RESUMING 2.15 P.M.

DISCUSSION RE TIMETABLE

MR BORICK: When Professor Cooper has finished his evidence-in-chief, I would like to start the cross-examination; I don't think I'm going to be all that long. Before I conclude, I would like a 10 minute break just to confer with my experts.

HIS HONOUR: I don't think that will be a problem.

MS MCDONALD CALLS

+DAVID ALBERT COOPER SWORN

+EXAMINATION BY MS MCDONALD

Q. What positions do you currently hold.

A. Currently I'm the Ciencie Professor of Medicine at the University of New South Wales in Sydney. I'm Director of the National Centre in HIV Epidemiology and Clinical Research also at the University of New South Wales, and I'm head of the HIV infectious diseases immunology clinical services unit at St Vincent's Hospital in Sydney, which provides care for people with HIV.

Q. What is a Ciencia Professor.

A. It is a special recognition by the University of New South Wales of high level achievement amongst the professorial ranks, and it's given to about five or six professors every three years.

Q. I want to ask you some questions about your background and your experience in relation to HIV and AIDS. Firstly, have you been awarded an Order of Australia.

A. Yes, I have indeed. I was very proud to have received that, and it was from the work that I'd done in the development - with, of course, many other people - of antiretroviral therapy to treat this dreadful disease, and I'm very proud of that achievement.

Q. When did you receive that.

A. Gosh time flies. I think it was three years ago.

Q. I'm not going to take you through everything you've done and all the experience you've had because it would take up all the time we have, but have you provided for the court a current curriculum vitae.

A. Yes, I have, I believe, yes.

EXHIBIT #P53 CURRICULUM VITAE OF PROFESSOR DAVID A. COOPER AO TENDERED BY MS MCDONALD. ADMITTED.

HIS HONOUR: You have seen that have you?

MR BORICK: Yes.

XN

Q. I'm going to ask that his Honour has the curriculum vitae in front of him, so we'll talk to the document and I will ask you some questions about what is in your CV. You've set out your education background and I won't take you through that. Then you go on to postgraduate training internship and residencies.

A. That is correct.

Q. From there, you set out for us your research fellowships. I want to move over to the topic of academic appointments because you have held a number of those. From 1981 to 1983, were you a research fellow in pathology at the Harvard Medical School.

A. Yes, I was.

Q. What did that involve.

A. That was my sort of postdoctoral training. I went to a very famous laboratory at Harvard Medical School in the Dana Farber Cancer Centre. Indeed, it was the laboratory in which human CD4 was first recognised and, without the work of that laboratory, we wouldn't have been able to understand the pathogenesis of HIV so well, so it was tremendous experience in learning about subsets of lymphocytes.

Q. Was that happening when you were there.

A. Yes, it was indeed, and the extraordinary thing, of course, was 1981 was when the AIDS epidemic was first discovered or described in the United States, and we were referred samples from patients to have a look at their CD4 cells in that laboratory, so it was a very exciting time.

Q. From 1986 to 1989, it appears that you held a couple of positions, one being the Director, National Health and

Medical Research Council of Australia, Special Unit in AIDS Epidemiology and Special Research at the University of New South Wales, and also you're a senior lecturer in medicine at that same university.

A. Right, that's correct and that special unit evolved into the national centre.

Q. Over the page in your CV, you set out professional positions and committee assignments: World Health Organisation, UN AIDS, Geneva Switzerland. Can you tell us about your involvement in that organisation.

A. Yes. In the early 1990s, I was invited to chair an advisory committee to be Director of the Global Program on AIDS of the WHO at that time, and this was on clinical research and drug development, so a group of us, about 10 or 12 international experts, advised the WHO on what they should be doing in terms of clinical research and drug development for this disease, so that was a great honour and a very exciting time for us to be advising the World Health Organisation.

Q. Have you continued to have any involvement with that organisation since then.

A. Yes. That committee was altered when UN AIDS was formed, so that that folded into the new UN AIDS mechanism, and WHOs role in the HIV epidemic was decreased at that time. It's since, of course, reemerged quite strongly and now I've got two roles with the WHO: the first is the chair of the Vaccine Advisory Committee. This is a combined WHO/UN AIDS committee on HIV AIDS vaccines which I chair, which means once or twice a year, to advise WHO/UN AIDS on priorities for vaccine development; and the second committee is the Strategy Committee of WHO about what they should be doing to assist member States in treatment and care and prevention of HIV disease.

Q. During the course of your answer, you referred a number of times to 'UN AIDS'.

A. Yes.

Q. Can you tell us what that is.

A. Right, so when it was realised in the early 1990s - late 1980s/early 1990s - that this was a very serious epidemic, the WHO and other members of the UN community felt that there was not enough emphasis being given to promoting, you know, treatment, prevention and care in this epidemic, so the UN resolved to form this special branch of the UN, similar to, say, UNICEF or UNDP, in which all UN agencies would be represented to promote the cause of HIV/AIDS around the world, and it has continued to do so and has been very, very successful under the leadership of Dr Peter Piot.

Q. I just want to ask you about a couple of aspects of your involvement in these organisations. In your CV you describe being a member of the Trial Management Committee at Petra, study on peri-natal HIV transmission in Africa. Can you tell us what that was about.

A. Yes. That was a very important study. As part of my advisory role to WHO in the Clinical Research and Drug Development Committee, we were particularly keen to increase the ability of antiretroviral therapy to prevent mother to child transmission, so we set up this study looking at dual therapy at that time, so to nuclear science, to prevent mother to child transmission in countries in Sub-Saharan Africa - so Tanzania, Uganda and the Republic of South Africa - and we did this as a consortium, and I approached AusAID, the Australian International Development agencies, who were very keen to assist in that, and they donated money to do this trial, which was eventually published in the Lancet with very positive results and, because of that, I was invited to become a member of the Trial Management Committee.

Q. You were also a member of the Comprehensive International Program for Research on AIDS (CIPRA) HIV Research Program in Thailand and Cambodia International Steering Committee. That is a mouthful, but what was that all about.

A. Yes, so the National Institutes of Health, which is the

largest public sector funder of HIV/AIDS research in the world, has a number of research programs which I'm involved in. A few years ago, they wanted to promote the ability of developing countries to carry out their own research, and the National Centre had been working for some time in Thailand and Cambodia on these aspects and, together with these partners, we applied for this CIPRA grant and were successful. We're now doing a study in Thailand and Cambodia, supported by the National Institutes of Health, which looks at whether early treatment of children with HIV infection is better than deferral, and that study is recruiting at this moment. What we're very excited about is that we have been able to assist a country like Cambodia, which was decimated in the Pol Pot years with only 500 doctors left at the end, you know, when Pol Pot was finally removed, and to have absolutely no, you know, sort of research training or abilities, and so this really upskills them and gives them technology transfer and being able to do clinical research, so it's a very important grant.

Q. You were also a member of the Smart Executive Committee.

A. Yes, Smart is the largest HIV clinical trial that has been done to date, again sponsored by the National Institutes of Health, and looks at whether continuous antiretroviral therapy is better than intermittent antiretroviral therapy. The trial completed in January of last year with a positive result showing that treatment interruptions were not very good for you with a two and a half fold rate of death and disease compared to staying on antiretroviral treatment.

Q. So that major study you were involved in, as recently as last year, showed that disrupting antiretroviral treatment had a negative impact on someone who had been diagnosed as HIV positive.

A. Right, so one of the premises of that started with there had been some reasonable concerns in the academic community that antiretroviral therapy, as well as being

efficacious, did have some trade-offs with respect toxicity, and so the study was done to try and spare the amount of antiretroviral therapy people took. We thought that it may be okay to have periods off antiretroviral treatment. The study was really quite extraordinary and resounding in the fact that if you interrupted therapy, you got sick and died at a rate two and a half times greater than if you stayed on treatment, and this has changed treatment guidelines internationally as a result of that study which we were involved in and helped run the study throughout the world.

Q. So the study was conducted throughout the world.

A. Yes, it was conducted in about 30 countries; we sort of divided up the world so there were different regional coordinating centres, and we coordinated sites in Australia and in the Asia-Pacific region.

Q. You have also been a member of the Treat Asia Steering Committee. What is that.

A. Treat Asia is a responsive non-government organisation - the American Foundation for AIDS Research, which you may recall was started with the assistance of Elizabeth Taylor to promote AIDS research, so it's a private foundation headquartered in New York - and it was interested in trying to promote treatments in Asia-Pacific, them thinking that a lot of effort was going into Africa and not enough was going into Asia, so this was set up about four years ago and we at the National Centre had technical advisers for this proposal, which has been very, very successful, in multiple sites throughout our region.

Q. Over the years, you have been involved in a number of editorial boards.

A. Yes, I've been on the editorial boards of major specialist HIV/AIDS journals, particularly the Journal of Infections Disease and the major specialist journal in the field, which is also called 'AIDS'.

Q. You have been on a number of government advisory bodies.

A. Indeed I have.
Q. And also you have had a number of memberships and assignments in professional societies. They are all set out in your CV.
A. Correct.
Q. You are also a member of a number of other international organisations.
A. Yes. I guess the one I'm most - the one that I'm most proud of is my presidency of the International Aids Society, which is a worldwide organisation of health professionals and scientists, an international professional society involved in HIV/AIDS, and I was president for four years from 1994-1998. It is a very successful organisation; it is the sponsor of all the World Aids Conferences, and there is a very large public advocate and policy organisation right now. The thing I did that I was most proud of during my presidency is took the World Aids Conference to the developing world, and it was under my presidency that we selected Durban, South Africa, in 2000, and I believe that that was a revolutionary meeting because, for the first time, the developed world saw the tragedy of the HIV/AIDS epidemic in Sub-Saharan Africa, and some of the things that have been developed, such as the Global Fund, UNGAS, World Bank, Gates, President Bush's emergency plan for the relief of AIDS, have all accelerated since that meeting, so it was a very important meeting and I'm very pleased that it did happen in South Africa.
CONTINUED

Q. What is UNGAF.

A. UNGAF was a special session of the United Nations which occurred in I think 2002 or 2003 and that launched the global fund for the treatment of HIV, TB and malaria.

Q. Now part of your curriculum vitae is a bibliography which sets out pretty much, year by year, the various publications that you have been involved in.

A. That's right.

Q. I'm not going to take you to them but there are many.

A. Yes, I think there is almost about 500 publications. They are most exclusively in the HIV field, although I have published in immunology and clinical medicine. The thing that I'm really again very proud of is the fact that I'm one of the 10 most cited clinical scientists in worldwide HIV/AIDS so those publications have been cited so many times that enable me to be called, you know, one of the top 10 - the top 10 clinical scientists in the world.

Q. I have noticed that in your bibliography, on occasions, at the end of the entry you included a letter in brackets. Have you done that to indicate that that particular indication is a letter as opposed to a peer review of an article.

A. That's correct. Most letters to medical journals are not peer-reviewed, they are reviewed by the editors of the journal and they are generally related to the correspondence about an article that was published.

Q. You have been involved in providing a statement for the court in relation to this case.

A. Yes, I have.

EXHIBIT #P54 STATEMENT OF PROFESSOR DAVID COOPER TENDERED BY MS MCDONALD. ADMITTED.

HIS HONOUR: You have seen it Mr Borick?

MR BORICK: Yes, I have.

XN

Q. Because time is short, I'm going to cut to the chase.

HIS HONOUR: You can take it that I read it.

MS MCDONALD: Thank you.

XN

Q. I'm going to put some propositions that have arisen in this court and ask you to comment. I ask you to do so based on your experience and involvement in HIV and AIDS around the world. The first is the proposition that HIV has never been proved to exist.

A. Well, that's absolutely wrong. It's a virus, it's been isolated on many, many occasions now from many different types of patients worldwide. Its genetic sequences is extensively known. It is probably one of the most studied viruses - indeed, micro-organisms that has ever existed and, you know, with a gene bank - for example, where gene sequences are registered, there are thousands and thousands of sequences of this virus that have been deposited in a gene bank from laboratories all over the world and there are variances of this human immunodeficiency virus, so to say that it does not exist is simply scientific ~~lunacy~~ truth.

HIS HONOUR

Q. When you say that the virus has been isolated many times, what do you mean by 'isolation'.

A. So there are a number of ways to isolate the virus. The most usual way is to culture it from white blood cells that are infected with HIV and that's been done on numerous occasions and people have taken micro graphs of that and there are many many pictures of that in the literature. Once that virus is purified, it's then genetically sequenced and those sequences are unique, just like every organism on the planet has unique sequences and markers. So that sequence is unique and because of the revolution in molecular biology, most people now handle the identification of that virus through molecular biological techniques which have been revolutionised over the last 20 years and used in almost all diagnostic proprieties and research laboratories around the world.

Q. The second proposition that I want to put to you is that HIV has not been proved to be sexually transmittable.

A. That is absolutely wrong. We have a generalised epidemic in sub-Sahara in Africa in which - in some countries up to 35 to 40% - for example in Botswana and Zambia, Zimbabwe, are infected and in order to have a generalised epidemic like that, of young people, you know, young adults, that essentially means that this has to be a heterosexually transmitted epidemic.

Q. What causes you to have the very firm view that this virus is sexually transmitted.

A. So, well it's - it is all sub-Sahara in Africa - I was pointing out the countries that are worse affected. So there is - you know, there is good data that the sexual partners that - HIV infected persons are at risk and can become infected with HIV should they not use condoms, so these could be sexual partners of people who developed HIV from blood transfusions or injecting drug users and other people in heterosexual and homosexual relationships. So the numerous cases have been followed in which there are pairs of people and the negative partner becomes infected with HIV and this is well-documented throughout the medical literature.

Q. The next proposition that I want to put to you is that the tests used for diagnosing are not reliable, particularly ELISA in the Western blot.

A. Right. Again that is absolutely wrong. Diagnostic tests in medicine are sometimes problematic and we say that diagnostic tests should be sensitive and specific and, you know, diagnostic medicine is sometimes not easy because we don't have the best tests for diagnosis to include a disease or to exclude a disease. In this case, we have one of the best tests ever. There is no diagnostic test in medicine that has the sensitivity and specificity of the HIV antibody test, whether it is done by ELISA or by Western blot. The test is 99. - very close to 99.9% sensitive and 99.9% specific. So there

is no better diagnostic test in medicine that I know of.

Q. The next proposition is that the antiretroviral medication does not work.

A. Well, that's again - again, that's absolutely incorrect. Potent antiretroviral therapy was introduced in 1996 requiring three drugs to fully suppress the virus and when that was introduced there was a revolution in the outcomes of people with HIV/AIDS. The death rate plummeted. Hospital wards were full of young, sick and dying people and they emptied out. Hospices closed and the outcomes of people with HIV just dramatically altered such that you now have people who are 70 or 80 years old with HIV doing very well on antiretroviral therapy. Before 1996, in our ward - we had a ward in St Vincent's hospital, which is the epicentre of the epidemic in Australia - we had 20 beds. It was always overflowing with the young and sick and dying, dying people, and it was a tragedy and we had usually, you know, four to six to eight deaths in a month in 1994/1995. It was the most horrible thing that any clinician could face and one of the horrible experiences that I have ever had and this applies to many of my colleagues around the world who I know very well from all the collaborations that we have done. That just completely stopped so the ward emptied out and the death rate is much, much lower. We would have perhaps two or three deaths a year from this disease right now.

Q. What sort of death rate was there pre the antiretroviral era.

A. This was a uniformly fatal disease. The statistics were extremely known. 50% of HIV people would develop AIDS within 10 years and those people who developed AIDS most would be dead within one to two years.

Q. I want to put another proposition to you and that is that blood transfusions, of themselves, cause a person to have positive antibodies or HIV antibodies and then it causes AIDS.

A. Well, that again is absolutely false. HIV of course can

be transmitted by infected blood products so that's only, in that circumstance, produce a positive antibody test but that's due to HIV infection. There is a well-described phenomenon in medicine which is involved in, I guess, diagnostic pathology for micro-organisms and immunological diseases and that is that people do make antibodies and the immune system is pretty specific and pretty good, but the way it works is that it takes chances to make sure that it covers everything and so, as the immune response to a particular organism is maturing, the antibodies, if you like, become more and more specific to the antigen that is causing that immune response. There are a lot of antibodies formed but at low levels and cross-react with other material in the body. This is probably the explanation for the phenomenon of forming cross-reactive antibodies with transfusions. So if you are transfused with blood products, there are minor genetics between the donor and the recipient. It will recognise that and it will make these low level antibodies, which are not specific, but can cross-react with numerous micro-organisms including HIV and there are - we do find small numbers of HIV positive, as with ELISA, some of whom have in fact had multiple transfusions. These are a manifestation of these cross-reactive antibodies. This can be concluded by the fact that the antibody - the amount of antibody does not go up over time. The Western blot is negative and the virus cannot be isolated from these people.

Q. Whilst on the topic of blood transfusion, in the early days of the epidemic, was it the case that there were a number of people who reported as becoming HIV positive as a result of receiving contaminated blood.

A. Absolutely, absolutely. That was one of the triumphs of the Australian response to the HIV/AIDS epidemic which was securing the blood supply earlier on and we were the second country in the world to adopt universal screening of our blood supply for HIV and completely eliminated transfusion associated with HIV/AIDS.

Q. It is eliminated in Australia now.

A. There are one or two small exceptions and that is what is called the 'window period'. So when you first become infected you don't make - you don't always make antibodies quickly enough and in that short window, in that one to two weeks, it is possible for an infected blood donor to be missed through the system. There has been one or two cases since universal screening.

Q. When was that; when was it introduced.

A. Universal screening was introduced in 1985 I believe. '85, yes, early '85/'86. I think up until that time we had a couple of hundred people with transfusion acquired HIV in Australia. Since then, there has been two cases which have been attributed to the window period. The blood banks have done a tremendous job introducing even more sophisticated technology to rule out the window period. I believe in the last few years there have been no cases of transfusions getting through the window period.

Q. Was there a particular case involving a young child that caused some controversy.

A. Are you referring to the Queensland babies or?

Q. No. Was there a case in which a young child became HIV positive. Excuse me. In Victoria, as a result of receiving some contaminated blood.

A. I'm not specifically aware of that case that you are referring to.

Q. I will speak to someone else about that.

A. Yes, there was certainly four babies in Queensland, that were premature babies, that were transfused just before universal screening from the one donor which was a very sad occurrence.

Q. What method is currently used in Australia for screening blood donations.

A. I'm not a blood bank - I'm not up-to-date with the latest technologies that the blood bank does use screening. I believe you have other experts who will tell you about blood testing. What we do in our

diagnostic laboratory to identify people who could be HIV positive is we do the ELISA tests and we do two different ELISA tests and we confirm that with the Western blot test.

Q. The next proposition I want to put to you - and I'm going to actually cite you something that was said in the evidence as part of that - the proposition is: 'There is a massive epidemic of HIV testing and positive tests, but there is no massive epidemic of HIV infection because no-one has proved it'.

A. Yes, well I mean that's - that's just a wrong statement. It is outrageous. There are - the death rate from this disease in South Africa is extraordinary, there are five million people infected with HIV in the Republic of South Africa. Deaths occur day after day, hundreds of deaths occur day after day still and the fact that the Republic of South Africa has only just introduced antiretroviral therapy, when it should have done so several years back, is due to this extraordinary denial-ism that some people in high level of the government of South Africa, including the president I believe, it just simply is not true. People die of this disease every day in South Africa.

CONTINUED

Q. You just mentioned then the introduction of antiretrovirals in South Africa. How recently did that occur.

A. So it has been happening fortunately, sometimes State governments are more sensible than Federal governments, so the provincial governments in South Africa, including the Western Cape and KwaZulu-Natal, Gauteng have had limited programs. In the last year the central government has started the rollout programs and these have been incredibly assisted by funds from President Bush's emergency plan for the relief of AIDS. President Bush has given six billion dollars for the relief of AIDS in Africa, which is really an extraordinarily positive thing for the United States, and the global fund also is a considerable donor to these rollout programs. We now have something like three or four million people in Sub-Saharan Africa on antiretroviral therapy and it is working, but there are not enough people on treatment right now.

Q. That was my next question: is it possible to assess the impact the antiretrovirals are having yet.

A. Yes, there is some important publications in The Lancet and the Journal of the American Medical Association, which coincided with the World AIDS Conference that was held in Toronto Canada in August of last year and these studies of looking at thousands of people on treatment identified that the death rates of the people on treatment had dramatically, dramatically declined. And the death rates unfortunately are not at the levels that we see - the improvement in outcome is not at the levels we see in the developed world and that is unfortunately because of access to people in poor countries, they tend to come in very late and very sick and don't access treatment early enough, and sometimes, as in any overwhelming illness, even antiretrovirals can't help them.

Q. I would like now for you to comment on the approach of attempting to come up with some sort of mathematical

equation to work out how many acts of intercourse would be required before someone is at risk of contracting HIV. I think you know what I mean by that; a process using a study and coming up with a statistical figure and then attempting to fix the number of sexual acts required before a person is at risk of becoming HIV positive.

A. That is a difficult thing to do. I am not an epidemiologist, I'm a clinical scientist, but I think Professor John Carter, who I believe is one of your other expert witnesses, will be able to address that, but essentially people have looked at cohorts of people at risk, whether they are an injecting drug-user or heterosexual men and women, or homosexual men and tried to come up with a rate, an average rate of infection according to the number of exposures. Now, as for any sexually transmissible infection, HIV obeys the rules, in that sexual transmission from male to male is much more efficient than male to female, which is more efficient than from female to male, and the rates that are quoted reflect that hierarchy.

Q. In your vast experience, can people become HIV positive through just one sexual contact.

A. Yes, I have - I mean, I care for about four or five hundred HIV infected people at any one time. I've probably cared for two and a half thousand HIV infected people over my career, and it is a pleasure to take care of these people and, you know, we get to know each other and we get to hear their stories, and it is extraordinary the number of patients I've had that have been infected on their first sexual exposure, even on occasion on their sexual debut.

Q. I want to turn to ask you some questions about some of the defence witnesses in this trial. Firstly, are you aware of a group of people who are referred to as 'the Perth group'.

A. Yes, indeed I am.

Q. Are you aware of a person by the name of Eleni

Papadopulos-Eleopulos.

A. Yes, I'm aware of her involvement in this case and some of the things that she said over the years, yes.

Q. Have you ever met her.

A. No, I haven't.

Q. Are you aware of a Dr Val Turner.

A. I'm only aware of Dr Turner from the correspondence around this case. I've never actually met him. I guess that Ms Papadopulos-Eleopulos is the sort of flagstaff of this group, so that is who I know the most, or have heard about the most.

Q. How is the group regarded in the scientific community in Australia.

A. Well, the group is regarded as not having any scientific credibility and we believe in the scientific community that their statements are wrong, mischievous and harmful.

Q. Are the views that they are expressing, and have been expressing in this court, part of any legitimate scientific debate that is going on.

A. I would say no. I've read some of the transcripts and I can't see anything in the points that they raise that is of any scientific validity or is even worth testing by scientific hypothesis. It seems to me, from reading some of the transcripts, that they're always referring to exceptions rather than rules, and sort of very rare exceptions, which are sort of beaten up into evidence that HIV doesn't cause AIDS. And this is, in my view, is a tragedy for all the work that we have achieved in this epidemic in Australia in trying to prevent people from becoming infected and all the successes we've had. I think it's very sad for, you know, for all the people in the developing world that we're starting to be able to help who might, with these views, start thinking that they're not going to get sick.

Q. Are you aware that a comment about a paradoxical outcome has been attributed to you during the course of the evidence in this matter.

A. Yes, I was aware of that, so I was invited to comment on a very nice paper from colleagues in Europe led by a group at the University of Bristow, very respected epidemiological group at the University of Bristow in the UK, and they submitted a very nice publication to this World AIDS Conference edition of The Lancet, looking at the outcomes of HIV infected persons in Europe, and what they noted is that there has been a dramatic decline in death rate in HIV infected persons in Europe over the - since highly active retroantiviral therapy has been introduced, but that death rate has been seen to plateau and seen to increase a little bit slightly. When you look at the data, it is clear - and this is what I commented on in my editorial, and it was also referred to by the authors - that this reflects some of the changes in the epidemic in Europe in recent years. So Europe is faced with a lot of immigrant populations who seek asylum in various countries in Europe, people from Anglofone Africa arriving at London Heathrow airport and seeking asylum, people from Francophone Africa arriving in Paris, people from North Africa coming to Spain or Italy, and these people, some of them are HIV infected, and that's why they seek asylum and seek treatment through the socialised health care systems in member states in the European Union. The problem is that, like with all sick immigrant populations, they have tuberculosis. The currently have tuberculosis and they often arrive very late in Europe because they've realised that they're sick in their own countries and they can't access treatment. And so what happens to these people is that they often do very poorly compared to the citizens, the average citizens of the United Kingdom, or France, or Spain. These people, there are increasing numbers of these people in Europe and because there's increasing numbers, it has affected the figures by this sort of slight increase in the death rate, and particularly the tuberculosis rate, which is an AIDS defining illness in recent years. So that's

what I was referring to about paradoxical.

Q. Was there anything in that study or article that supports the suggestion the antiretroviral medication doesn't work.

A. Absolutely nothing in that study that suggested that the medication wasn't working. They clearly showed that the death rate from 1996 onwards had decreased in the way that numerous cohorts around the world have shown, and they did not attribute that change in the death rate to any toxicity, it is simply due to unfortunately people accessing treatment too late.

Q. I had better make sure that we are talking about the same statement. Can I just see P 18. The article that you have been referring to, is it an article entitled 'HIV Treatment Response and Prognosis in Europe and North America in the First Decade of Highly Active Antiretroviral Therapy: A Collaborative Analysis'.

A. Is it The Lancet of August?

Q. Yes, August 2006.

A. Who is the first author on that?

Q. The first author is M. Egger.

A. Matisse Egger, yes, that's correct. So when these very large studies are published in major medical journals, the journals sometimes call for an editorial comment and they ask experts who are not involved in the study to write an editorial and my colleague, Greg Daw and I, wrote an editorial based on that paper for an edition of The Lancet.

Q. Another study that has a mention in this hearing is a study that has been referred to as the 'Rodriguez Study'.

A. Right.

Q. Are you aware of that particular study.

A. Yes, indeed I am.

Q. Could you just tell us about your understanding of what that study was about and what the results showed.

A. Right, so, I have to take you back one step and that is that in the mid to late '90s, there was a very important

cohort in the United States called - or two important cohorts called Max and Wise: Max is a cohort of several thousand homosexual men in several major cities of the United States; Wise is a cohort of similar numbers of heterosexual women, particularly minority women, black and Hispanic women in the United States, and they followed that cohort over many years and they provided a lot of information about outcomes of people with HIV. These were the first two cohorts which showed a relationship between viral load and outcome. So if you had a high viral load, your disease progressed faster than if you had a low viral load, and that was generally very well accepted by the HIV research community. This Rodriguez paper analysed - but one of the things that has concerned people is that not everybody with a high viral load automatically progresses very, you know, fast, and there are some people indeed with low viral loads that progress quite rapidly. So this study by Rodriguez is an attempt to sort of explain some of that diversity, and what they show is that viral load is not the only factor in their work that explains the progression of disease and the CD4 cell decline. Although they don't explain what the other factors could be, I think that it is tantalising to suggest that we should be looking for other factors that the immune system affects - sorry, that the virus affects within the immune system which might contribute to that CD4 decline. So it is a hypothesis and it doesn't discount the well known relationship between viral load and outcome.

Q. When you say it is 'tantalising' to now look for other factors, what sort of things do you have in mind, or would that be speculation at this stage.

A. I think one of the exciting things that people are looking at right now is the genetic susceptibility to the virus. It's well known, for example, that there are genes that affect outcome of infection with malaria. There is good evidence that survivors of the bubonic

plague in the later middle ages had a genetic advantage by having some different genes to other people, and this is a very hot area of research, suggesting that there are in our genes genetic diversity which allows some people to not have a bad outcome with this virus, whereas other people seem to progress - with other genes some people progress quite fast. This is very important, of course, in trying to identify what would be the best components of an HIV vaccine. So these are one of the factors that are being actively pursued right now, and there is a lot of evidence that there are at least 10 or 20 genes which can contribute to a fast or slow progression.

CONTINUED

Q. Again, just to make sure that we're talking about the same study, is the study that you have been referring to entitled 'Predictive value of plasma HIV RNA level on rate of CD4 T cell decline in untreated HIV infection'.

A. Yes, that is the one that was published in JAMA, the Journal of the American Medical Association. I think the last author is Lederman.

Q. The last one is Lederman and the first one is Rodriguez.

A. Correct.

Q. What do you say to any suggestion that this article is support for the proposition that HIV does not cause death.

A. I think that the article is by no means suggesting that. It is suggesting that HIV may cause disease in other ways than just the amount of the virus and that is perfectly consistent with many other infectious diseases and post responses. Not everybody - in any pandemic, and every epidemic, not everybody is wiped out. Some people survive and they survive probably because of some protective factors in their genes.

Q. I want to turn to the question of transmission of the virus by a mother to a child. Is that one area which there have been great developments in the western world through the use of antiretroviral medication.

A. Yes, this is one of the triumphs of antiretroviral therapies. Prior to the availability of antiretroviral therapy, mother to child transmission was around 20-25% and mainly occurred in the last trimester of pregnancy during child birth and with breast feeding. We were one of the first groups in the world, with my colleague, John Zeller, to document transmission of this virus. Since antiretroviral therapy has been available, all women with HIV infection in pregnancy are highly recommended to take antiretroviral therapy to render the viral load below detection in their blood and genital tracts and that has had a dramatic outcome, in that we just almost never see HIV-infected children any more in the developed world. The only time we do see it is in

the sort of immigrant populations I was referring to in that other paper, in the Lancet, of immigrants who come to another country, don't realise they're HIV-infected, and deliver, without the knowledge of HIV infection which is a real tragedy. Paediatric HIV in the developed world has essentially disappeared over the last five years.

Q. You just mentioned, as part of that answer, that you and your colleague were the first to document breast milk transmission. What did that involve.

A. What that involved was some work in the early days of transfusion, transfusion prior to 1985, when the blood was screened and we identified a woman who was transfused for post part of haemorrhage; in other words, she bled after delivery of the child, so that she could not have transmitted the virus to the child during pregnancy or delivery, however, it subsequently turned out that that child was HIV-infected and the only hypothesis was that that child must have been infected by breast feeding, which this woman did, as is, of course, normal practice. That description led to an enormous amount of subsequent work, showing that there was HIV in the breast milk, showing that the immature gastrointestinal tract of an infant could absorb the HIV virus and leading to change in policy at the World Health Organisation, where a woman could safely bottle feed in the developing world: in other words, access to clean water for boiling, that this should be a recommendation for such women.

Q. In the developing world, a massive change of recommending breast feeding to, if possible, using a formula.

A. It is a dramatic thing. The recommendation is only if it is safe for the woman to do so, so only if the woman can safely bottle feed a sterilised formula. Now, a lot of the research in the developing world, on mother-to-child transmission, is concentrating on how we can prevent breast milk transmission without

interrupting that very important part of mother-to-child development.

Q. You have just mentioned that part of this process, in terms of documenting the breast milk transmission, was showing that HIV was present in the breast milk; how did you do that.

A. I'm sorry if I misled you there. I didn't do it. What I'm saying is because of that work identifying that case, the scientific community then started looking at breast milk and showing that there was indeed HIV in breast milk.

Q. Though you yourself didn't do it, other members of the scientific community did it.

A. Right, correct.

+CROSS-EXAMINATION BY MR BORICK

Q. I want to ask you some questions about what you have told us today and then I want to go back to your report you have handed in; all right.

A. Sure.

Q. His Honour asked you the important question 'Has the virus been isolating'; remember that.

A. Yes.

Q. You said there were a number of ways to isolate it.

A. That's correct, yes. Different laboratories have different approaches.

Q. What are the other ways in which it is isolated.

A. The usual method of isolation is called viral co-culture, where you take the cells from the person who is HIV-infected, stimulate them to divide, and culture them with fresh uninfected cells and those cells then start producing virus. You then maintain that virus, usually on replicating cell lines.

Q. What do you mean when you say 'Take cells from a person infected with HIV'.

A. You take blood, you separate the white cells, particularly the lymphocytes and stimulate them and then culture them with normal uninfected lymphocytes.

Q. Yes, but how do you know that that person's infected

with HIV.

A. You find a virus in that culture supernode and you identify that virus by various techniques and that includes standard microscopic techniques of electromicroscopy. You can do it by reverse transcriptase and you can do it by molecular techniques of identifying the virus. They all pose legitimate read-outs for the presence of the virus.

Q. You have to do all of that before you can say that the cells are infected with HIV - that the virus exists in the cell.

A. No. You don't do that with every person because what has happened now is that we know the genetic blueprint of this virus and, so to show that someone's infected, you identify the gene of the virus and that is a much more rapid thing to do with the revolutions in molecular biology that I talked about before.

Q. What is the genetic blueprint of this HIV, of the virus.

A. The genetic blueprint is a sequence.

Q. You said it is unique, everybody knows what it is. You tell us what it is.

A. It is a genetic sequence which makes you and me different from any other plant or animal or virus or bacteria. It is a genetic sequence.

OBJECTION: MS MCDONALD OBJECTS

MS MCDONALD: Could the witness finish his answers?

A. It is a genetic sequence that is basically the principles of DNA and molecular biology that every organism is unique and has a unique genetic sequence, and that unique genetic sequence identifies one microorganism from another and it also identifies one person from another, which you probably know, in terms of DNA evidence in legal matters. It is a very unique tool to identify an organism.

XXN

Q. You referred to the revolution in molecular biological techniques; what were you referring to there.

A. I was referring to the ability to amplify small amounts

of genetic material to manipulate them and sequence them and this is due to what is called PCR technology, or polymerise chain reaction.

Q. Who founded PCR.

A. One of the AIDS denialists. He won the Noble Prize for it. I can't remember his name. It escapes me right now. He won a Noble Prize for that discovery.

Q. Can you remember what he had to say about the use of his techniques for the diagnosis of HIV.

A. No, I can't remember it.

Q. Can't remember it or don't want to remember it.

A. Sorry, I just simply can't recall what he said because it is just wrong.

Q. If you can't remember what he said, how can you say it is wrong.

A. Because it is just simply wrong. If you tell me what he said, perhaps I can help you but I can't recall exactly what he said about it, but it is definitely dismissed in the overall scientific community.

Q. I will come back to that a bit later. You referred to the fact that there are many, many pictures of the virus; do you recall that.

A. Yes.

Q. Produce one. Can you produce one.

A. I can refer you to publications of them but I haven't got one now. The other expert witnesses have indicated those that are available.

Q. My precise question is can you -

A. They're on the front of every textbook of virology.

Q. They are not. Can you produce one.

A. I haven't got one.

Q. One actual paragraph.

A. There are tonnes of photographs of it in the scientific literature.

Q. Yes, or no: can you produce one paragraph.

A. I haven't got one with me. I would be very happy to send you one.

Q. We will look forward to it, thank you. You have

referred to the ELISA and the Western blot tests and I don't quite understand what you're saying about them. Are you saying that the ELISA, for example, is a specific diagnostic test for HIV.

A. Indeed it is. It is 99.9% sensitive and 99.9% specific which means if it is positive, it is almost certain that you're infected and, if it is negative, it is almost certain that you're not.

Q. If that is the case, why do we bother with the Western blot or nucleic acid testing, or any other testing if it is so specific.

A. We don't always rely on that. In some settings we just use two ELISA's with different platforms and that is enough. It is a public health choice. In the developing world, for example, it is not really necessary because the prevalence of HIV infection is so high that ELISA testing is the most cost-effective. In the developed world we like to exclude very rare events and so we'll do Western blot testing.

Q. You can be HIV-positive in Papua New Guinea but not in Australia.

A. No, that is not true. It is a public health fund and cost benefit analysis which allows you to do that. Unfortunately, Papua New Guinea doesn't have enough money to have the standard medicine that we do, I wish it would.

Q. In Papua New Guinea you can be diagnosed positive or found to be positive on one ELISA test, can't you.

A. I'm not sure of the recommendation. Most developing - I don't know specific PNG, but in most developing countries it is two different ELISAs.

Q. What do you need for a positive result in Australia.

A. You confirm it with a Western blot, it is normal practice.

Q. You say do one ELISA, positive, confirmed by one Western blot.

A. We usually do two ELISAs and a Western blot is our particular laboratory algorithm.

Q. Why do you do two ELISAs.

A. Because, as I said before, this is not a great diagnosis to have, for all the reasons that I have explained, and we like to be - we're fortunate in our society that we are able to afford the best diagnostic technology. We go out of our way to make sure that it is really positive.

HIS HONOUR

Q. Is it your position that one ELISA positive test, in your view, is 99.9% accurate and the reason for doing two and/or a Western blot -

A. Yes - no, I think that that quota is for two different platform ELISAs. I think it would probably be - for one ELISA it would probably be around - a bit over 99. I think the second ELISA gets you very close to 100.

Q. Your view is that if you test positive on one ELISA, it is somewhere around about 99% certain that that test is positive.

A. It does depend on the population. If you have a population that you're testing in which there are many HIV-infected persons, then the chances of having a false positive ELISA are very low. If, however, you have a low-risk population, such as blood donors, where you have to make an exclusion declaration and so forth - and it is very rare to find an HIV-infected person these days amongst blood donors in Australia - it is more common to get a false positive ELISA. It depends on the population you're testing.

Q. That is a mathematical question; is that correct.

A. Yes, indeed.

XXN

Q. Why does it depend upon the population, because the population test is different to the specificity test, isn't it. If it is 99.9% specific, that's it, it has nothing to do with the population, has it.

A. Yes, that is absolutely correct. In a low-risk population you're going to see more false positives than in a high-risk population, as a percentage.

Q. I'm saying population has got nothing to do with it and I'll give you an example. Assume, would you, that there is 1 in 1,000 people in Australia with HIV; okay.

A. Yes.

Q. We accept 99.9% specificity which is 1 in 1,000.

A. Right.

Q. Put those two together, 1 in 1,000 people have found to be positive, but there's an error rate of 1 in 1,000, so that leads to a 50-50 chance of being a false positive, doesn't it, on those figures.

A. I'm not really sure about your logic there. I think you should probably question Professor Elizabeth Dax, who is the chief of the National Reference Lab and she can give you the figures of the rates of false positives in the Australian population.

Q. If it is any consolation to you professor, it took me two hours to get my head around that. I'm doing the best I can with it. You have referred to the Rodriguez study.

A. Yes.

Q. That was a study that occurred in Europe and North America.

A. I think so.

Q. It is here, that HIV treatment response and prognosis, in Europe and North America.

A. That is not the Rodriguez one, is it? That's the RCC collaboration.

Q. You're quite right, P18 I'm referring to. Their interpretation of the study was that 'the virological response, after studying HAART, improved over the years but such improvement has not translated to a decrease in mortality'. That is their interpretation. You'll accept that, will you.

A. Yes.

CONTINUED

Q. My understanding is that you regarded that - you used the word paradox - but you explained it by saying that so many large numbers of people are migrating into Europe and North America and that could explain it.
A. Correct.
Q. The data they have got came from 22,217 patients who were aged 18 years and over, were antiretroviral naive before starting HAART, and who started therapy between 1995 and 2003.
A. Right.
Q. That doesn't fit in with your proposition, does it.
A. No, I think that they are saying that the mortality is certainly decreased compared to what it was before 1996. I think the other thing that's important to mention is that even with treatment, HIV is a fatal disease. Survival has improved but some people still continue to die of this disease. I was trying to explain to you that I thought my interpretation of the continued death rate was due to migrating populations into Europe and the sort of slight increase that they have seen over the last couple of years, but that it's quite true that people with HIV do still continue to die, they just don't die at the rates that they used to.
Q. HIV, by definition, is a virus; that's right.
A. Yes.
Q. What is the disease HIV.
A. Well, we sometimes call it HIV disease or we call it AIDS. They are the clinical manifestations of HIV infection.
Q. But that means HIV equals AIDS, is that right.
A. No, not always, because AIDS is simply a state of the immune system where you're susceptible to various opportunistic infections, and these infections are a read out of the parlous state of your immune system, so people can have HIV and asymptomatic HIV infection; the problem is that without treatment, they will progress to AIDS.
Q. But you can have AIDS without HIV; there have been

plenty of examples of that, haven't there.
A. Can you have AIDS without HIV?
Q. Yes.
A. No, I don't think so.
Q. Take tuberculosis, that's AIDS, isn't it. If you're HIV positive and you have tuberculosis, that's AIDS.
A. That's correct - it's not fully correct, it depends where the tuberculosis is, but if it's dissemination, yes, if it's pulmonary tuberculosis, no.
Q. I will come back to that in a minute, too, but if you have tuberculosis in whatever form, if you are HIV negative, then you have tuberculosis, don't you.
A. Yes.
Q. So how does it happen that if you have an HIV positive ELISA test, and you haven't had tuberculosis, you have AIDS, but if you're negative, you have tuberculosis.
A. Sorry, I just can't follow that. So the surveillance definitions - or the definitions of the diseases which define AIDS are made in the presence of a positive HIV test, so in order to have AIDS with tuberculosis you have to be HIV infected.
HIS HONOUR
Q. HIV is the fundamental before you can have AIDS.
A. Right.
Q. If you haven't got HIV, whatever disease you might have, it's not AIDS.
A. If you don't have - there are plenty of people who get disseminated infections that might be due to other causes of immune impairment, so people with cancer who are treated with chemotherapy or radiotherapy get impaired immune systems, people who are lucky enough to receive heart or kidney or bone marrow transplants for serious illnesses sometimes get their immune system impaired because of the increased need of antirejection drugs, and those people suffer opportunistic infections which also occur in people with AIDS, such as tuberculosis, or cryptococcyl diseases, or leishmaniasis, or a whole host of them, but in order for

a person with tuberculosis, or cryptococcyl disease, or leishmaniasis or whatever, to have AIDS they have to be HIV infected.

XXN

Q. That is, have an HIV positive test result.

A. Correct.

Q. So if we were in Papua New Guinea and one ELISA test was sufficient and a person had tuberculosis, the person had AIDS; if the same person lived in Australia, they would have tuberculosis.

A. No, that's just illogical.

Q. It's not illogical.

OBJECTION: MS MCDONALD OBJECTS

MS MCDONALD: If the witness can finish.

XXN

Q. Please explain.

A. All right. Let me try. If you are HIV infected in Australia or Papua New Guinea and you have tuberculosis, you have AIDS. If you're not HIV infected, no matter where you are around the world and you have tuberculosis - which is a common, very common, sadly, you know, infectious disease that we're not doing too well with either - then you just have tuberculosis.

Q. Take out the words 'HIV infected' and come back to what you agreed with when I put it to you. You have got an HIV positive result, right.

A. Right.

Q. If you have an HIV positive result in Papua New Guinea which is, let's assume, one ELISA test.

A. Let's assume two.

Q. All right, two, and no confirmatory test, all right.

A. Yes, let's do that.

Q. You've got TB - well you've got AIDS, that's Papua New Guinea.

A. Correct.

Q. In your laboratory, if you had two ELISA tests positive but no confirmatory test, you wouldn't be able to say HIV positive, would you.

A. No.
Q. So the person coming out of your laboratory would have tuberculosis and not AIDS.
A. No, but we would confirm the HIV positive test before saying that that person has tuberculosis - has AIDS, sorry.
HIS HONOUR
Q. The position is, isn't it -
A. Can I just interrupt you? I'm sorry. One of the important things is also the clinical perspective, all right, so that, you know, if you've got an HIV positive test in a young homosexual man or a young injecting drug user, and they present with tuberculosis, that really ramps up the chances of them having AIDS. If it's some lower risk older person from the community, and they have tuberculosis, then of course the chances of them having AIDS is much, much less, so it's a clinical balance as well as the test.
Q. I was just going to put the proposition which I think is obvious, but I just want to confirm it: that different countries have a different basis upon which you can arrive at a final diagnosis, and that's a decision that's made by that particular country depending on its resources, etc.
A. Yes, that's a public health - that is purely a public health decision. I mean a Western blot costs $100 so, you know, spending $100 on something is a lesser priority than providing drugs to treat that person's tuberculosis.
XXN
Q. You refer to the mother to child transmission, and you referred to the figure of 25%; in other words, 25% of mothers can have transmitted HIV to their baby.
A. Correct.
Q. But you start with the proposition that the mother is HIV infected first, don't you.
A. Yes, indeed.
Q. So you've got 100% of infected mothers and 25% of

infected babies.

A. Correct.

Q. Why aren't all babies infected. Why don't you get 100%.

A. There is very good data now that that is related to a number of factors. It's related to the viral load in the mother; some mothers with very high viral loads are much more likely to transmit than mothers with very low viral loads, and similarly in breast milk as well, there is data for that. It's also related to childbirth and how traumatic the childbirth is. For example, there is very good data in twins, in twin births, where the second twin is much more likely - the twin who is born second is much more likely to be HIV infected than the first twin who comes out, and that is simply because the birth canal is much more traumatised and much more bloody, so there is all sorts of reasons why some children are infected and others aren't.

HIS HONOUR

Q. For the same reason, I suppose, that there are all sorts of reasons why someone who is having a heterosexual relationship with an HIV positive male may not necessarily contract HIV.

A. Right. I mean, you know, just as I was saying, I've had patients who were infected on their sexual debut. I've got many gay men who are discordant, who remain discordant, and they have the occasional - they generally use condoms most of the time, but they have the usual slip-ups, so yes, it goes both ways.

XXN

Q. I want to just take you to your report you provided to the court. You referred first of all to Cox's postulates.

A. Yes.

Q. And they are set out at - it's my p.2 of the report.

A. Yes. I think a number of the experts refer to Cox's postulates.

Q. Just assume we have had a paper where someone has conducted a study of Cox's postulates and how they have

changed over the years, but basically in 1878, Cox published some papers and his first statement had three postulates and, in 1884, they increased to five, and I think I can take it they have changed over time. From where did you get your three postulates, what particular publication or era.

A. I think it was just from, you know, this is just medical school days. This is standard, you know, microbiology 101, so I just remembered them as I remembered them but, you know, the principles are pretty well-known to any microbiologist or physician.

Q. I can understand that. Immediately after setting out the three postulates, you said and I quote 'HIV fits all three of the postulates and, therefore, meets Cox's postulates'.

A. Right.

Q. Meaning HIV fits all of Cox's postulates, all three of them, as the cause of AIDS.

A. Right.

Q. You go down a couple of paragraphs to postulate three and, after you refer to ethical considerations you say 'However, in the absence of the fulfilment of this third postulate, there exist other postulations which strongly suggest that the transfer of HIV from an infected host to an uninfected host causes disease'. Is that not a contradiction between the statement 'HIV fits all three of the postulates' to the words 'In the absence of the fulfilment of the third postulate' followed by a strong suggestion.

A. Not really. I think that, you know, fulfilling Cox's postulates, transferring the pathogen from the infected host causing disease, is something that no research committee in this country, or indeed probably any other country in the world, would allow, so we have to have indirect evidence of that, and I have given you some good examples, I believe, of the indirect evidence in the absence of being able to ethically transfer the virus from one person to another.

HIS HONOUR: I think we have fallen onto 'circumstantial evidence' in the legal world, indirect or circumstantial evidence.

MR BORICK: Now you'll want a discourse on Chamberlain's case.

XXN

Q. We'll come to the circumstantial evidence in a minute. Just following on from that, you use the expression 'In the absence of the fulfilment of the third postulate, there exist other postulations which strongly suggest'. That's the point I'm making to you; that you're really saying there the third postulate has not been fulfilled, but there is a strong suggestion that it may be. That's what you're really saying, isn't it.

A. Yes, I think that's what I'm saying. If you want me to say 'very strongly' or whatever, I can, I just can't say that the postulate is fulfilled because it's unethical to fulfil it.

MR BORICK: That's going to put a gloss on the Chamberlain concept of circumstantial evidence.

XXN

Q. In relation to postulate one, you say 'The epidemiological relationship between exposure to HIV and AIDS has been demonstrated in numerous different studies that document that patients with AIDS, regardless of where they live, are infected with HIV'. That is your statement.

A. Yes.

Q. What test was used to prove that relationship.

A. Whatever the public health recommendation in the country where the study was done.

Q. No, but what test - this is your statement - are you referring to.

A. The evidence for exposure to HIV in the numerous studies are, if the study was done in the developing world it would be two ELISA tests on different platforms. If the study was done in the developed world, it would usually be two ELISA tests and a positive Western blot.

Q. How was the specificity of the test for those pathogens, how was that determined for each of those tests.

A. The specificity?

Q. Yes.

A. I think you need to question Professor Dax about it. I mean she's basically spent her life and done an enormous amount of work nationally and internationally in documenting that the diagnostic tests for HIV in this country and around the world are the most sensitive and specific that they can be, so I would have to say, you know, consistent with licensed tests. So, like every diagnostic test in medicine as critical as this, it has to be licensed by a regulatory agency, which is the Department of Health in Australia, the TGA, the Therapeutic Goods Administration, the Food and Drug Administration in the United States, and the European Medicines Evaluation in Europe. These are licensed tests that guarantee a certain level of sensitivity and specificity.

CONTINUED

Q. You postulate to isolation pathogen to AIDS patients. 'Multiple HIV isolates have been cultured from AIDS patients, the virus has been cultivated and propagated in human T-lymphocytes, Macrophages and certain immortal tissue culture cell lines developed for the purpose of invitro propagation'. The question is: how do you detect the virus in the culture.

A. The detection methods I think I alluded to before are several. They include assay reverse transcriptae enzyme of the virus. They include an antigen test relying on the specificity relying on the antibody reactions. They include PCR technology to quantify the virus in those co-cultures, so all of those are used in my laboratory at the Centre of Immunology in St Vincent's in Sydney. We have a freezer full of these virus isolates from hundreds of virus AIDS patients checked in these ways.

Q. In this context, what do you say is the significance of the detection of the protein P24.

A. It's a standard methodology. It is a specific test for the presence of antigenic components of the virus. P24 is part of the core of the virus. It's a very robust antigen and the technology to detect is cheap and reliable.

Q. P24 was first discovered by Montagnier in 1993 in material in which he later admitted contained no retroviral particles; do you accept that.

A. No, I don't.

Q. That is you don't accept that he made that admission.

A. I think it was a mistake. I think there are numerous cultures since in which they have P24 antigen and you can have viral particles there. I think perhaps in his hands at that time when it was so difficult, you know, when everyone was struggling to try and isolate this virus that some anomalies were found and that has not subsequently happened.

Q. It is your position that the protein P24 is unique to HIV.

A. Yes, unique.

Q. Do you accept that the protein P24 can be found where there was no HIV, for example in the placentas of healthy women or bile culture blood of negative donors. Do you understand the question.

A. Yes, I do. So, what you are getting at is issues of what - according to endogenous retroviruses - as we have evolved over generations and generations we may have been infected with different retroviruses over, you know, over the generations and these retroviruses have gone into our DNA and are in fact quite harmless and sometimes they will have, you know, they can activate the genome to produce this P24 in very low levels. The issue which I think you are missing is that, the fact that this P24 antigen is specific to HIV so - and just, I was saying before, every organism has a unique genetic footprint, blueprint. The P24 antigen of HIV is unique protein.

Q. You are saying it is specific or unique to HIV.

A. The P24?

Q. P24.

A. Right, but I mean, you know, you look - you know, you look like your brother. You know, you may look like your brother, sister or parent or sibling but your generic material is slightly different. In a court of law we can prove that your hair is different from your sister's or your father's hair. Now, you know retroviruses are families. They are families of viruses. You know dominion evolution has allowed different organisms to evolve over time and there are some unique features of living organisms which have common structure to allow them to reproduce and survive. So that there are different retroviruses and P24 is one of the components of retroviruses which allow them to be retroviruses. The issue is that the HIV P24, just like you're different from your sister's hair is different from some other retrovirus and that can be detected antigenically or it can be detected genetically.

Q. I'm going to ask his Honour to adjourn for a few minutes

to enable me to take some instructions. What's your time frame.

A. You know, I'm yours for however long you want me this afternoon.

HIS HONOUR

Q. That's an invitation I wouldn't make to counsel.

A. That's up to his Honour of course but unfortunately I'm only available today.

Q. What I'm going to do is adjourn for about 10 minutes, so that will give you a break as well.

A. Thank you so much.

Q. If we could resume in 10 minutes would that be convenient? I'm asking you if that would be convenient to you.

A. Yes.

Q. We are going to hang up and we will get you back in 10 minutes time, approximately.

A. Okay, thank you.

ADJOURNED 4.00 P.M.

RESUMING 4.20 P.M.

HIS HONOUR

Q. Can you hear me; hello.

A. Yes, I can.

MR BORICK: I will just mention this briefly to Ms McDonald and the prosecutor - there are two prosecutors - I have some questions that I want to put to the Professor now. I haven't got a transcript of what went before. What I have got in mind, if my friend has a look at them, I prepared some written questions that he can then respond to. Would there be any trouble with that, if the parties agree to it?

HIS HONOUR: If the parties are agreed to it and Professor Cooper is prepared to do it, the answer is I'm prepared to do it on that basis. This is an application for leave, it is not a trial.

MR BORICK: Yes.

HIS HONOUR: Ms McDonald, do you have any problem with that?

MS MCDONALD: I don't have a problem, in principle, so long as it is a sensible limit.

HIS HONOUR

Q. Professor Cooper, did you hear the exchange that we just had.

A. Yes I think so, you want me to respond to some written questions.

Q. Yes but they are put to you - the prosecutor will have a look at them and I will have a look at them to ensure that you are not flooded with a series of questions. Is that course acceptable to you.

A. Thank you your Honour, that's fine.

XXN

Q. You said early today that once the virus is purified then you sequenced the genes; do you remember saying that.

A. Yes.

Q. Would you be able to provide us with any papers or studies which demonstrate the purification of HIV particles.

A. So again I'm not, you know, a card-carrying laboratory virologist. It is something that you should ask one of the other expert witnesses, Dr Dominic Dwyer. You purify viruses by gradient centrifugation - by splitting very hygiene - I would defer this to expert witnesses like Dr Dominic Dwyer for that.

Q. What I was actually asking was: whether you could provide us with any papers that demonstrate the proof of purification of HIV proteins or would you like to leave that to one of the other experts.

A. I thought your question was HIV viral particles.

Q. It was. HIV particles.

A. Yes. So yes, I mean, there are standard laboratory techniques for purification of viral particles and I prefer you would address that to, you know, the experts in laboratory virology like Dominic Dwyer.

Q. You referred to the gene bank; do you remember that.

A. Yes.

Q. Are you referring to the gene bank in the Los Almanos laboratory.

A. Yes, that's one of the major gene banks around the world.

Q. Is that the one that you were referring to.

A. Yes, I was yes.

Q. Are you aware that the custodian of those sequences is Dr Brian Foley.

A. No, I don't know who the custodian is. I know that they are held at Los Almanos and very special sequences where we have publications where we submitted those sequences to Los Almanos.

Q. Are you aware that there has been a recent intensive debate in the British medical journal, on loan, between Dr Foley and the Perth group, members of the Perth group.

A. No, I'm not aware of that.

Q. I have to provide you with a transcript, but would you be aware that Foley has admitted that what is called 'HIV genome' is a Tly(a)RNA which originated from material which was not purified.

A. No, I'm not aware of that. What I'm aware of is that when you - I have several publications and there's numerous other publications in the literature when you isolate special sub-types of the virus which might have special genetic signatures, the journal will not publish your article unless you submit that sequence to gene banks so that it is publicly available for other scientists to look at and analyse.

Q. When I was putting some questions to you about the first postulate, there was some discussion about whether you use one or two ELISAs; do you recall that.

A. Yes.

Q. In that context, are you aware that the Mandela study, that's the Nelson Mandela study from which the figure - there are five million South Africans infected - that study was based upon one ELISA and the ELISA test kit which they used in that study is not licensed in

Australia; were you aware of that.

A. No, I'm not aware of that, but I think it's important to go back to the, you know, the public health issue that where you have - where you have a very high prevalence of HIV; in other words, up to, you know, 40% of the population or in some ante-natal clinics - for example, in Johannesburg where, you know, 40 to 50% of the pregnant women are infected, then even if you do one ELISA test, the chances of having a false positive in such a population are extraordinarily low.

Q. The other point that I was making in that question is that the test kit used in that study is not licensed in Australia.

A. Well that I don't know. I have colleagues in South Africa who have surveyed their populations and they use reliable assays. So, for example, I'm involved as an advisor to the national institutes of health for a project that they are undertaking with the South African defence force where they are treating enlisted men and women in the South African defence force who have HIV/AIDS and I can assure you that the testing that the NIH would have done in the South African defence force, where they have hundreds to thousands of infected service men and women, would be an FTA licensed test.

Q. Now, the next question relates to a document called P18 which is the document 'HIV Treatment and Response and Prognosis in Europe and North America'. Do you know the document that I mean.

A. Yes, I know of it.

Q. For convenience, could we refer to that being the MAY study; the reason being that correspondence should be addressed to MAY; all right.

A. Correct, yes.

Q. I just want to clarify something here. I read out to you the interpretation just as it appears in the paper, but is the paradox that you referred to this: that although the May study shows that there was a reduction in the viral load over time, it was not accompanied by a

reduction in the death rate'. Is that the paradox.

A. Yes, if that's what I wrote, yes that's it.

Q. In relation to tuberculosis you said that only multiple TB is an AIDS-defining disease; is that right.

A. I'm sorry I missed that.

Q. I'm sorry I had my head down. I think you said that in relation to TB, only multiple TB is an AIDS-defining disease.

A. I mean, disseminated tuberculosis is distinct from pulmonary tuberculosis so, generally, clinicians working in HIV medicine distinguish between pulmonary and extra pulmonary tuberculosis, so extra pulmonary tuberculosis has - it is much more likely to be associated with a more severely impaired immune system than pulmonary tuberculosis.

CONTINUED

Q. You aware that since 1993 in Australia, TB found anywhere in the body, including in the lungs, is an AIDS defining disease.

A. No, that is not correct. It's an AIDS defining disease if you have HIV infection.

Q. You said that reverse transcription in culture is proof of isolation, is that right.

A. Yes.

Q. Is reverse transcription specific for a retrovirus.

A. Only retroviruses can have the reverse transcription enzyme, that's correct.

Q. So it is specific to a retrovirus.

A. Yes.

Q. Just on that topic, are you aware that one of the discoverers of reverse transcription, Professor Baltimore, says that 50% of our DNA is obtained by reverse transcription.

A. I don't know what the context of that is. Usually DNA synthesis is by a process which resembles reverse transcription, which is done by an enzyme called DNA polymerase.

Q. That is probably one of the matters where I will be more specific in a written query to you.

A. Sure.

Q. The next two, I will just put them to you now and then provide you with a little more information. You referred to the observation that laboratory or health care workers may become infected with HIV on the basis of accidents that exposes them to the virus. Such workers became HIV positive following the event of these risk factors of infection. Do you have any figures or studies to support that proposition or observation.

A. Unfortunately we had a health care worker some years ago in our service at St Vincent Hospital who became infected exactly in that way, unfortunately. She was working with AIDS patients and underwent a needle stick, an accidental needle stick injury and sero-converted, and, in my view, she had no other risk factors. So

that's personal experience. And there's numerous reports in the literature of health care workers with no other risk factors getting HIV through infected needle sticks.

Q. Have you got any figures on the death rates emerging from needle stick accidents.

A. Well, no, I don't, because - I simply don't have any figures, but there is no reason to suppose that their outcomes wouldn't be any different from any other HIV infected person, and probably better because they're within a health care setting.

Q. Would it surprise you if I said that nearly 800,000 needle stick incidents are reported annually in the United States. Does that figure surprise you.

A. No, not at all. It's depressing, isn't it?

Q. The next figure is that there have been 200 deaths from hepatitis B per year, but up to January 2002 only 57 cases of deaths have occurred unrelated to hepatitis B and directly related to needle stick. Would those figures surprise you.

A. Sorry, deaths due to HIV needle stick?

Q. No, 200 deaths have been discovered due to hepatitis B each year, per year.

A. As a result of needle sticks?

Q. Needle sticks, yes.

A. Right.

Q. Would that figure surprise you.

OBJECTION: MS MCDONALD OBJECTS.

MS MCDONALD: In my submission, to make that question fair, my learned friend has to include what sort of needle stick injury we're talking about, one where the blood is from somebody who has been diagnosed as being HIV positive, because that is quite a different scenario from any old needle stick injury.

MR BORICK: I will withdrew that question and be more specific if I am allowed to put it in writing.

XXN

Q. Do you know the numbers of laboratory and health care

workers there are in Australia.

A. No, but I wish there were more. I'm not sure of the exact numbers, but thousands, I would suspect.

Q. Do you have any figures as to how many of the laboratory or health care workers may belong to AIDS risk groups such as drug users or who are gay men.

A. There are certain industries in which there is an overrepresentation of the traditional HIV risk groups in an industry, and the health care industry is not exempt from that, and the situation is even worse in Africa, where the rates in some health care settings amongst health care workers are even higher than in the general population and reflect what you are referring to. But it just depends on the country. Yes, that is correct, but there are certainly situations in which it is quite clear that even a health care worker from a risk group has been infected from that particular needle stick injury and not by other means of transmission.

Q. You understand what I am really putting to you here; I'm saying that your observation which is marked point A in your report, that is relating to laboratory health care workers, cannot assist you to fulfil or to argue that Koch's third postulate is fulfilled. Do you understand that is what I am putting to you.

A. Yes, I understand what you are trying to do. I just have to say to you that there are very clear cut documented cases of health care workers who have had needle stick transmission from an HIV infected patient to them by a needle stick accident. That has been proved by genetic analysis of the virus isolates from the person to the health care worker.

Q. Can you provide some documentation.

A. Yes, I think I could. I think I could, it would be a bit of a search in the literature, but there are examples of that. The best example, of course, is the other way round, is the Florida dentist.

Q. I am about to come to that. You have no doubt heard of Harrison's Internal Medical Textbook.

A. Yes, I have.
Q. It's the Bible, isn't it, in a sense.
A. One of them, yes.
Q. And you have no doubt heard of Dr Faucci.
A. Yes.
Q. Do you realise that in that textbook Dr Faucci talks about the Florida dentist case and he says 'To this day that case remains controversial', are you aware of that.
A. Yes, I am aware of that.
Q. It is a pretty significant statement about the Florida dentist case, it is a very controversial matter as to whether the dentist passed it on to the patient, isn't it, for a variety of reasons.
A. Yes, I understand that it is. I understand it is controversial. It was my understanding that the virus isolates amongst the dentist and his infected patients were again consistent. There is a similar case within Australia in which a surgeon in Sydney infected several patients that underwent minor procedures, and again in that setting, the virus isolates in the contaminated equipment from the index patient were the same as in the subsequent patients in that list on that day.
Q. Is that documented anywhere, that case.
A. Yes, very, very well documented. It's a publication in The Lancet some years ago. And indeed the genetic evidence was used to prove that the surgeon had been, sadly, at fault.
Q. P.3 of your report at point E, you refer to simian immunodeficiency virus called SIV, S-I-V, and you argue that the fact that these SIV strains, as you say, caused AIDS in monkeys provided an animal model fulfilment of Koch's transmission third postulate, which is the transfer of the pathogen to an uninfected host causes disease. My proposition to you is that it is completely invalid to use SIV as though it were HIV for the purpose of arguing that the third postulate has been fulfilled.
A. It is a different organism, it is a different organism, but animal models have been used extensively in AIDS

research and we know that the HIV virus evolved from simian viruses, so we know exactly where and when that happened, so it is not unreasonable to use those simian virus models to prove aspects of HIV transmission.

Q. My proposition to you is: it is totally invalid to use it. Do you understand what I'm putting to you.

A. I disagree with that.

Q. You disagree, yes, I understand.

MR BORICK: That completes what I want to put this afternoon, with the proviso of the written material.

HIS HONOUR: When do you think you will be in a position to put your written material?

MR BORICK: I would like to have it ready by Monday.

HIS HONOUR

Q. Are you in Australia for the next week or two.

A. I am going to Thailand next Wednesday working on our project there in Thailand on treatment.

Q. How long will you be away.

A. Be away from Wednesday to Sunday next week.

Q. So you will only be away for a relatively short time.

A. Indeed.

Q. So if the questions are sent to you early next week, would you be in a position to respond, say, within a week to ten days.

A. Yes, I should be able to do that.

Q. We will arrange for any further questions to be submitted to you.

A. Thank you, your Honour.

Q. When you're answering them, can I just remind you - I hope you don't mind me doing this - but you are still under oath. So any answer indeed will be answers given under oath.

CONTINUED

+RE-EXAMINATION BY MS MCDONALD

Q. During the course of your evidence you have talked about using two ELISA tests and using different platforms, what do you mean by that expression 'different platforms'.

A. By different platforms I mean using - I guess it is hard to explain simply, it is the configuration of the assay and which antigens you use and which antibodies you use and how they react with each other and how they read out. Generally you try to use an antibody in the second ELISA which targets a different antibody in the region. Or you might use a viral other than the first ELISA or the second ELISA.

Q. The second and final matter I wanted to us ask you about, this case in Sydney in relation to the surgeon who infected patients.

A. Right.

Q. You told us that case is very well documented, was it also in fact very well investigated at the time.

A. Extremely well investigated. Just to be quite clear, the surgeon was not infected but through his surgical practices, probably reusing local anaesthetic vials they were contaminated by the first patient who happened to be HIV infected and then by reusing the local anaesthetic vials on subsequent patients they became infected. I think Dr Dwyer actually did the work on the sequencing and he will be able to tell you how those sequences were identical through the index person and the subsequent unfortunate people who were infected in that way.

Q. How many people were infected.

A. I think that there were four or five, something like that.

Q. Was that then the subject of a special inquiry by the Medical Board of the New South Wales Health Department.

A. Yes, it was.

Q. Obviously there are ramifications -

A. There should be a report on that somewhere, it was very

well-known at the time, and I believe the transmission report was published in the Allianz a couple of years after the event.

HIS HONOUR

Q. That concludes your evidence at this stage.

WITNESS STANDS DOWN

+THE WITNESS WITHDREW

CLOSED-CIRCUIT TELEVISION DEACTIVATED

MR BORICK: I should be here by a 20 to 10 tomorrow.

HIS HONOUR: I will list it for 9.40.

MR BORICK: That is Childs.

HIS HONOUR: Yes.

MR BORICK: Then we have got Dr Turner to finish.

HIS HONOUR: To complete.

MR BORICK: My understanding is we go to Professor French. Perhaps it might be an idea if my friend tells us what is in store for us.

MS MCDONALD: I hope not to be too long with Dr Turner tomorrow. Then we have Professor French for the rest of the day. On Monday we have Elizabeth Dax and Dominic Dwyer who will obviously on quite discrete areas. On Tuesday we have Professor Gordon who will be more of a generalist. They will also be talking specifically about Mr Parenzee's case. In there somewhere Professor McDonald. Then on Wednesday we have Professor Kaldor and then on Thursday we have Gustav Nossal.

HIS HONOUR: We are going to have to find times for addresses. Perhaps if you can give my associate some idea as to when we might be able to find time for addresses and how long you might need to prepare addresses.

MS MCDONALD: It might depend on where we go with written submissions, which has become more appealing the more I have thought about it given the nature of the case because this might effect whether we have some or any oral submissions to supplement.

HIS HONOUR: I think that we will have to have some oral submissions but I think if they are supplemented

with written submissions.

MS MCDONALD: The oral submissions first and then the written submissions?

HIS HONOUR: Yes.

MS MCDONALD: I would think that would be the appropriate course.

HIS HONOUR: We will have to find some time to do that.

ADJOURNED 4.51 P.M. TO FRIDAY, 2 FEBRUARY 2007 AT 9.40 A.M.