HOUSE OF LORDS

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Witnesses: Mr Rhon Reynolds, Dr Emmanuel Cormier, Ms Mary Kerr and Ms Lisa Bright

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Members present

Lord Fowler (Chairman)
Lord Gardiner of Kimble
Baroness Gould of Potternewton
Baroness Healy of Primrose Hill
Lord McColl of Dulwich
Baroness McIntosh of Hudnall
Baroness Masham of Ilton
Lord May of Oxford
Lord Rea
Baroness Ritchie of Brompton
Baroness Tonge

Examination of Witnesses

Witnesses: **Mr Rhon Reynolds**, [Advocacy Specialist Europe, International AIDS Vaccine Initiative], **Dr Emmanuel Cormier**, [Clinical Immunology Manager, Internationial AIDS Vaccine Initiative], **Ms Mary Kerr**, [VP and Head of Europe, ViiV Healthcare], and **Ms Lisa Bright**, [General Manager UK and Ireland, Gilead Sciences].

Q387 The Chairman: Good morning. Thank you very much for coming. Just so that we have you all absolutely positioned, perhaps the first thing might be if you could give me a couple of seconds' introduction on your role, starting from the end and moving down.

Dr Emmanuel Cormier: Hello, my name is Dr Emmanuel Cormier. I work for the International AIDS Vaccine Initiative here in London. I am the clinical immunology manager.

Mr Rhon Reynolds: My name is Rhon Reynolds. I am the policy and advocacy officer for the International AIDS Vaccine Initiative and I am based in the Amsterdam office.

Q388 The Chairman: Just tell us a little about the organisation itself.

Mr Rhon Reynolds: The International AIDS Vaccine Initiative is a global, not-for-profit, public-private product development partnership. I have a whole spiel here for you, which I could read through.

The Chairman: No. We will have it for the record at some stage.

Mr Rhon Reynolds: We have offices in Africa, India and the US, where our headquarters is based. We conduct research to identify the best HIV vaccine candidates to take forward to trial. We also conduct policy and advocacy research and, as I mentioned, we do R&D projects.

Q389 The Chairman: What kind of budget do you have?

Mr Rhon Reynolds: Off the top of my head, it is about $90 million. We get public and private investment into the International AIDS Vaccine Initiative specifically from the Department for International Development and a number of other European donor Governments.

The Chairman: Okay. Thank you.

Ms Lisa Bright: Good morning, my name is Lisa Bright. I am the general manager for Gilead Sciences in the UK and Ireland. Thank you very much for giving me the opportunity to give evidence to you today. Gilead is a global pharmaceutical company. We focus on developing medicines for high unmet medical needs, particularly in the areas of HIV and hepatitis. That is particularly relevant for the UK. The chances are that seven out of 10 people in the UK on antiretroviral therapy for HIV are taking Gilead medicines. We take that responsibility very seriously and we are involved in a range of other initiatives that support prevention and testing, given that we have such a high proportion of people here with undiagnosed HIV.

Ms Mary Kerr: Good morning, my name is Mary Kerr. I am the Vice-President and Head of Europe for ViiV Healthcare. For those of you who have not heard of ViiV Healthcare, it is a joint venture established when GlaxoSmithKline and Pfizer merged their HIV portfolios. ViiV Healthcare is a relatively new entity. It is a privately owned company and it is 100% focused on HIV.

Q390 The Chairman: Thank you very much. That is excellent. We have a lot of questions to get through and I think we need to keep the questions short and the answers reasonably brief. I am going to start, if I may, on the possibility of an HIV vaccine. I see that in 1984, the then United States Health Secretary, Margaret Heckler, who I remember meeting in Washington, said, "We hope to have a vaccine ready for testing in approximately two years…yet another terrible disease is about to yield to patience, persistence and outright genius". More than 25 years later, we are still waiting. What are the prospects now?

Mr Rhon Reynolds: We are going to take this in turns. My colleague Emmanuel is a scientist. This is the one thing that we hear time and again. We have even heard from a former Prime Minister here the promise that we should have one in a short time. The reality is that this is one of the most complex viruses that we have ever had. There is a slide that we could share with you in one of the packages that I prepared showing that the variance in the HIV virus is quite huge. It has not been without effort. There has been some success since the early days of our efforts. This year alone, we had proof that an HIV vaccine could prevent infection in humans. This was with the recent Thai study in 2009, called RV144, which provided the first demonstration that a vaccine could prevent HIV infection. There were two AIDS vaccine candidates given a few months apart—a so-called prime boost combination—and they were found to be 30% effective. This is just the beginning. There has to be a lot more research specifically on this candidate.

One of the really exciting things that IAVI has been doing, which my colleague Emmanuel can expand on, is searching the world to find people who have antibodies that can broadly neutralise the virus from spreading. To date we have identified that there are 15. This is novel and ground-breaking. If we can replicate these antibodies, it will give really significant results.

Q391 The Chairman: What do you think about that, Emmanuel?

Dr Emmanuel Cormier: I want to go back to your initial comment that in 1984 it was projected that in two years we would have a vaccine. That was in the context of the success of the hepatitis B vaccine. The idea was to provide a vaccine that would elicit antibody responses towards the pathogen of hepatitis B.

Q392 The Chairman: So she was talking about hepatitis B and not about HIV?

Dr Emmanuel Cormier: That was an example. The failure behind that is that HIV and hepatitis B are very different in their variability, for example. The initial thought was that it would work easily like this. Looking at the broadly neutralising antibody in the context of HIV infection, we have learnt that the emergence of breadth in antibody responses is a long process in the context of infection. If we could force a person's immune system to elicit this breadth through a vaccine, we would be in good shape for preventing infection.

Q393 The Chairman: The science base is obviously extremely complicated. What about the resources being devoted to this? One piece of our evidence tells us that an AIDS vaccine is not a very attractive target for pharmaceutical companies. You have huge outlay, a high risk of failure and impoverished markets at the end of it, so it is not a natural target for pharmaceutical companies. Is that your impression?

Mr Rhon Reynolds: This is the raison d'être for IAVI's existence and for other models like us. There were no incentives for pharmaceutical and biotech companies to take this on. That does not mean that we are not looking for partnerships. Obviously, once we get to a product, the scaling up and growing out of it mean that we would have to partner with the pharmaceutical industry and definitely with the biomedical industry in particular, because of the new technology and innovations that they would provide to this effort.

The resources needed for this effort are undeniably significant because of the long path ahead. I am not sure whether I have fully answered your question, but the point is that it is

unsustainable. One of the things we have been considering is how you look at innovative mechanisms to fund this kind of work.

Q394 The Chairman: Do you feel under-financed, as an overall position?

Mr Rhon Reynolds: I would not say under-financed. The amount of resources that have led to this effort has been steadily decreasing. Private sector donations to this effort went down in 2009 from 10% to 3%. Just last week a thing called the G-Finder report was launched, showing that funding for HIV/AIDS R&D went down by 0.9%. It is about the decrease in resources that are being lent to the effort over time.

Q395 The Chairman: I was not quite clear about those figures. Are they for the UK?

Mr Rhon Reynolds: The G-Finder report is global. There is also the resource tracking report on HIV vaccines and microbicides.

Q396 The Chairman: Let me put it another way. Do you feel what the UK is doing is sufficient in this area?

Mr Rhon Reynolds: One of the things I would have to do is to sing the praises of the UK, which has taken the long-term view on this epidemic in investing in the broader response around treatment and prevention, but also the long-term response in DfID's research strategy, investing in IAVI and in the international programme on microbicides and other research efforts. The UK has led the way in the European context. In a global context, I think it is third after the United States in funding towards this effort as well.

Q397 Baroness Gould of Potternewton: Taking the points that you have made on the science and the funding, the thing that I have in my head is that it has taken 25 years to get where we are and things are obviously looking better, in the sense that people now understand and recognise the position, but can you give us some idea of the expectation for the future? Are we going to wait another 25 years before we can get a vaccine or do you see it happening reasonably quickly in the future?

Mr Rhon Reynolds: I will not make the mistake that past politicians and others have done of guesstimating on what date we will have a vaccine. I am as hopeful as everyone around this Committee that we will have a vaccine tomorrow, but if we look at the history of all other viruses, it has taken a long time. Look at polio. That does not mean that we should give up on the effort. I have only started working at IAVI in the last two years and I am excited about this. We have had results on the CAPRISA studies, showing that microbicides had something like 30% effectiveness among women. We have had the PReP study among men who have sex with men, showing something like 41% effectiveness. Then of course there are the Thai results and there are going to be more results. The point is that we need to continue the political and financial support to continue this momentum.

Q398 The Chairman: But the truth is that at the moment we are still in the position where we were in 1986, with no vaccine and no cure.

Mr Rhon Reynolds: I would say that we have a lot more information than we had 25 years ago.

Q399 Baroness Tonge: I have been in touch with IAVI since 1997, when I first came to the House of Commons, and I have had the regular newsletters from Seth Berkley, who should be sainted for his persistence. I am slightly worried about this. I feel that the advent of antiretroviral drugs put vaccine research back a few slots. I wonder if that was reflected in your funding, particularly in the USA, when George Bush made a big thing about antiretrovirals and the global health fund and they were being pushed out all over the world. Do you feel that that is when your funding started to diminish? Did people lose enthusiasm politically for vaccines when they knew that the antiretrovirals were there?

Mr Rhon Reynolds: I know you want me to answer one thing, so I will respond to that first and then let Emmanuel add to it. As we have seen with a lot of donors, the economic downturn has had an impact on our funding.

Q400 Baroness Tonge: Yes, but before that was there a downturn for the vaccine research when the antiretrovirals were being pushed so hard?

Mr Rhon Reynolds: It was in 2009 when we saw the big drop of around 10%. Some years back there was the Merck trial, which was disappointing news. That was also a hard hit for the momentum that was behind it.

One of the things that we know from the AIDS 2031 project, looking at the HIV/AIDS response over time, is that even if we scaled up we would still not end this epidemic. If we have even a partially effective vaccine that is even 50% effective and distribute it to 30% of the population, it would reduce the epidemic by 24%, or a 5.4 million reduction. The prediction is that even after 2031, we still need a vaccine as part of the response. The point is that we have more people living with HIV. The cost of sustaining these people on lifelong treatment is unsustainable. In the history of any epidemic, the answer has always been a vaccine. Lives depend on this. That is my response.

Dr Emmanuel Cormier: To go back to your comment, one compelling number is that even with all these drugs that you could give to people, for every 1% globally that you put on treatment there are 2% who get infected. Just that difference in numbers tells you that although treatments are available, they are not sufficient to block infection globally. That is probably even more true in developing countries than it is in the UK or countries that can afford medication. That is the compelling number.

Baroness Tonge: So one on treatment, but two get infected?

Dr Emmanuel Cormier: Correct

Q401 Lord May of Oxford: I want to offer you a conjecture that is more about the sociology of science in this area and get your reaction to it. Our first vaccines go way back, long before we had the faintest understanding of the immune system. That has been the history of most vaccines. They have been derived without a real understanding of how they

work, but they work. By the time HIV came along, we had brilliant molecular description of events between the virus and the cell, which is a huge advance, but we still do not have an understanding of things as simple as how the immune system assembles itself somatically and why it does not go on for more years in puberty or fewer or whether the hygiene hypothesis about allergies is right. That is not a molecular biology kind of thing; it involves going beyond the description of molecular events that enable us, when we understand them, to design antiretrovirals, to ask questions about, in a sense, the dynamic behaviour of this complex system of very labile things that have lots of escape mutants, like malaria and HIV. It is an area that is not merely not very funded, but most people who work in immunology do not recognise that it exists. The immunology texts are still like the ecology texts of the 1960s—they are descriptive rather than fundamental. We still do not have an understanding of the pathogenesis of HIV, I would argue. We can describe the molecular events, but we still do not really understand it. You handle the initial infection and the first few escape mutants and eventually the thing crashes. It may be that we will accidentally be able to build a vaccine by finding some people who have peculiarities, and we can generalise, but personally I do not think we will get it until we have understood the dynamics of that system better. What is your response to that? It is really about the sociology of the people working in the area.

Dr Emmanuel Cormier: First, HIV is a very complex system. I agree that we have a tendency to focus on one area and not see the big picture and try to connect everything. People are trying. System biology is a process that people use to try to take information from the various areas and make it a rational system, or something more complete. I think we have learnt a lot along the way of discovery. That brings me back to a comment I wanted to make earlier on broadly neutralising antibodies. In the field of vaccinology, we all understand that the best way to block a virus is to have an antibody-driven immune

response. Right now, with the emergence of discoveries in the field of broadly neutralising antibodies, we are much closer to getting a vaccine that would address our needs. This is very encouraging. It has happened in the last two or three years. We are starting to digest information and then, from that information, get new plans for vaccines. That is the exciting part for us to come. In terms of timelines, vaccine discovery goes from anywhere from two years to 100 years.

Q402 The Chairman: But if we were the Government, we would be sensible to plan on the basis that there was no vaccine, would we not? That is the sensible way of planning for the future, isn't it? We are all very hopeful, but that is the position as it stands.

Mr Rhon Reynolds: What would save the Government more money in the long term? We have ballooning treatment costs. That is not to say that these have not been really effective in saving lives; it is just about sustainability. That is the long-term view that we hope for and the effort that we hope that policy makers and others will make to continue advocating a vaccine, because it makes good sense.

The only other thing I wanted to add is in terms of not knowing and the Thai study. If Anthony Fauci, one of the leading scientists at the NIH, was a betting man, he would have bet against RV144. The results that they found were unexpected. The investigation has to continue. IAVI and others are doing that work to find out why that works. The point is that this science is complex and the virus is complex.

The Chairman: I want to move us on, if I may, to take it more generally.

Ms Mary Kerr: Could I just make a comment about the role of pharma? Not all pharmaceutical companies are involved with HIV research; in fact, not many are. Not all pharmaceutical companies have a vaccine capability; in fact, few companies have a vaccine capability. So when you put that together with the complexity of the science and the

dynamism of the virus, you can see that it is not surprising that there has been a limited focus. GSK, the shareholder of ViiV, has some early work on a vaccine for HIV.

The Chairman: Thank you. I would like to take us on to go generally into research.

Q403 Lord May of Oxford: I wondered what you thought the emphases ought to be in research? We have heard quite a few people who seem to feel that we do such a good job now in managing with mixtures and handling the fact that escape mutants appear, and so on, that in some sense everything is okay. My own view would be that, first of all, these people forget that it is not a question of whether resistance will eventually emerge, even to the most sophisticated things, but when. Do you think the focus should be simply on trying to aim for yet more efficient ways of suppressing the virus or that much more attention ought to go into trying to find a cure? Is there any hope in that? Where should the research emphases be?

The Chairman: Let's try to bring the other two into this now. Lisa Bright, would you like to start?

Ms Lisa Bright: Both are very important. All of us want to see an eradication of the virus. In Gilead we have a very small team working on a cure. That is going to be an incredibly complex task, and who knows whether we will ever get to that point.

Q404 Lord May of Oxford: Are there many people working on it?

Ms Lisa Bright: There is a small team at Gilead dedicated to looking at that. In the interim, as you point out, we also have to look at what we can do here today. We know that one of the biggest challenges that we still have, even though antiretrovirals have had a phenomenal impact in extending life expectancy for somebody with HIV, is that one of the key factors that defines that is adherence—whether somebody can adhere and continue to take their medicine. If we go back maybe 20 years, HIV was a very different situation, it was pretty much a death sentence and people were taking 30 tablets three or four times a day. Now, if

you are diagnosed at 35 the chances are that you are going to live an almost normal life expectancy. A big factor in that has been that drugs are better tolerated, although nothing is perfect. Also, you can now take one or two pills once or twice a day. That has had a huge impact. Antiretrovirals have taken us a long way, but I still think there is significant room for improvement. In terms of the research priorities, we still need to think about the fact that HIV is a long-term condition now. People are living with HIV for a long time and there are some additional challenges that come with someone living with HIV into older age.

The second thing is, what is the right time to start treatment? We have to consider not just the impact on the individual, where we know that early diagnosis has a very good outcome, but also the impact on onward transmission. Obviously, somebody who has undetectable virus is far less likely to infect somebody else. We need to continue to discuss that balance between the needs of the individual and the public health issues associated with onward transmission.

The one other area on research that I think is very important relates to prevention. All the work from the fellowship programmes that we fund in the UK and all the Department of Health pilots suggests that testing—I very much think that testing is a preventive tool because if you are aware of your own status, you are less likely to infect others—is very highly acceptable among the general public. We are talking about acceptability in the 80-90% range. The challenge is that healthcare professionals are far more reluctant to offer testing in a broad range of settings. An interesting piece of research is what it would take to encourage healthcare professionals to feel more comfortable in expanding access to testing.

Ms Mary Kerr: I agree with what Lisa has said. To go back to the question on research and the unmet need, given that there are almost 100,000 people living with HIV one of the major areas of focus is on keeping them well for the duration of their life. As Lisa says, the population is ageing, it is a chronic condition, they remain infective and there are complex

morbidities and co-morbidities. There are many challenges that will only start to emerge as we move forward with an ageing HIV population. Within that, some of the research priorities are very much in the fundamentals, making sure that the efficacy, the resistance and the adherence continue to be strong. We need to pre-empt the emergence of resistance by continuing to progress highly effective antiretrovirals.

At the same time, tolerability should not be underestimated as an important factor. Tolerability is one of the major drivers of adherence. As Lisa says, adherence is one of the major drivers of efficacy. So it is really important to continue to invest in developing compounds and medicines that improve tolerability for patients to take. When I talk about tolerability, I am talking about renal disease, bone disease, cardiovascular disease and CNS morbidities. Clearly, HIV itself is associated with many toxicities. Antiretrovirals treat HIV but they do not diminish some of those toxicities. Indeed, they themselves are associated with toxicities. The constant search for medicines with a better toxicity profile is very important.

Finally, one element of the disease—the impact on the immune system—still requires a lot of exploration. Antiretrovirals do something to improve the immune status of the patient, but they do not restore the immune system. Diseases associated with immune senescence, for example malignancies, are really important to progress. The message is still that there is a lot of unmet need in the area.

Q405 Lord May of Oxford: Setting aside where the areas are going, overall who are the prime funders of HIV research in the UK and how much will your organisations be spending on it this year? What is the balance between private and public? You have hinted at that already.

Ms Lisa Bright: I shall start and then maybe everyone else can add to that. My understanding is that in the UK the balance of spending from an R&D perspective is that

roughly 50% comes from pharma, 30% comes from the Medical Research Council and universities and the remainder comes from charitable organisations.

Q406 Lord May of Oxford: Including Gates, presumably, so it is not all UK charities.

Ms Lisa Bright: Yes, absolutely. On the question around the balance, my response is that it is less about balance and more about making sure that there is enough research happening and that there is great collaboration. The progress we have seen in HIV over the last 20 or so years has been as a result of excellent collaboration between the private sector, the public sector, the third sector and patient organisations and patients themselves. The criticality as we go forward is that that collaboration continues to happen. Gilead invests over $1 billion into research and development every year. The vast majority of that goes into HIV or viruses.

Q407 The Chairman: Is that worldwide?

Ms Lisa Bright: Yes, that is worldwide. In the UK, we have 346 people currently engaged in the Gilead-sponsored HIV study in over 27 centres. That means that most of the key centres are involved in some way with Gilead HIV research. Over the last two years, that was probably about 500. On top of that, we invested £1 million last year in research, not necessarily on treatment but on prevention strategies, particularly around testing. This is incredibly important, because we still have 22,000 people living with undiagnosed HIV.

Q408 Lord May of Oxford: That was the question. Putting it all together, what fraction of global expenditure on all aspects of HIV does the UK contribute? Maybe that is a tricky one.

Ms Lisa Bright: I am afraid that I do not have the answer to that, but maybe one of my colleagues does.

Mr Rhon Reynolds: I think it is in our submission. All together, the amount of money spent on HIV is about $40 billion. Only 2% of that goes towards HIV vaccines research. IAVI

spends $72.5 million on HIV vaccines R&D, and that only represents 8% of the expenditure on HIV vaccines already.

Q409 Lord May of Oxford: Out of a $40 billion total, is it too hard to say how much comes from the UK?

Mr Rhon Reynolds: I could not say that specifically, but it is definitely in our submission. Most of the money that countries have been spending goes towards the global fund. The funders of HIV vaccines in the UK are DfID, the Wellcome Trust and the MRC. That comes to about $23 million. You also asked whether anyone is working on a cure. There is a Nobel laureate from the ANRS based in France who is working on a project towards a cure. This looks at all intervention, including treatment and new prevention technologies.

Q410 Lord May of Oxford: Can I just ask quickly, in the 50:30:20 split, did you count Wellcome in the 20 as a charity?

Mr Rhon Reynolds: That is philanthropic as opposed to—

The Chairman: I think we might put this on paper for you so that you can give us a considered reply to the specific questions that we have asked.

Ms Mary Kerr: I would just like to make a general point to say that the UK position should be congratulated for the level and quality of research that is done, which is of international recognition, driven by many of the individuals who are known to the experts. The research done in the UK is of extraordinarily high quality and we acknowledge the international UK role of the MRC, the Wellcome Trust and the NIHRs in funding research. ViiV has data that I could share with you in the public domain. Last year we spent £100 million on our pipeline assets. Within that there is funding for collaborative research projects.

Q411 The Chairman: I am sure that pipeline assets is a well known phrase in your industry. What does it mean?

Ms Mary Kerr: It basically means the medicines we have in development that have not been approved by the regulatory agencies and are not available to patients.

Q412 The Chairman: But they are not all HIV—or are they?

Ms Mary Kerr: They are all HIV. That number is just HIV. ViiV is 100% focused on HIV. It is hard to estimate how much of that is spent in the UK, but we are very keen to engage UK physicians because of the quality and the level of the work that can be done here. We have 15 active sites in the UK involved in the pivotal studies and others involved in collaborative research projects. We are very keen to find ways to improve the opportunity to involve more UK physicians in research. In that respect, there are a number of areas of improvement that we could seek collaboratively.

Q413 Baroness McIntosh of Hudnall: I wanted to pick up on what you were saying, Ms Kerr, about the necessary monitoring of the long-term effects of being on antiretroviral drugs. By definition, because they have only been available since 1996, we do not have a long period of exposure to work on. In terms of the co-morbidities that you were referring to earlier, is there research going on, undertaken either by you or elsewhere, looking at the population who are currently taking antiretrovirals and longitudinally assessing how they are responding? You suggested that some of the co-morbidities that you mentioned might have occurred anyway, some of them might be related to HIV and some of them might be related to the drugs. How is that long-term research being monitored? That will have a big impact on Governments' ability to assess what their costs are going to be over time.

Ms Mary Kerr: Indeed. This is a challenging area, not just in HIV but across all medicines—monitoring and understanding the profile of a medicine when given chronically. This sort of information is often not available as a result of pivotal studies. In HIV we are very fortunate to have a number of large cohorts globally and in the UK, who monitor patients over time and can get a fairly good estimation and assessment of the profile of medicines when given to

certain populations. Clearly, some of those cohort studies have some challenges and results need to be interpreted terribly carefully. They are not randomised controlled studies, therefore issues that confound outcomes need to be carefully managed. Nonetheless, they are a very good and well used source of information in the community about long-term care.

Q414 Baroness McIntosh of Hudnall: Who is responsible for co-ordinating or collating the outcomes from all of that? Who pulls together all the data collected from various patients?

Ms Mary Kerr: The cohorts themselves are organised and self-organised. UK CHIC is a cohort, which will collate the data internationally. There are cohorts in the US and across Europe. Maybe Lisa would like to comment on that. There are a number of self-organised and managed and very well organised cohort groups. Another approach is meta-analysis. Data can be collected over time that is generated in isolated settings and randomised studies and pooled to do a statistical analysis to understand what trends are emerging. There are various approaches to understanding profile in the long term.

Q415 Lord Gardiner of Kimble: Should the United Kingdom be more prominent on HIV research? Other than funding, what can be done to enhance the role of the United Kingdom within HIV research? Going on from that, in 2008 the National Institute for Health Research was set up to stimulate clinical research in this country. Do you think the new funding arrangements have impacted on the ability of the pharmaceutical companies to invest in research in the UK? How do you see the pharmaceutical industry's relationship with the public sector in the UK?

Mr Rhon Reynolds: I have an answer, but we are not a pharmaceutical company. Outside of funding, one of the things that we have been advocating in the UK is stronger science, technology and innovation in the development response. Health-related R&D is fundamental in the fight against poverty. Development also requires building strong economies capable of

generating and redistributing wealth. We think PDPs—product development partnerships—such as IAVI can accelerate the development of access to new health tools for diseases of poverty, such as an AIDS vaccine, by working to strengthen science, technology and innovation capabilities, especially in developing country contexts. That is one way, outside of just funding, that the UK could do that.

One issue that we did not get a chance to respond to on research priorities is that IAVI's mission is to drive through and get as many vaccine candidates as we can to achieve higher levels of efficacy. We are looking at designing and developing vaccine candidates that can elicit broadly neutralising antibodies and the continued engagement of developing countries in research and development. IAVI is working in countries such as Kenya and Uganda. I think Emmanuel can talk about this. These countries are doing the level of research that is happening in any other developed country context. I just wanted to add those two things.

Ms Lisa Bright: If I may add to that, from a UK perspective I reinforce what Mary said, that we have excellent research here in the UK. That is borne out not just by the key centres that we have—St Stephen's AIDS Trust, Chelsea and Westminster, Imperial, Royal London and so on—but the number of key opinion leaders that we have and the quality of the guidelines. One of the challenges is that we could clearly always do more. Every country should aspire to do more HIV research. I am sure the Committee is well aware of the report that came out in January this year by Professor Rawlings from the Academy of Medical Sciences. That looked at how we can improve the competitiveness of the UK as a place to do research. It came out with many interesting issues, but there are a couple of key points for here. One is that there is quite a lot of bureaucracy around the regulatory and approval processes in the UK, which creates a lot of duplication and means that getting studies up and running in the UK can take a lot longer than in other countries. Many of us who are involved in research and development would welcome the implementation of the

guidelines, particularly around a national body that can try to accelerate a lot of the approval processes. While the NIHR[1] investment has been very welcome, the reality is still that approval at trust board level, and the regulatory and complex approval, which absolutely needs to be there for patient safety, can probably be streamlined a little. The public-private relationship is very strong in the UK in the public, private and third sectors. That is borne out by a very specific example that I can give you. We work with a range of stakeholders in HIV on a campaign called "Halve it", which is a coalition of experts—clinicians, patient advocacy groups and policy makers. We are very fortunate that the Department of Health and the HPA act as observers on that. We work together to try to develop a plan that will help to halve undiagnosed and late diagnosed HIV in the UK. That is a really good example of collaboration that has developed in this space over many years.

Ms Mary Kerr: On the matter of research in the UK, I agree that the partnership is already very strong and the UK presence globally is strong and prominent, but there are certainly opportunities for improvement. To pick up on the point about clinical trials governance and regulation, there are clearly opportunities to speed that system up. It is quite noticeable when you look at recruitment into clinical studies that the UK is a slower recruiting country. That means that UK physicians and patients do not get exposure or access to medicines before they are approved and can shape the medicine development.

That is one area, but there are a number of others, some based around knowledge exchange, including simple things like collaboration between academia and industry, which is a systematic occurrence in the country. We build collaborations based on trust and mutual agendas. There is a very strong skills base in all the life science industry, particularly focused on postgraduate and post-doctoral scientists. This is an area where the UK generally is going to have to be very cautious, moving forward in the future with new funding arrangements

[1] National Institute for Health Research.

for universities. Of course, there is the general underpinning of financing in an environment that creates funding in financing. To go back to your point, the UK is in a good position to build and develop, moving forward.

The Chairman: I want to jog forward a bit now. We are going to come back, but I would like to do something on treatment costs, to get that clear in our minds.

Q416 Baroness Ritchie of Brompton: To put this in context, there has been an estimate by the British HIV Association that by 2013 the costs will be between £720 million and £758 million, yet at the same time the Government has said that expenditure on HIV and AIDS in 2009-10 was £760 million. It would be interesting to hear what effect you anticipate on HIV treatment and care from the prospect of competition based on price that is coming out of the Health and Social Care Bill. Following on from that, will that new dynamic change the kind of HIV drugs that pharmaceutical companies are going to be able to market to the NHS, particularly as existing treatments come off patent? Those are the areas that it would be interesting to have your thoughts on.

Ms Mary Kerr: Obviously, the Health and Social Care Bill is very new for us and we are still trying to understand the impact it will have. Our understanding is that the focus is less on price and more on quality. The principle of the approach is around universal access at the point of need, which does not depend on a postcode, but depends on the need of the patient; a focus on quality and improving outcomes; and fundamentally, for the industry, to ensure continuity of research, we need fair reward and recognition for innovation. The price will be based on the value of the contribution and the outcome.

Therefore, I believe that we have common goals. We are very keen to work together through the ABPI[2] and the industry association, in partnership, to shape the process moving forward. That is something we are very willing to engage in actively.

[2] Association of the British Pharmaceutical Industry.

Ms Lisa Bright: I agree with Mary. I think there are going to be some opportunities. We are very pleased that value is going to be considered as we think about medicines. In the context of HIV we should be very aware that when we value medicines, we need to think about not just the value to the individual, but the value to the broader public health agenda by reducing onward transmission.

Coming back to the proposed changes in the NHS, we are all still very unclear about exactly how that is going to pan out for HIV. It creates some risk and some opportunity for us. There is a risk that we need to understand better how the interface and accountability is going to work between those who are procuring prevention services and those who are procuring treatment services to make sure that the person with HIV does not fall down the gap in the middle and that linkage to care is lost.

There is an opportunity at the same time to think about the care pathway for somebody with HIV. It is so different from 20 years ago, when you were expecting this to be a death sentence and there were very complex regimens. People are living with HIV for a normal life expectancy now. It is a long-term condition. But the care pathway probably has not changed that much. There is probably an opportunity in there somehow to think about how somebody living with HIV who is stable, treated and well could be managed in a slightly different setting on an ongoing basis, while still under the guidance and supervision of a specialist. It will create some opportunities to think about that pathway.

From a generic perspective, we all appreciate the value that generics are going to bring to the NHS, because I am sure it will enable the NHS to save some money. Will it change the innovation that we bring in HIV? Absolutely not, because there are still significant areas of unmet need. We are still going to need to see that innovation. We are bringing several new medicines for HIV to the UK over the next couple of years.

Q417 Baroness Gould of Potternewton: Can I take further the point about value? The *Equity and Excellence* White Paper talks about value-based pricing and aligning prices to the value to the NHS and the patient. Is not one of the difficulties that it is almost impossible to identify accurately what impact it costs an individual patient over a lifetime in terms of their treatment? No matter where you go, you are given different figures. Surely, if we are going to look at value-based pricing, we need much more information and knowledge of real and actual costs. I do not know whether any research or work is being done on how to achieve that.

Ms Lisa Bright: I think we have all talked about this. It is such a complex area. We know that HIV treatment is incredibly cost-effective. NICE sets a barrier in terms of the QALY. HIV comes well under the threshold that NICE would usually consider for treatment. While NICE has not reviewed HIV medicines, if we look at other health technology appraisal systems, such as SMC or All Wales, they have approved almost all the antiretrovirals for HIV that have gone through. You are absolutely right that there needs to be more looking at the cost. There has been some interesting research to show that the direct lifetime cost to the NHS of one missed diagnosis is between £280,000 and £360,000. There is some emerging work around cost-effectiveness, but there is an awful lot more that we still need to gather.

Q418 The Chairman: Of the costs of £750 million a year that we are now talking about, do we know how much is antiretroviral drugs?

Ms Lisa Bright: I do not have an exact figure. I would be happy to try to provide you with something in writing on this, but my understanding is that that figure is probably going to be somewhere in the region of 40% to 60% of total costs on treatment.

Q419 The Chairman: Tell us about generics and what the time frame is there.

Ms Lisa Bright: My understanding is that we may see some generics in the UK over the next 12 months, but I do not have any further information.

Ms Mary Kerr: Just to comment generally on generics, ViiV healthcare supports their use once the patent has expired, as long as it is within the regulations in the country, so this is something that we can embrace. There is no concern with generics as such, but we should look at the advances that have been made, for example, with fixed-dose combinations over a time. When we look at how effective treatment is, the various combinations have revolutionised and transformed the lives of patients. The concern is probably that we do not roll back the clock and go back to the time when we were separating out some of the combinations that have supported adherence, which is considered to support efficacy. We need to guard that we focus on quality and not sacrifice it for the sake of price.

Q420 The Chairman: Just to try to be specific, do you foresee that generics will dramatically reduce the cost to the National Health Service?

Ms Mary Kerr: In the coming period, there is one ViiV healthcare medicine that will lose patent—imminently today or tomorrow—which means that generic *Epivir* may appear on the UK market. Generic *Epivir* is used in a very limited way as a single medicine, so it does not really pose the potential for a big cost reduction. I am not aware of others in the coming years. When we get to 2013, there may be some other genericisation, but in the coming years that it the only one.

Q421 Baroness Tonge: Our brief says that Dr Keith Radcliffe said in his evidence that 75% of the cost of HIV treatment is on drugs, so it is quite high. I wanted to tease out something that you said. I am very used to hearing about patient pathways. You said that the patient pathway for an HIV/AIDS patient may become more like that for any other patient. I am very interested in this. If AIDS is now a chronic disease with an almost normal life expectancy, why is the patient pathway any different now from that for a patient with, say, diabetes or one of the chronic lymphomas? I cannot understand why it is still singled out.

Ms Lisa Bright: The advances that people with HIV have seen over the last 20 years are incredible. We still recognise that, at the end of the day, HIV is still an incurable serious disease. Even though the fears about resistance have not been borne out—I think we were all worried that we would see huge levels of resistance to therapy 15 or 20 years ago, but that has not happened—it is still basically a long-term, incurable disease.

Baroness Tonge: So is diabetes.

Ms Lisa Bright: Yes, I understand. There is still a key role for a specialist to oversee and to be really engaged in managing somebody with HIV, but on a day-to-day basis this is probably an opportune time to think about whether there is a role for non-specialist settings to support somebody with HIV.

Baroness Tonge: As with diabetics.

Ms Lisa Bright: Yes, whether it is a specialist nurse in a secondary care setting or greater day-to-day involvement from general practitioners. If somebody is stable and treated well, there is an opportunity to think about how that might evolve, but clearly, if somebody has breakthrough resistance or is failing with treatment, it is very important that they are still under the supervision of their specialist.

The Chairman: I am going to jog back a bit now.

Q422 Baroness McIntosh of Hudnall: I will try to compress this question, which is about the use of therapies as prevention rather than just as treatment. We have already had some evidence about the potential of antiretroviral drugs to be used preventively as well as for treatment. Do you have a view about that strategy? Secondly, what is your view on whether the focus in the area of prevention needs to be more on this sort of issue, developing therapies that can be used preventively, or on behaviour change? What impact do you imagine that either of those is likely to have on prevention?

Ms Lisa Bright: There is some really interesting new science emerging around the use of antiretroviral drugs prior to exposure. We have talked about some of those today, including the use of gels or the use of tablets for men who have sex with men to try to reduce the risk of acquiring HIV. There is some very interesting science going on at the moment. Gilead does not have a clinical development programme in that area, but we actively support those initiatives that we have talked about through the provision of medicines. It is a very important area of research and we should continue to watch how the debate evolves, as clinicians start to debate the pros and cons and how it could be used in real life. There is still some really good discussion to be had in those areas.

There is a real opportunity for us to think about the importance of testing as a means of prevention. If somebody is aware of their status, they are far less likely to infect other people. Not just that, but if they are diagnosed, we already know that 50% are diagnosed late. Thinking about testing as a preventive strategy to prevent onward transmission is incredibly important. There are some behavioural issues that are flagged earlier around acceptability to the general public, but what else can we do to encourage and broaden out testing beyond the specialist setting, which is very pertinent to the issue of prevention?

Q423 Baroness McIntosh of Hudnall: Can I ask about using drugs preventively. This may be a question for Mr Reynolds. It is about identifying populations of people to whom you might want to give these therapies, given that you are trying to get to them before they are infected. When you think about the possible benefits of doing that, how widely would you expect to have to go in recruiting people into taking drugs which, as we have already heard, have potential side-effects, when they are not infected themselves?

Mr Rhon Reynolds: Every opportunity involves some considerations, and some of them are ethical. Do not quote me, but when we do not have universal access to treatment, there are some ethical issues around who should get treatment—someone who is uninfected or

someone who is infected and does not have access to treatment. This is a debate that is happening in civil society and at the WHO, which has introduced some of the modelling around scaling up testing and getting people on early treatment, but also using treatment as prevention.

There was an interesting study launched by Bill Gates last year in Vienna at the International AIDS Society conference. It showed that even if we scaled up treatment as prevention, if we had microbicides and if we scaled up behavioural prevention modalities that work, we still would not get to where we all want to be, which is decreased infection. We would still need an HIV vaccine. I mentioned some of the positive results we have had from it, so it is undeniable that we need to take this into consideration, but at the same time we need to ensure that the people who need treatment gain access to it and that the new prevention tools that become available are scaled up rapidly and we still have a holistic approach to respond to the epidemic, continuing the research that is needed to get us to zero.

Q424 Baroness Gould of Potternewton: Is there not a further dimension to this? It is right that one has to continue with the research, and you made a point about making sure who should get the treatment, but does this not go back to the previous question about cost? If we are going to find that we are looking at value, this is going to be the big question. Is it really of value to use a small amount of resources, which this certainly will be, on treatment as prevention rather than making sure that you treat patients? The other point that goes with this is that if it is possible to have treatment as prevention, how are we going to raise awareness among the particular groups that they should be involved? If you have not got anything wrong with you, are you likely to go ahead and do it, even though you may be part of the at-risk community? It is a much wider issue than just the question of the treatment being available.

Ms Mary Kerr: It is a very wide public health issue. I do not know whether the Committee is aware that the EMA has just released a concept paper on the matter, inviting interested parties to join the discussion. They raise a number of issues, triggered by the data that has become available showing a reduction in the risk of infection and the incidence of infection in two different populations. Obviously, the data is very interesting and investigational, but generally one would agree that it is not enough to move forward and recommend this as an approach at the minute. However, it is interesting.

The points that you raise are really important. For example, will the use of prophylactic treatment increase resistance? What does it do to adherence? Will it raise tolerabilities? Will it reduce change behaviours? Will it increase risk behaviours? Will it reduce the use of condoms? There are all sorts of complexities that need to be addressed, but in the first instance this paper is being shared for discussion, so you may want to get a copy.

Q425 Lord May of Oxford: I am an evolutionary biologist. Whether we are talking pesticides, herbicides, antibiotics or the early stages of antiretrovirals, resistance will appear. The conversations that we consistently have and even some of the questions that we ask implicitly assume that we have cracked this problem for antiretrovirals. Am I alone in believing that this is untrue? The more people you give it to, the longer they live, the higher the probability that it will emerge sooner rather than later, but that it is going to emerge eventually in a form as refractory as we see now with antibiotics is, in my opinion, inevitable. Does that never cross any of your minds?

Ms Mary Kerr: I think you are right that it is definitely a consideration, but we can only go on the evidence we have at the minute. When you look at the UK population who are treated with antiretrovirals, the vast majority are treated very successfully with a range of products.

Q426 Lord May of Oxford: I understand the evolution of what has happened so far, and I have even been part of it—not in treatment, I am happy to say—but I think it ought to be part of the consideration of whether you use them more widely for prevention. You mention all sorts of complexities, but never that.

Ms Lisa Bright: Resistance is an incredibly serious issue. Mary is right that we can only go with what we have. What is important is how we monitor resistance. We have a really good resistance database in the UK. Obviously, there are some other good ones in other parts of the world as well. Any resistance test that is done on somebody who is newly diagnosed or somebody who fails on treatment is captured. We have a good way of getting an early warning signal, but none of us knows long term. We can only base it on the evidence that we have today.

The Chairman: We have almost run out of time, I am afraid. I am just going to ask Lady Masham to ask a question about testing.

Q427 Baroness Masham of Ilton: Recently, the Health Protection Agency recommended an expansion of the range of settings where HIV tests are offered. The expansion of testing is an area of research that Gilead Sciences has funded through its Gilead UK and Ireland Fellowship Programme Award. Why do you fund these studies? What conclusions can be drawn from the pilots that you have been involved in? Beyond expanding the range of settings where tests are offered, what more needs to be done to increase the uptake of testing? And what do you think about the new health service, as will be, with public health doing some things and health doing other things? You have already said that the patient might fall between two stools.

The Chairman: Brief answers, please.

Ms Lisa Bright: The reason we are involved in the fellowship programme is that we are very committed to seeing successful treatment for people who live with HIV. The fellowship

programme is our way of supporting locally based, innovative testing pilots that happen across the country. We have funded over 25 of those over the last two years and invested more than £1 million in them. They have taught us a lot. I will give you some headlines of what we have learnt. Most importantly, the fellowship programme is there to generate best practice—what worked and what did not—and to try to facilitate sharing between local providers of testing services about what worked.

Key learnings are that without some kind of seed funding, the many excellent initiatives and ideas that are there already would not have got up and running. Having some form of funding has been key to some of these pilots taking place. The second thing is that while not all projects worked—some of them really did not work in the sense of identifying undiagnosed people—they gave us some really good learning. The projects that worked have been shown to be very cost-effective. We are about to publish some data in May on some projects showing that the cost of a positive diagnosis can be as low as £2,000 to £4,000, which is incredibly cost-effective.

Q428 Baroness Masham of Ilton: Which were the most successful?

Ms Lisa Bright: Some of the most successful projects were replicating existing projects from the US, where there is routine testing in A&E or emergency admissions. Another key project that worked really well was routine offering of testing for new entrants to general practice. The fact that you happen to live in an area of high prevalence is, in itself, an independent risk factor for HIV. Offering routine tests at general practices in those areas was shown to be very cost-effective.

Q429 Baroness Masham of Ilton: And in prisons?

Ms Lisa Bright: Yes, we did sponsor a project in prisons that I can provide you with some more evidence on. That significantly reduced the late diagnosis. At the point at which people were diagnosed, it had a significant reduction, so people were picked up earlier.

The other key lesson is that acceptability of testing is high among the general public, although it is somewhat lower among healthcare professionals. That is something that we need to work on.

The Chairman: Okay. You say you are publishing this in May. We will be publishing after that, so perhaps you could let us have that. We have raised a great number of questions this morning and you have been very good and patient in your answers, but I think there are probably quite a lot of follow-ups to this. Perhaps we could now correspond with you on the basis of what we have done this morning and see if we can get even more information in this area. I am afraid we have gone over time. In the mean time, thank you very much for coming this morning.