trying to describe to you using all those techniques that indicate a virus is there. When I was talking this morning about the development of the tests we were talking about the material that was put into the test wells or onto the Western Blots and at that early time to put that material onto those tests that material was not isolated or the virus purified, it was grown in some culture and

then probably purified to some extent but not completely so there was just no cellular protein, that is actually not probably entirely possible but it did make for non-specificity in the tests at the early time, that's true. So, no, I'm sorry Mr Borick but you are confusing my words and the way they are applied to different techniques and different situations. So I'm sorry you can't tie them up that way, it's not sensible. That's like saying a word only has one meaning, I'm sorry but words have more than one meaning in the English language, and so it's a different situation, you are trying to apply a blanket meaning to the term 'isolation' and I don't accept that I'm sorry.

Q. Have you read the evidence given to this court by Ms Papadopulos, where she described Montagnier's tests exactly as he carried them out and then she gave a series of criticisms of his tests. Have you read her evidence on that topic.

A. Yes, I have read it but I'm sorry I don't really understand it and I can't reiterate it to you and I also - I have looked at that in the past and, again, this may be one of those sort of half truths but I think what's really crucial here is that many people went on to isolate the virus to prove that the virus existed by many other techniques add I just don't see the relevance of harping back to that one paper, even though it's an accepted reference, as the first group of people that actually isolated the virus.

Q. I'm not harping back to it, it's the paper which you cited in support of your proposition that HIV causes AIDS and -

A. It's the paper that I cited that HIV was isolated.

Q. And that HIV causes AIDS.

A. No -

Q. You cited him on it.

A. I think if you again will go back to the quote and I think you read it more than one way 'Immunoassays were developed and first implemented in 1985 soon after the

discovery of HIV, and as the aetiological factor for the development of acquired immune deficiency syndrome'. Well that would be the starting point, taking virus or taking tissues from people who had acquired immunodeficiency. That was what I tried to explain to you earlier when you asked me how would I isolate a virus, one of the ways I do it is go back to people who had an illness that we thought might be attributed to a virus, and so here it was clear since 1981 when the syndrome was described that something was causing it, and in 1983 both Montagnier and Gallo put that all together and found the same virus or a virus with very similar characteristics.

Q. Are you able to make any comment at all upon Mrs Papadopulos's explanation of the tests which Montagnier carried out.

A. No, I'm sorry I'm not.

Q. And I take it it follows that you're not able to make any comment on the criticisms that Mrs Papadopulos advanced to this court on Montagnier's tests.

A. No I'm not at the moment.

Q. Is the expression 'reverse transcription' one with which you are familiar.

A. Yes, it's a term I'm familiar with, yes.

Q. Did Montagnier have anything to say about reverse transcription.

A. In that particular paper?

Q. Yes.

A. I expect he did, yes. It's a pity we haven't got one in front of me, I don't have one, but I expect he did.

Q. Is reverse transcription specific to retroviruses or -

A. Yes, reverse transcription is characteristic of those particular group of viruses, the retroviruses, yes, but -

Q. Would you accept that Montagnier said that the particles he saw, the photographs were typical type-C particles. Would you agree that's what he described them as.

HIS HONOUR: Mr Borick, have we got that paper because

I think if you are asking the witness to comment on a paper by Montagnier, it's fair to the witness that she should at lest have a copy of the paper in front of her.

CONTINUED

MR BORICK: We will get it, your Honour. I had thought because she cited it in her very recent article that she would be familiar with it.

HIS HONOUR: I don't know that you can presume that. If you ask me about judgments I had cited in recent judgments I don't think I would be able to tell you exactly what was in them. I might be able to tell you generally so it perhaps might be an idea if the witness had the paper.

XXN

Q. Do you agree that all the mainstream experts say that HIV is a Legge virus with a typical conical shaped cord.

A. That would be a usual description of the virus yes.

Q. It certainly could not be described as a typical type C particle. Do you agree with that.

A. I'm sorry, I don't know. As I told you, I'm not a virologist and I'm not sure what virologist call type C particles altogether.

Q. Have you published anywhere that HIV has a type D cylindrical nucleocapsid core.

A. I'm sure I have because that's what you're suggesting but it's not something that would immediately spring to mind, no. This is virology. It's not to do with testing per se and I am really not an expert virologist although I know peripherally some virology but to do with the integrity of the tests, not their structure function or minute biochemistry.

Q. We can refer these questions then to Dr Dwyer, is that right.

A. Possibly.

Q. Would you agree that viruses only grow in cells.

A. Under normal circumstances, that's true.

Q. What do you mean by 'normal circumstances'.

A. Infection, yes, they grow in cells.

Q. Would you agree that to obtain viral proteins or RNA the virus must first be purified.

A. No, I don't agree with that because you can find fragments of RNA in the plasma that are not cell or

virus associated and this has been one of the contentions about viral load that the viral load doesn't altogether reflect the actual number of particles in the plasma but overall the viral load gives you an indication of how active the virus is in the body.

Q. Are you aware that Montagnier claimed to have purified the virus back in 1983.

A. According to his papers you mean?

Q. Yes.

A. I don't know the details of that purification. I could look at the paper and assess that but, yes.

Q. It is within your knowledge at the moment common knowledge that in the purified virus he said he had found three proteins P24, P25, now known as 41, and P80 which reacted with antibodies and patient serum. Does that sound right.

A. Yes.

Q. Are you aware that he claimed P24 to be HIV but not the others.

A. No, but I could -

Q. You can accept that.

A. Yes, I can accept that because when we talk about proteins having particular molecular weights there are many proteins of similar molecular weights.

Q. Would not the presence of non protein suggest that the virus was not purified or, rather, indicate that the virus was not purified.

A. If you wanted the virus there with absolutely nothing else I suppose you could make that definition but one of the diagrams I showed you this morning showed you the virus is, as part of its clever avoidance of the immune system, budded with the human protein, so I think that might be quite difficult. I don't know what those proteins might have been or how they were purified or the molecular markets etc. etc. but it's possible that they were not. I can't tell you. They may not have been antibody reactive; I think that's what you are saying.

Q. Are you aware in 1997 Montagnier admitted that he had not purified the virus.

A. I have read that.

Q. Do you accept that is what he said to the French journalist.

A. I don't know that but I accept that if you say so.

Q. Are you also aware that in the material he called purified virus that is in 1983 he did not have any particles with the morphology of retroviruses.

A. I really would like to see the material. Again it's not the type of literature I am particularly familiar with and I'm not sure which paper we're quoting or where we're coming from.

Q. In your evidence this morning when you spoke about the virus not being isolated you -

A. This is to do with putting material on the test in the first instance. We are not talking about purifying the virus or isolating it, whichever one you want to use, I think those terms are interchangeable perhaps.

Q. In evidence this morning you spoke of 1985, the problem was the additive was made from cellular preparations of HIV.

A. Yes.

Q. That was the problem with purification, wasn't it because -

A. It was the problem with finding material to put on the tests that had purity that would not offer any non-specific testing. It has nothing to do with isolation of the virus and the type of questions you have been asking me per se. It has to do with the specificity of the tests and I think we need to separate those two lines of argument.

Q. If you want a purified virus you can't have any cellular debris in it and still say it's purified.

A. That's semantics quite frankly, that's semantics, because if you want to have a preparation there where you say there is a virus there you can identify etc. then you can say you have isolated the virus perhaps,

but if you want to have the absolute crude chemicals that make up that virus perhaps you will have to go further with your purification, use different methods, use affinity columns and so on but I don't see that ties up necessarily what I was saying this morning about materials deliberately put on the tests that delivered non-specificity because it was grown in human cells. We knew what the virus was, that we had to take that virus and grow it up in human cells to make sensitive tests so we can identify people who had been exposed but I can't see that twisting that to whether the virus is absolutely pure in Montagnier's hands or Gallo's hands or anybody else's hands has relevance to the specificity of the test, I simply don't see that.

Q. Since the first tests were based on Gallo, how do you know in the test kits the antigens are HIV proteins.

A. It was based not on the proteins but the background of the virus that was isolated by those workers, which there weren't only those two experiments. There was a raft of clinical information. There was lots of people who had been infected with the virus. We talk about blood transfusion. We know that if you have those particles in your blood and you transfuse your blood to somebody else that that person will become infected etc.

Q. Do you agree antibodies induced by one protein can react with another protein or proteins known as cross-reactions.

A. That is a possibility but also I would cite that over the years that these possibilities have been absolutely minimised in that the way the tests are set up, in the way they are conducted and in the choice of antigens on the plate, so that you are looking at highly specific combinations.

Q. You agree with the proposition that antibodies induced by one protein can react with another protein or protein.

A. In certain circumstances that's true.

Q. If that happens that can result in false positive tests.

A. Yes, that's also true but please let's talk about statistics and it does occur but it's in a very small proportion of tests.

Q. Is it the fact that cross-reactions exist that is distinguishing truth and false tests are the bugbear of virology are a serious problem.

A. Yes, it is a problem that there is non-specific binding in immunological tests and that is why we have created a raft of other tests so that those very few tests and again I emphasise that the number of tests that demonstrate false reactivities are minimal, they are really very small, these tests are extraordinary specificity and that's why we have a system of labs in this country from screening labs to reference labs and a national reference labs so we have a system to define the non-specificity.

Q. Can you explain how a scientist distinguishes between cross-reactions and a true reactions.

A. I think I already have. I think I explained to you this morning about strategies, testing strategies, evaluated kits, using those properly in situations where there's quality management systems, checking systems, etc., that there are other methods available, that we can check for instance the RNA in the plasma or the DNA in the cells etc. so I think we have pretty much covered that.

Q. Yes but as I understand you, you are talking about what other people have told you as how this is done, you yourself.

A. No, that is my job, that is my job, that is really what I do or part of what I do is to make sure that these tests only exhibit very small minimal false reactive reactions and only allow into the country on our lab's recommendations those that have minimal non-specific binding, that is high specificity and to seek in numbers of samples the possibility that those tests will deliver false reactive results and we exclude those that give high possibility of those giving non-specific results and then we guide the labs in using a body of data to

make sure that those labs follow protocols that can be used to distinguish true from false reactivity.

Q. What you are saying as I understand it is that the HIV antibody tests are validated and are highly specific.

A. Yes.

Q. You state you pretty well say that in your report to the court, don't you.

A. I do.

Q. Does your report contain any proof of the validation of the high specificity you are referring to.

A. My report but no not particularly, but my laboratory publishes every evaluation in our newsletter of the evaluations we conduct for the blood service, those evaluations must demonstrate specificity greater than 99.97% something like that and for diagnostic labs the specificity is less, don't make me go into that but it can be a little bit less but I have also told you that in Australia we monitor the specificity of the tests used in the blood and we did until recently monitor the specificity of the tests used in diagnostic laboratories and found those to be less than 99% in all cases and in the blood service it's more or less 99.9% specific for the HIV tests. They of course are the selected population who have been selected because they are donors.

Q. You have talked about tests in South Australia and rafts of tests what proof is there of validation of a high specificity of the antibody test, specific terms.

A. I thought we were talking about science here.

Q. Yes.

A. So we are talking about numbers, proof, scientific information, so in Australia there are annually around a million donations made that are all tested for HIV, every single one of those donations of tested for HIV so that gives you numbers. Of those that are reactive which are less than say .2%, they are found to have non-specific reactivity so it's a very small number. If we put those .2% on western blots or we follow them with

other supplemental tests we find that the binding in those very few numbers is non-specific, that is, we cannot define exactly why those sera react in the tests. We don't know the answer to that. It may be because there are other antibodies that cross-react with the protein. It may be because the person has an infection against antibodies but by and large we don't really know.

Q. Highly specific means that there are few false positives.

A. That's correct.

Q. Is a false positive a positive test that occurs at the absence of HIV.

A. It's a reactive test and just because it's reactive on one test doesn't mean it's reactive on another, that's exactly why we have testing strategies to demonstrate reactivity on one test and demonstrate it's lack of reactivity in the next one.

Q. Do you agree a false positive is the reactive which occurs in HIV.

A. No, because we don't talk about positive tests, in first screen we talk about reactive for exactly that reason, we don't talk about positive first tests because that can give the wrong impression to physicians or other people that that first test is then truly possible because obviously it is a sensitive diagnosis and you don't want to make a mistake so no, I do not agree with that because it is not one of the terminologies we use.

Q. One of the main test is the ELISA test.

A. That's not true, we don't use it anymore.

Q. It used to be millions of people were tested as positive on the ELISA test.

A. That's very true.

Q. That means there is a very good chance millions of people have been diagnosed incorrectly.

A. I disagree with that absolutely and entirely, absolutely and entirely.

HIS HONOUR

Q. Why do you disagree with that.

A. We are talking about a very small rate followed by subsequent testing which sorts that out so we would not make a diagnosis just because one test was reactive and we would follow any reactive test with supplemented testing that sorts out the two, so many people may have been diagnosed and not millions, we are talking about Australia because there aren't millions of people with HIV positive in Australia but many would have been tested internationally using ELISA in the early tests but that is exactly why we have two tests because the likelihood of two tests being reactive in a person who is falsely reactive in the first round is very low.

CONTINUED

Q. Before everything improved, in the bad old days, instead of what's happening now, lots and lots of people got diagnosed as having been HIV-positive on the strength of one ELISA test.

A. I think that's a half truth, I don't think lots and lots of people did. Some people did, it's true, but we very quickly wised up that this was not the way to go about it and, I mean, very quickly.

Q. Isn't it true, in the world today, there are still countries and jurisdictions where one ELISA test is sufficient -

A. I don't know.

Q. - as a test of positive.

A. I don't know of anywhere.

Q. Papua New Guinea.

A. That's not true. In Papua New Guinea, I set up the testing system in 1993 on a very strict regime of supplemental testing. The Central Public Health Laboratory in Port Moresby was trained to do Western blots - they don't do them very well. When they were first trained they used to send every sample to us as checked, so it was double checked, and now Papua New Guinea is changing because of the situation I described this morning. Papua New Guinea is becoming a highly prevalent area. The population has a greater than 2-3% prevalence of HIV and maybe more. That's what we know about. They are using rapid tests now and the minister of health, who I was speaking to last week, is looking more and more to having two rabbit tests available, so that they can actually diagnose more quickly and role out antiretroviral therapy. In Papua New Guinea, in fact, they did not use the ELISA widely, they used particle agglutination assays, which is another platform that works very well in tropical countries, so I reject that statement entirely.

Q. We could look for the numbers elsewhere but, in general terms, would you agree that if people were diagnosed

HIV-positive on the basis of a single ELISA test, there is a very strong risk of false diagnosis.

A. No, I would not because I have explained to you about positive predictive value, so you would not be able to estimate in any given population - generally you would have to go to populations and the specificity of the test being used, you would have to know that and the specificity of the algorithm. Algorithms are set up so the sensitivity and specificity is 100%. That is how the algorithms are constructed.

Q. In terms of the isolation in identification of a virus by an antibody test, what has the percentages in the population got to do with that at all. Percentages have got to do with how many people have got HIV, nothing to do with specificity; would you agree with that.

A. No, it hasn't got to do with specificity. I thought I explained that.

Q. Are you agreeing with me, that population trends, or the percent figures you're talking about, have nothing to do with specificity of the ELISA test.

A. The specificity is the characteristic of the test but the chance that that specificity - that the reactivity will represent true or false reactivity certainly changes with populations. In a particular population, the specificity will be characteristic of the test.

Q. How can the specificity of the test be altered by the number of people in the population who are, say gay, homosexual - how can the specificity of the test alter.

A. I don't believe I said that.

Q. That is what you're implying, I am suggesting.

A. It certainly was not and I would plead the court that that be not inferred to me at all. I would not suggest such a thing. I would suggest that if you were testifying in a population where there was high prevalence, that the prediction of your test being truly positive at any one time, if it were reactive, is higher when your prevalence is higher, than if it is not, so this is what we were talking about, again, this morning.

In the general Australian population, the prevalence is very low, therefore, the ratio of truly positive to falsely reactive groups may be relatively high. The chance of your reactive test being false reactive may be higher than the chance of it being truly reactive. That's the positive predictive value, but if the prevalence were high, then the true reactivity would exceed the false reactivity and we know that the specificity of the test gives you a measure of the false reactivity. In this particular population, it is well below 1%. In most countries it is, but in those tropical countries it may be - the specificity may operate at a slightly lower level, depending on what test were used and how it were used. Again, the prevalence might be higher, so the predictive value might be the same.

Q. The specificity is going to vary, the tests are going to vary, according to the number of people in any particular community who are exposed to HIV.

A. No, the predictive value is going to change, not the specificity necessarily, although, it is true, the specificity may vary a little bit between populations. We know that to be true too.

Q. Would you agree with the proposition that a false positive rate of an HIV antibody test should be calculated before the test is introduced into routine clinical practice.

A. I think it should be estimated, yes. It is not a rigid thing. You talk about HIV testing or any testing as though it is rigid. It is not, because populations have different characteristics, that is why we have a valuation system in Australia, so that we can see how these tests operate in Australian people and their plasmas.

Q. Do you recall that Dr Turner drew an analogy between HIV and pregnancy tests.

A. I do.

Q. You say that's a false analogy.

A. I do.

Q. Isn't he simply using the pregnancy test concept to illustrate how one should go about determining the parameters of tests, in general, including specificity.

A. That is what he was trying to do, yes, I believe so, but the analogy is not valid. The reason it is not valid is, also I explained this morning, when you use an HIV test, it may be that that is your only way to make your diagnosis - it is the only port of call - because people, early infection, or blood donors, for example, who may have no signs of infection, they don't have a clinical screening, so those tests have to be received with pregnancy. What usually happens is that there is some indication that the woman might be pregnant but I draw to your attention the Chicago study quite some time ago, where people who came into casualty, as a form of valuation, were given pregnancy tests out the back, there was no history and, under those circumstances, in fact, those tests were highly non-specific. Without that clinical screening, such as we use in HIV screening as the first test, so without the clinical screening, the non-specificity is quite clear and those tests are non-specific. It is apples and oranges because with HIV testing we have very clear cut, high-performing tests, that are used in specific ways and in highly managed systems under clear guidelines, whereas with pregnancy tests, they're used in non-laboratory settings, quite often by untrained people. They're not set up in the same way as HIV tests, which are set up in staged steps, which are very carefully controlled and that is why they are so highly specific and sensitive, whereas pregnancy tests are - it doesn't matter so much if you get it wrong with pregnancy. It may be a personal disappointment or difficulty but it is not a life-threatening situation.

Q. Do you agree with the proposition advanced by Dr Turner in relation to the determination of parameters of tests applied in the valuation of all diagnostic tests, be

they antibody tests or any other tests - for example, heart attack, blood clot on the lungs.

A. I am not quite sure that I understand.

Q. I'm saying that there has to be ways in which diagnostic tests are properly assessed in relation to the establishment of the specificity - any diagnostic test.

A. Yes, I didn't understand what it had to do with blood clots on the lungs, I'm sorry.

Q. I just gave you those as examples.

A. I don't think that was a very good example.

Q. Would you agree that to calculate the false positive rate of an antibody test for HIV, you need a method of determining the presence or absence of HIV.

A. You would need - yes, you would need to have samples that did not exhibit the presence of antibody as your negative controls, yes.

Q. You accept that you do need a method of determining the presence or absence of HIV; that's the starting point.

A. HIV antibody.

Q. I suggest that in determining the presence or absence of HIV is a procedure which must be independent of the antibody test -

A. I think those experiments have been done. I think you're confusing things here. It is clear, from a huge amount of data, that if somebody is exposed to the virus, they develop an antibody response. That can be followed -

Q. First you have to have -

A. That is clear. There is a myriad - a huge amount of evidence to saying that when somebody is exposed they develop an antibody response that can be followed by different tests that have been clearly evaluated to show that antibody is present. In terms of isolating the virus for attributing negative, there's a jump there that is not necessary to make. Yes, we have shown that if you're exposed to the virus you develop an antibody response, therefore, if you want to evaluate a kit in this day and age, you take what you know to be a well

performing test, in a group of people who you do not consider to have been likely to have been exposed to the virus and you call that your anti-HIV negative population, so you collect a lot of those people, as people's plasma, and that is your negative bank. By the same token, there's a whole group of people who you consider to have been exposed, they might have had the risk factors, they might have had positive tests in other areas and they become your positive population. Or you may collect a series of plasmas from people with rheumatoid arthritis, for example, that is shown to make sticky antibodies, or other antibodies that might react in the test or people who have shown false reactivity. They form another group or a group of samples or a panel that you would use. Not everybody would collect these panels, that's why we have the national reference laboratory because we have a huge bank of these samples that we have categorised, put away and have a lot of information about and then when the new test comes, we will put it up against the background of samples, but we could not afford or hope to afford that if there was a virus in every single sample and nor do we do that necessarily to make our anti-HIV-positive diagnoses.

Q. You seem to be suggesting that the antibody test actually diagnose HIV and AIDS.

A. No, AIDS is a clinical diagnosis.

Q. Are you suggesting that the antibody test diagnose HIV.

A. Yes, certainly, the presence of the HIV - exposure to HIV, yes, because people who are not exposed to the HIV do not mount a clear specific response to the tests, such that you get a reactive EIA, followed by whatever supplemental test you might use - a Western blot, an RNA a cellular DNA, a P24 antigen test or whatever.

Q. Don't you need the actual virus before you can start to use any testing process.

A. That was the isolation of the virus way back. Then we go on, once that was isolated, then we could grow that virus.

Q. You can't isolate HIV by an antibody test, can you.

A. You can identify -

Q. Isolate it is the question.

A. No, you can't isolate it - but, well, actually you may be able to. If you can isolate your antibody and put it on a column which is called an affinity column. What you do is you bind the antibody to a gel, a specific gel, using a chemical reaction, then you run your plasma or your cell preparation on these affinity columns several times over, the virus will then bind to the antibody on the affinity column. You will then wash the column and you will end up with a virus preparation. It may not be isolated using exactly the characteristics you want me to describe, but it will be a fairly pure preparation. The reverse of that - the flip side of that - is preparation of plasma products, where they use huge columns and methods of isolation to make sure the virus is removed from the plasma, so that it will not pass on in plasma products which are given to many more people than a blood donation, for example. You can - if you want to follow that line of argument - you could use antibodies to purify your virus, yes.

Q. What is being put to you is that you have to have a procedure totally independent of the antibody test in order to say that you've got a virus and that is generally known as the gold standard.

A. I've read this several times over, this gold standard, and I don't know what gold standard we're searching for here but, it seems to me, that if someone is ill and it can be shown that that person is infected by a series of tests which, in high probability, indicate that person's been exposed to the virus and then, if you really want to go for it, you could take that person, you could isolate that virus or grow that virus. That can be done but it is expensive, it is laborious, it requires specialised facilities where you don't pass the virus and so on. Yes, if you took a person who was antibody-positive, you can, certainly, and that does

happen. The indirect way we look at the virus is the RNA tests or the DNA tests. That is an independent - as far as I can see, that could be called the gold standard or you could call isolation of the virus the gold standard, or, I mean, in an individual patient. I think the gold standard these days is the genomic sequence and that is done for resistance testing, in part, or, if you really want to, you can sequence the virus of a patient in its entirety.

Q. You have prefaced all of that by saying 'if one is ill then they're infected'. What about if a person shows no clinical signs, and we know that happens in millions of cases. What happens in that situation.

A. You can do the same thing again, if that person is found to be anti-HIV-positive. In almost all situations you can do that, it is just we don't do that.

Q. I didn't quite understand what you meant when you said that the gold standard here could be a genome sequence; is that what you said.

A. Well, that could be -

Q. Have I understood you correctly.

A. You could call that your gold standard, yes.

Q. What do you mean by that.

A. I'm struggling to find what you mean by a gold standard. What do you mean by a gold standard? I find that a very difficult concept, in the light of what you have been saying. I don't know what the gold standard is in your terms but, for me, if someone were HIV-positive and I could take that person's plasma or cells and either grow the virus or sequence the virus, I would say that were a gold standard because it is compared with a huge amount of information and data that is beyond that particular patient.

CONTINUED

Q. I will explain it to you as carefully as I can from the point of view of saying you are totally and utterly wrong. You can't take a person say they are HIV positive and then use that to prove that a virus has been isolated; do you understand that. First you must isolate the virus, then you can test the person but you can't assume that for the purpose of isolation that HIV exists; do you understand that. That's what we are putting to you.

A. No I don't think you understand the concept Mr Borick.

Q. I'm doing my best to explain because you said you can't explain what's been put to you. You are getting a bit of an inkling of it.

A. No, sir, I'm sorry I don't understand what you are talking about at all.

Q. What about the expression 'gold standards' itself, what do you understand by that expression. Forget about HIV.

A. Okay so - this is getting a bit ridiculous but what about if you have a metre, you want a metre, so somewhere there is a gold standard a metre, in Geneva, and it's actually now, I understand, a light beam not a physical - so you can't actually touch that gold standard any more but it exists. Now, is there a gold standard that we can touch, that we can see? Well there is because there's the sequence of the virus, which we know has conserved areas and that we can compare and say that's unique to the virus. There are ways we can isolate the virus, there are ways we can examine the virus under a microscope, etc., but I don't know which one you want to choose as the gold standard, I wouldn't be prepared to choose any but all I know is if somebody is found to be HIV positive, anybody, that you can then take that person's tissues or plasma and find the virus. Now I can't see the relevance of why you need somebody else's virus or a gold standard before you perform those myriad of tests. I'm sorry but I'm trying very hard to understand your concept of gold standard and I don't.

Q. Have you heard of it before, as a scientist, you

understand that the term is used in science.

A. I know what it is. Thank you Mr Borick I think I am trained in science and you are not.

Q. What is the gold standard.

A. For a physical measurement it's the litre, the weight, and it is being used in virology probably a little erroneously but I don't think it's something that we ought to spend a long time on because there's so many other ways to look at it and I don't know what you want as a gold standard, what you want me to explain as a gold standard. What I find is if somebody is anti-HIV positive and you take either the tissues, the plasma, the serum, that one way or another you can find the virus. You can find its RNA, you can find the virus with its sequence and so on. And Dr Dwyer's going to have to leave soon but Dr Dwyer might want to elaborate on that.

Q. Have you read the report that Dr Dwyer has provided to this court.

A. No, I have not seen that.

Q. I just want to put the first paragraph so I'll read it to you. Dr Dwyer has told the court that 'Laboratory confirmation of viral infections (and infection caused by any other organism) can be made both directly and indirectly. Direct methods include: isolating, or culturing the virus, or detecting viral genetic material (RNA or DNA), using a range of molecular assays (nucleic acid testing or NAT) from the relevant clinical specimens. The main indirect method of detecting virus infection is virus specific antibody testing. In general, virus isolation and detection of viral genetic material by NAT - nucleic acid testing - are the "gold standard" tests for confirming infection. Although some viruses cannot be readily cultured using current laboratory techniques'. Do you agree with what I read to you from Dr Dwyer's report, it's in effect that antibody tests are an indirect means of diagnosing a virus but virus isolation is a gold standard test for

confirming infection.

A. That could be considered that way certainly. That's what I was trying to intimate to you, that if somebody is exposed to the virus and develops antibodies we know for sure that that person has been exposed to the virus and if we go back then we can do those tests and if you want to take every patient, as we tend to do now anyway, that once somebody has been diagnosed in fact we do look at their genetic testing in their RNA, their nucleic acid testing.

Q. Has the specificities of the various antibodies' tests, the ELISA and the Western Blot tests, been proven by using HIV as a gold standard.

A. Well, when we look at our panels, by and large if you want to make RNA testing your gold standard then in many cases yes because when we collect our specimens to look at our sensitivity, which is what where we use positive samples, we would have the history on those people and they would usually have viral load testing done, but if you are asking about specificity in the negative samples then, no, we would not use RNA testing on every sample because the Commonwealth would not grant a budget to do that, it's impractical. But at the same time if we were to evaluate an RNA test, then we would use that RNA test in those same samples and not get an answer. So there's ways to check that if you like, but every sample that we put into a specificity evaluation would not then have an RNA test or be, you know, we wouldn't attempt to isolate the virus, no. There is no way we could afford the time or the money. We don't have the resources to do that.

Q. You are aware of an organisation called Abbott Laboratories.

A. Diagnostics, yes.

Q. They are manufacturers of the HIV test kit packets.

A. Yes, they have actually just been sold.

Q. In their test kit packet inserts, and we have the documents been tendered in this courtroom, there is an insert which says 'At present, there is no recognised

standard for determining the presence or absence of HIV 1 antibodies in human blood'. Are you aware of that insert.

A. Yes, I've seen that insert.

Q. What is your interpretation of that statement.

A. I think there is all sorts of things that companies have to do to protect themselves and I don't think this relates to gold standards that you're looking for. All it says is if you want to compare the result that you get in an Abbott HIV 1/2 go AXSYM, that you can't immediately compare it to a result that's a tangible, you know, hands-on result like you seem to want to be able to. There are now antibody standards available since that was written, the National Institute of Biological Standards in the UK do make antibody standards that you can purchase and in a particular test you would expect those standards to deliver a given sample: cut-off ratio, so in a sense that is a standard that you can use to see if you are in the ballpark of the same value that other people get for that standard. I would also submit that in Australia we have a system that looks at standard samples that are sent out to every HIV testing lab in the country. Those quality controls, so-called, are delivered to the labs on an annual or semiannual basis and the labs can put in the results in that standard sample every single time they make a run of the assay. So we know the mean and standard on that particular sample in every laboratory on the sample, we can see how it varies from day-to-day and we can follow that because the results come up instantly through the Internet and if they are out of whack - if they are out of the mean to standard deviations we call the laboratory and say 'Would you like to examine your system you seem to have aberrant results for the last few runs' or something like that. So that's kept - in Australia we keep a very close watch on the laboratories in that fashion. So Abbott Diagnostics don't have a system like that but they have

been pestering us for many years to give them the data that we have that could provide them with that information.

Q. The question was this: the incidence in the test kit packet reads 'At present, there is no recognised standard for determining the presence or absence of HIV 1 antibodies in human blood'. That's pretty straightforward, you agree. It's set out very clearly 'No recognised standard for determining the presence or absence of HIV 1 antibodies in blood'. Simple enough. As director of NRL responsible for approving antibody test kits, have you found out why that statement was included and found out exactly what it was meant to convey.

A. I can't tell you if we challenged Abbott Diagnostics on that particular statement, no. I would suspect that Abbott inserts that to protect itself because companies are very clever at that. The companies are very cautious about false negative reactions because if they are found to have false negatives in their tests very quickly - excuse me your Honour - the lawyers come after them. So it's a precarious situation for those companies that are always in fear of being sued. So it doesn't surprise me that that statement is there, no.

Q. My question was, as director of NRL responsible for approving antibody test kits, have you yourself, as director, made any effort to find out why it was there and what it means.

A. No. But I have looked at the package inserts of numbers of other companies' package inserts and not found a similar statement.

Q. Have you ever heard of a Dr William Brattner, retro-virologist from the United States.

A. Yes, I know Dr Blattner quite well.

Q. He is highly thought of.

A. I think so, he is an associate in the Institute of Virology in Baltimore, Maryland and he's an expert on human T cell lymphotropic virus.

Q. In a paper published in 1989, 'Retroviruses' Viral Infections in Humans, Plenum Medical Book, referred to in 25, Dr Blattner has said, and I quote 'One difficulty in assaying the specificity and sensitivity of human retroviruses is the absence of a final gold standard. In the absence of gold standards for both HTLV 1 and HIV 1, the true sensitivity and specificity for the detection of viral antibodies remains imprecise'. Have I got the right -

HIS HONOUR: The quote in slide 24 is not as full as the quote you've given but that's the reference -

CONTINUED

MS MCDONALD: I also had a note that that slide has been withdrawn based on the fact that that paper cannot be produced.

MR BORICK: We say we have handed up a copy. I accept that Dr Blattner -

HIS HONOUR: Read the passage again.

XXN

Q. 'One difficulty in assaying the specificity and sensitivity of human antiretrovirals is the absence of a final gold standard. In the absence of gold standards for both HTLV-1 and HIV 1, the true sensitivity and specificity of the detection of viral antibodies remains imprecise'.

A. And I would put to you that that was written in 1989 when sequencing was not readily available but as Dr Dwyer has suggested that may be considered as a gold standard as may isolation or any of the direct means of examining virus and if you wanted to make those gold standards you could.

Q. So first of all you accepted that that is the view held by Dr Blattner in 1989.

A. Absolutely if that's a true quote but Ms McDonald says that was withdrawn.

HIS HONOUR

Q. The slide was but assume that is an actual quote from the paper I understand your evidence that's 1989 we are 2006 now a lot of water has gone under the bridge.

A. Yes.

Q. Plus the evidence you have given previously about sequencing previously.

A. Yes.

Q. Which didn't exist in 1989.

A. No, certainly not readily.

XXN

Q. That's your response to the statement.

A. That is.

Q. What is meant by the statement 'the absence of a final gold standard'.

HIS HONOUR: I'm not sure that that is a very fair question because it is a question of a definition, what Professor Blattner might regard as a gold standard and what this witness might regard as a gold standard it is unfair to take the quote as it is. You have to give her the paper.

A. I think it is what perspective you come from.

XXN

Q. What do you understand that to mean when he refers to a gold standard.

MS MCDONALD: If my learned friend wants to cross-examine on this article he can produce the article. It's just not fair.

MR BORICK: Here it is. I suspect the witness is not going to be just able to look at that in the witness box now.

HIS HONOUR: If you want the witness to read the article she is not going to be able to do it in the witness box. It is unfair to her. I don't know if you can quickly tell us if Professor Blattner defines what he means by 'gold standards'.

A. I can't tell you that but I suspect that as I say it depends what perspective you come from what you might consider a gold standard and what I might consider a gold standard may not be the same gold standard that Dr Turner or Mrs Eleopulos want to consider a gold standard. I don't know what they want to consider a gold standard or what they want me to admit that might be their gold standard or my gold standard.

HIS HONOUR

Q. My understanding and Mr Borick will correct me if I'm wrong you take the analogy of a pregnant woman they say you have to have a pregnant woman take as your basis before you can test other people to see if they're pregnant and if you haven't got a pregnant woman you can't say a whole lot of people who test in the same way are pregnant because you don't have the basis to say they are pregnant.

A. My analogy of the foetus would be the isolation of the virus from the tissues of that person, from the sequence of the virus that you would look at, the presence of an RNA or a positive DNA test, those direct ones as Dr Dwyer has suggested.

HIS HONOUR: Do you want to tender that article or not?

MR BORICK: Yes I'll tender the article. I think the pregnancy analogy is a bit to what you put.

HIS HONOUR: I didn't say it was Mr Turner's understanding. I said it was my understanding.

MR BORICK: The baby is the ultimate test. That tells you whether the test was right or wrong.

HIS HONOUR: I understand that. I very much understand that.

EXHIBIT #A16 CHAPTER 21 RETROVIRUSES WILLIAM A BLATTNER TENDERED BY MR BORICK. ADMITTED.

HIS HONOUR: If you want the witness to be provided with a copy and want to go away and ask the witnesses questions by correspondence I am prepared to do that.

MR BORICK: Yes obviously I have other questions to ask in relation to the other documents which were provided.

HIS HONOUR: I will make sure that the witness is provided with a copy of that chapter of the book to read.

XXN

Q. In the book which you coauthored with Constantine 'All serological confirmatory tests which I understand would include the lease and WV tests have guidelines and criteria that must be met to when the result fulfils the requirements to classify the samples of HIV positive, negative or indeterminate. These criteria have been determined in two ways, first manufactures of test kits have predetermined the requirement for results based on individuals classified as positive or negative by other means (clinical status culture etc.)' and does the

expression clinical status culture etc. refer to an independent means of establishing the presence or absence of HIV for evaluating the antibody tests'.

A. It could do. I think it's yet another - I think really it's what we have been saying all along that when you are trying to establish the means to make a diagnosis you weigh in all the factors that you possibly can. They may be direct factors if you want to call it that or indirect, and I'm struggling, I'm sorry, to see why - it's essentially the same question to me and I feel like I've answered it.

Q. You have said that in effect, as I understand it, the independent means of establishing the presence or absence of HIV for evaluating antibody tests depends upon clinical status culture etc. Have I correctly quoted you.

A. I believe so. I have no reason to suspect that you are not.

Q. Have I correctly ascertained what you meant when you refer to clinical status, culture etc.

A. I expect so.

Q. By that do you in fact mean that they act as the HIV gold standard.

A. I wouldn't have put it that way but you could - as I have said, it depends on what you choose. If you want a gold standard under these circumstances, it depends what comparison you choose.

Q. By the expression 'clinical status' in that quote do you mean AIDS.

A. In terms of, yes it could mean that or it could mean that somebody who had an anti HIV assessment and loss of weight or chronic diarrhoea that may come into the weighting of a positive sample. I think we can't isolate any one thing. When we do this we take into account the weight of the scientific evidence so it may be when you are setting up your criteria that you choose all these different things and take into account certainly when we set up our serum panels in the NRL

take up all samples available concerned with any one specimen then test that specimen by as many different tests as we have available to us and if they all are reactive or positive whatever they might be we say that is a positive panel sample. Similarly were we to check negative samples and find evidence that there was reactivity or presence of a virus then we would not use that as a negative sample. We may use it as a cross-reactive sample depending on the characteristics of what's found but we certainly wouldn't use it as a negative one.

Q. Do you agree - that a positive test is included in the definition of AIDS.

A. Positive test meaning what?

HIS HONOUR

Q. Of HIV.

A. An anti HIV positive diagnosis. Is that you what mean?

XXN

Q. A positive HIV test, HIV positive, that is what I have been referring to in this courtroom. Not sure where the 'anti' comes from.

A. Because that is the antibody testing. I want to make quite sure I understand you here. Are you saying someone must have an HIV anti-positive result before diagnosing with AIDS.

Q. The definition is a requirement that there be a positive HIV test or anti-test, whatever you want to call it.

A. Certainly that would be true in Australia. It's not necessarily in different parts of the world.

Q. What other parts of the world.

A. Sometimes when tests are not available the diagnosis is made clinically.

Q. Whereabouts.

A. Some parts of Africa. That's what WHO is trying to eliminate and make sure everybody has a HIV diagnosis and make sure these are ruled out.

CONTINUED

Q. In Australia, an HIV-positive test is part of the definition of AIDS; is that right.

A. You wouldn't make the definition - yes, I suppose you could put it that way.

Q. In effect, you're saying, or what is being said, is that the evidence that HIV is the cause of AIDS is a positive antibody test.

A. I think you're leaving out a lot of information in making that leap. There's a huge amount of information between that first statement and that second statement. I just can't understand why it is ignored here and I think we've gone over it and I think Dr Dwyer could perhaps supply better clinical information to the court as to what lies between those two statements than perhaps I could. I honestly have not seen a patient for many years.

Q. We have had other sources that HIV is the cause of AIDS and the evidence of HIV is a positive antibody test. Is there anything wrong with that. That's what the current majority view is.

A. I think you're making a leap there. If somebody is exposed to the virus, there is no doubt they mount an immuno response to that virus, which can be defined through anti-HIV tests. If you want to confirm that, then you can look at other sources of testing, as I have said, which include nucleic acid testing, culture, virus isolation and so on.

Q. Would you accept that the current view is that HIV is the cause of AIDS.

A. Do I?

Q. Yes.

A. Certainly, I do.

Q. Do you accept that a positive antibody test is sufficient to prove AIDS.

A. No, AIDS is a clinical diagnosis. If somebody is found to be anti-HIV-positive they have been exposed to the virus. Over time, without treatment and care, there is absolutely no doubt in my mind that that person will

develop the syndrome called AIDS, where, finally, their immune system is suppressed sufficiently for those illnesses, or those infections, known to define AIDS, will appear.

Q. Do you accept that the diseases which constitute AIDS have causes other than HIV.

A. Of course, by definition they are opportunistic infections. They're the type of infections that would invade when someone, or are more likely to invade when someone has a depressed immune system. It doesn't say they can't exist in other circumstances, of course they can and I think Professor Cooper explained that quite clearly last week.

HIS HONOUR

Q. You can get tuberculosis without having tested antibodies to HIV.

A. You certainly can. Tuberculosis is one of the greatest killers in the world.

Q. If you have tested HIV and you develop tuberculosis, you have AIDS.

A. That's an AIDS defining illness, yes.

MS MCDONALD APPLIES TO INTERPOSE WITNESS DWYER

LEAVE GRANTED

WITNESS STANDS DOWN

+THE WITNESS WITHDREW

DISCUSSION RE TIMETABLE

HIS HONOUR: I want to get on with this and I want to get the submissions done. I'm out of the jurisdiction from the middle of March and I really think that this matter ought to be resolved as soon as possible. The work involved in marshalling the material that we have all been through is, to say the least, quite voluminous and I'll be assisted if people are assisting me with that. That will take time. Unfortunately, all our resources are stretched but this matter really must start to take priority - it has to take priority - because it is unfair to the defendant to keep this matter going any longer than I possibly have to and,