

HOUSE OF LORDS
MINUTES OF EVIDENCE
TAKEN BEFORE
THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY
(SUB-COMMITTEE II)
GENOMIC MEDICINE

WEDNESDAY 11 JUNE 2008

PROFESSOR PETER FURNESS, DR JOHN CROLLA, DR IMRAN RAFI and
PROFESSOR STEVEN O'RAHILLY

Evidence heard in Public

Questions 178 - 234

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WEDNESDAY 11 JUNE 2008

Present

Colwyn, L
Northesk, E
O'Neill of Bengarve, B
Patel, L (Chairman)
Perry of Southwark, B
Winston, L

Witnesses: **Professor Peter Furness**, Vice-President, Royal College of Pathologists, **Dr John Crolla**, Chair, Joint Committee on Medical Genetics, also representing the Royal College of Physicians, **Dr Imran Rafi**, Royal College of General Practitioners, and **Professor Steven O'Rahilly**, Professor of Clinical Biochemistry and Medicine, University of Cambridge, examined.

Q178 Chairman: Good morning to all of you and thank you for coming. Welcome to the panel that have come in their spare time to give evidence to us today and a particular welcome to Professor Steven O'Rahilly who I know was called in at the last minute. My first question relates to translation of the genomic information and genomic science. We have had differing views given to us on this. On the one hand we have the view that DNA and RNA-based tests are already being used in clinical medicine and on other hand we are told it will take years before many of the genomic science knowledge will be translated into clinical medicine. Which bit is true, and how fast is the science moving so that we are able to plan its translation into clinical medicine? The memorandum from the Royal College of Pathologists states that there will be an exponential increase in genomic tests. What are the cost implications of all of this? Who is actually monitoring or making pronouncements about which tests are good and which tests are not so good?

Professor Furness: I am Professor Peter Furness. I am Vice-President of the Royal College of Pathologists and President Elect. I am a histopathologist by training, but I have also been heavily involved in a College initiative looking at how we evaluate new diagnostic investigations. You have just asked a whole series of questions, all of which have really very complicated answers.

Q179 Chairman: Simplify it for us!

Professor Furness: You started with what was given to us as question one on the list of possible questions, which concludes, “Are these differences disease specific? Or are they a reflection of the different types of genetic tests?” The answer is both. The word exponential came from a discussion that we had with Professor Finbar Cotter, who is a hematologist, who has described in his laboratory an increase of three-fold in the number of genetic tests being undertaken in the space of two years. Elsewhere the increase has been less dramatic. I know my colleague Dr Crolla has some information about the increases annually of about 20 or so per cent in a different area. The problem is that this is so enormously broad. Leukemia is mentioned as an area where genetic tests of a sort are already very important because in some types of leukemia there are consistent, reliable and relatively straightforward changes that you can look for. Other types of cancer are much more variable. For example, we have recently seen developments in expression profiling which give improved prognostic information in breast cancer, a common cancer compared to leukaemia. I have already mentioned a relatively simple and long-standing set of genetic investigations for leukaemia and compared that to a technically completely different investigation looking at what the genes are doing and how they are being expressed. There was a good example in *Nature* a few years ago which took what we thought was a single disease entity, largechalbetale (?) lymphoma, which we thought had a very unpredictable response to treatment and demonstrated that by looking at the gene expression of these tumors you can split them into those that will respond and

those that will not. That was in 2002 and it is still not in routine practice. I have only been talking about acquired mutations in tumours. I have not even been addressing the underlying changes which I think stimulated this Select Committee's inquiry, which are to do with population-wide screening of an individual's inherited genome, I have been talking about mutations in that genome. There is another question in here that is talking about cervical cytology, which I think is actually related to assessing the genome of viruses rather than humans. You have in here such a vast spread of potential in a whole lot of different areas that the Select Committee is going to have to be careful to pick out the different elements and recognise that there are advantages to be gained in a whole lot of different areas as a result of different technologies. Saying exponential is probably mathematically inaccurate because it is going to be very jagged. In some diseases there is going to be a development that becomes very valuable very quickly and in others it is going to take longer and then suddenly there is a breakthrough, but that is the nature of the whole process. You asked a question about the expense. That is immensely difficult to discuss even, but the costs vary depending on the different tests that are required. At the moment I am told that sequencing someone's entire genome costs about £10,000, but the extrapolation suggests that that will probably come down to £1,000 within a few years. We are already in a situation where I am told if you want to sequence ten genes from one individual economically you may as well sequence the whole thing. There is a very rapid change. The costs will come down, but they will remain substantial if you have large numbers of patients compared to what we use at the moment.

Q180 Chairman: We have to write our report so that a common person understands it and not scientists like you.

Professor Furness: I do not envy your task!

Q181 Chairman: The summary would be that where the science is going suggests that there will be the translation of the science into clinical medicine, both diagnostic and the testing of diseases?

Professor Furness: Yes. The translation will be difficult, though, for the reasons we have explained.

Q182 Chairman: Do any of the others want to comment?

Professor O’Rahilly: I am Steve O’Rahilly. I am a Professor of Clinical Biochemistry and Medicine at Cambridge. I am a practicing physician and biomedical researcher and I am here for the Academy rather at the last minute. To give some concrete examples sometimes gives a good flavour for what sort of sudden jumps can occur. When you are sitting in a regular diabetic clinic the assumption is that everyone looks the same because the people have got a disease called diabetes and it is all the same. Our wonderful researcher from Exeter Andrew Hattersley recently decided to look at people who have had diabetes from birth and by using genetic techniques he found that a very large number of people who had diabetes in the first few months of life had a particular mutation. All of those individuals, even after 30 years, could be taken off insulin and put onto a tablet and they will become insulin free, having been a slave to this injectable drug for many, many years. It shows dramatic changes in their health benefits. The problem is it is a rare condition, but it is a real example of where the use of genetics suddenly unleashes a real change in clinical practice. A lot of the genome-wide association studies, et cetera, are wonderful insights into the biology of disease but their immediate translatability is not obvious. On the issue of dissecting the heterogeneity of what we think is a common disease, you go to a doctor and he thinks you have got diabetes, he thinks you have got obesity, but in fact those diseases are sub-dividable. What genetics is doing increasingly is actually helping us to subdivide those into separate entities, some of

which may end up having specific therapies. That is where the rubber of genetics hits the road of clinical practice.

Dr Rafi: I am Imran Rafi. I am a GP in Surrey. As an end user, we are not really doing a lot of genetic testing in primary care, but we are simply being exposed more to aspects of genetics. For example, population screening, the sickle cell haemoglobinopathy programme, is going to impact on primary care. There are tests that specialists use that we are increasingly aware of that do affect patient management. For example, where patients are prescribed Azathioprine for whatever disease they are being treated for, the expectation now is that they get tested for a certain enzyme which affects Azathioprine metabolism. I think our exposure in primary care is going to increase. We have seen that with cancer care in that where perhaps 20 or 30 years ago we would get a letter from the specialist saying, "This patient has got breast cancer. We plan to give them surgery and then radiotherapy or chemotherapy," now we get letters which come back stating that this patient has got breast cancer and we also get information back about the tumour and the tumour biology. I think that over time clearly patients will get more multi-gene profiling which will aid their treatment. Primary care does have to be ready. I think our exposure will clearly increase over time.

Q183 Chairman: Would anybody like to comment as to who should be looking at the risks and benefits of genomic tests? Is anybody looking at it?

Professor Furness: The UK Genetic Testing Network is in relation to conventionally inherited disease.

Dr Crolla: I am John Crolla. I am here representing the Joint Committee on Medical Genetics and the RCP. I am a clinical cytogeneticist with a special interest in the translation of genomic technologies for high resolution analysis of the genome for inherited disorders. My expertise is very much on the constitutional side. I think this is an extremely complex

issue, as Peter has already underlined, and I think it is going to be of some importance to unpick how the translation of genomic science is going to be implemented with the greatest effectiveness. Your question here is whether genomic science to the clinic will take many years and will be rapid. I think the answer is that in some cases it will be relatively rapid, as we have seen from Andrew Hattersley's work, but in other areas it is going to have to be much slower because the evidence base needs to be built up. I think there is a danger of impatience and pushing things a little bit too quickly so that we do not get a thorough evidence base on which to make prognostic, therapeutic and diagnostic points and I think that is an important thing. Which body oversees this? There are various models that have been discussed. The RCPATH and the Public Health Genetics and Genomics Unit in Cambridge have looked at the implications of genomic medicine and molecular pathology testing in the broader context and have made several recommendations which I am sure are available to the Committee. My view is we need caution and we need time because the pace with which the technology is evolving can overtake the way in which we have to analyse and interpret the data.

Q184 Lord Winston: I am very grateful for Dr Crolla's caution. I am really troubled, gentlemen, because I am worried that you are looking at this through rose tinted spectacles. When we talk about a £1,000 or a £10,000 genome sequencing I am inclined to say, "So what?". I agree that the single gene defects for certain rare diseases may be jolly useful, but it seems to me that what we are not taking account of the epigenetic effects which occur during development which may radically change somebody's response to environmental influence later on, which therefore means that the genome may pay very little respect to the development or otherwise of the disease that we really want to screen for, including diabetes. I wonder if you would comment on that because it seems to me to be absolutely critical in

understanding whether or not we really can use the genome to really benefit large swathes of the population. I am seriously doubtful about that.

Professor Furness: I think when we had the meeting in this room a few months ago we heard the evidence about the prospects for identifying increased susceptibility to common diseases from such large investigations, which is essentially a tool to permit targeted population screening, so we then get into the question of evaluating the cost-benefit analysis of population screening programmes. We have seen already the difficulty and the arguments around introducing the screening programmes that we have already got such as cervical screening and breast cancer screening, which are technically much simpler but, nevertheless, there are enormous and prolonged arguments about the costs and benefits. I am sure you are entirely right to be cautious there. One of the problems that were highlighted by the report which John Crolla has just mentioned from the meeting which I co-organised is the difficulty of generating exactly that evidence of clinical utility. Will it actually affect patient care? It is very difficult to generate that sort of evidence. There is a problem with funding research to provide that sort of evidence which we have discussed. Even if the evidence is there - and it is usually pretty flimsy - there is a problem with evaluating and allocating the responsibility for evaluating that sort of evidence. The basic science is moving ahead at enormous speed such that the relatively cheap whole genome analysis will soon be with us, but the tools for turning that into logical decisions for the whole country we feel are not in place.

Professor O'Rahilly: I share some of your caution about the practical applicability of some of this technology, but I would point out a few things. While epigenetics and programming are clearly important, that does not mean that the data which supports the heritability of many common and complex diseases is not true. I think everyone who works on them would say that the heritability is pretty reasonable for many of the diseases. There is a genetic component. It is not the whole story but it is the epigenetic and nutritional and heritable

programming that is layered on to a heritable predisposition. Secondly, the driving force behind a lot of these large scale genetic studies is not necessarily to make them into a diagnostic for public use, it is to understand disease pathways and biology and to aid the pharmaceutical and biotechnology companies who might be able to perturb those pathways to treat people irrespective of their genome type, but understanding how a disease happens and what the components are of it are potentially enormously helpful to industry in terms of its attempt to find better therapeutic services. With some of these diseases there are very limited amounts of therapeutic services, so if you know that pathway B is involved in the development of that disease you may be able to manipulate that pathway. Thirdly, I think it is a mistake to say that we can easily spot and say genetics is a very useful tool for these rare individuals with single gene disorders and these syndromes and then the rest of the diseases are something different. One is going to segway into the other very readily. In my own field of obesity genetics, for example, ten years ago people just thought if you are fat you are fat, it is just a bunch of fat people. In fact, the heterogeneity are ten different monogenic disorders that people just look fat, but they have a single gene that is causing them to be obese on a particular pathway and on one very rare occasion we are able to do something about it. The principle would be these things that look like they are all the same and they are not in your category of the interesting monogenics will turn out with appropriate research to be all the time rather simple genetic disorders lying within and hidden within the complex phenotypes that are present.

Dr Rafi: I suspect that in ten years' time I will probably be doing essentially the work that I am doing today, which is still trying to promote good health, trying to change people's behaviour and reducing weight, reducing heart risk and so on. I think where genomics will help will be as an extra tool where perhaps, as stated already, we can target the patients who

are particularly at high risk and use genomic information to aid management in those patients. I suspect the nature of the job will not change.

Dr Crolla: Having introduced the note of caution, I want to underline the enormous excitement and enthusiasm for the translation of genomic technology into diagnostics. There is a lot of enthusiasm within the NHS infrastructure, particularly within the genetics laboratories and in the evolving molecular pathology discipline. There has to be caution but there is also a great excitement and enthusiasm. What we do need to really have time to do is to do a proper evaluation and have the infrastructure developed so that we can do this translation in a systematic way. I think that is a point that needs to be addressed really quite urgently because it has implications right across the spectrum in terms of who we recruit, who is going to be fit for purpose in five years' time in order to do this diagnostic work, to do the interpretation, how are we going to train them and how are we going to embed these technologies and, also, horizon scan because this is another major issue. Peter has alluded to the fact that there are various estimates as to how quickly one can move from the whole genome scanning to epigenetic analysis. I just want to balance the caution with the enthusiasm, but we do need to get the structures in place to get the right people to deliver the service to the population via the NHS.

Q185 Lord Colwyn: The Academy of Medical Sciences described the high risk for Crohn's disease and type 2 diabetes in individuals who carry several of the susceptibility genes. In America last week we saw examples of other genes and other high risk diseases. For example, for type 2 diabetes and Crohn's about 0.1 per cent of the population have a 10-20 increased risk of developing these diseases. Given that this test will soon be available for 50 or so of these common diseases, is it likely that these tests will show a significant proportion of the population have a 10-20 fold increased risk of at least one common disease?

Professor O’Rahilly: I saw this document yesterday for the first time. I was not involved in its genesis.

Q186 Chairman: Did you agree with it?

Professor O’Rahilly: I know who did this and you do not ask barbers if you need a haircut! Peter Donnelly is the leader of the Wellcome Trust Case Control Consortium who has been a major driver behind the data, and of course he would be bullish. He would not be in the job if he was not bullish about the power of this technology. As an end user and not someone who has been centrally involved in this I would be a little more cautious about those interpretations. For example, in type 2 diabetes, where 5 per cent of the population get the disease, a 50-fold increase would mean 250 per cent. You cannot get that increased risk, the background is too common. There are certain disorders which the novel genomics have found such as adult macular degeneration where the predictive power of some of the snips that have been had are enormous, they really have had a huge increased risk. If you could find those people at risk when they were 50 and design some clever preventative therapy based on the knowledge of the disease and stop people going blind that would be a wonderful use of genomics, to prevent blindness in old age on the basis of understanding the people who are susceptible and doing something about it. That would be really bullish and possibly achievable based on looking forward based on the knowledge. Crohn’s disease is a relatively uncommon disease and it is the best example where the genome-wide scans have found many genes with a strong influence. Yes, you probably could find a group of people in the country who would be highly predisposed to Crohn’s. It would be a relatively small number of people. For things like type 2 diabetes we have found new pathways, we have found new genes, but the ones we have found to date represent a very small proportion of the risk. In fact, the nay-sayers of this say that if you compare the power of asking someone two questions, how fat are you and do either of your parents have diabetes, then you get just as

much predictive power as using the combined genes that are currently available for type 2. They are real, the data is believable, but together they represent only a small fraction of the genetic heritability of type 2 diabetes. What is coming out of these genome-wide association scans is really a case of it is a glass half empty and a glass half full, it is exciting that for the first time we have found new genes that are predisposed to these diseases and they are real and they are believable and they are not false positives, they truly really are involved, but despite throwing a large amount of effort at it they represent only a small fraction of the heritability and probably there is going to be tremendous heterogeneity based on the fact that the genome is much more variable than we thought it was. The nightmare scenario is that everyone's disease is unique and that everyone with type 2 diabetes has it for a different set of reasons and that is going to be hard to handle. There are other failures of the genome-wide association studies. The hypertension and the bipolar disorders so far have not proven particularly tractable to this approach even though their heritabilities are quite high. At the best end this could really provide tremendous predictive power for certain diseases, the macro degenerations, the Crohn's disease, but as you get down to other diseases then I think you have to be cautious. I think it will be tremendous for finding new pathways, for understanding potential routes to disease, for helping the pharmaceutical industry, but in terms of us all having our personalised print, my personal opinion would be that we need a huge amount more information before we go down that route.

Professor Furness: I do not propose to get into discussions of guessing how and to what extent this will impact in terms of what is possible, but I think the example of Crohn's disease does provide a very useful illustration of what is meant by clinical utility, "We can do it. Is it worth doing?". If you could easily screen the population and detect the one per cent who are at high risk of developing Crohn's disease it might look like a useful screening procedure, except for the fact that people who have developed Crohn's disease present with abdominal

pain, diarrhoea, constipation, a whole load of symptoms that make you think at that point you now need to do something about it. You probably do not need to do anything beforehand, in which case the clinical utility of knowing what you are susceptible to is zero, arguably. Another example would be if we could identify a constellation of genetic changes which meant that someone was at very high risk of developing high blood pressure. That is a disease that causes lots of damage with no symptoms. If you find it early you can treat it, prevent the damage and prevent the strokes, heart attacks and so on. So there you would probably have a very good case for whole population screening. If you do screen the whole population you will presumably pick up a few of the rare diseases like Huntington's, where if you have got the mutation you are going to get the disease, it is definite, but if there is nothing you can do about treating the disease, again we are back to clinical utility and do people really want that information. The number of questions that are going to have to be answered in terms of decisions on what the health service should do in this country are legion and systems that we have at the moment such as NICE, which look at the small number of big issues, are not set up to cope with the profusion of questions that are going to be generated on what we should do with these techniques.

Q187 Lord Colwyn: Can you make any comment on the Polish screening survey which I think found that in the whole of the population, looking for breast cancer genes, there were 4,000 carriers? Were there any lessons to be learned from that and also problems with lower penetrance genes?

Professor Furness: That is not an example that I put forward, but I would think it would be an excellent illustration of where you could then target breast screening programmes, as we currently know them, on those who are at higher risk potentially if a cost-benefit analysis demonstrated that that is worth doing.

Q188 Lord Colwyn: Should infants be screened for low penetrance genes just after birth?

Professor Furness: I think you are sitting next to a notable philosopher who can analyse that rather better than I would.

Q189 Chairman: In scientific terms is it worth screening infants for a whole batch of diseases with high penetrance?

Professor O'Rahilly: We do screen infants for diseases already that we can do something about. I think screening people for things we cannot currently do anything about should be in the realms of research. It is not in the realms of translation as a general practice. I am not familiar with the studies you mentioned, but it is perfectly reasonable to do research studies saying what would we find if we did this, but moving it into clinical practice is a different issue. It has to have a health benefit for the individual.

Q190 Lord Colwyn: Early screening would surely give you some views on lifestyle and how it should be led in the future. Is that not important?

Professor Furness: It depends on the disease. If you are dealing with a disease where we are not aware of lifestyle changes that can impact on the outcome, where is the value? If you are dealing with heart disease, for example, you are probably right.

Chairman: We heard for instance that the NIHR are looking at a plan to screen all infants for some 23 different diseases, some of which will not have a treatment.

Q191 Baroness Perry of Southwark: Are we not pushing the translation imperative a little too far for the stage which the science has reached? In any research there has to be a very long period of blue-skies, non-applicable research before anything emerges that could become applied. Outside the field of medicine that is true as well. What is happening, surely, is that we are learning an enormous amount now about disease and about the genetic component of

diseases and that in itself is very valuable knowledge. Maybe down the line further than we can see now, for some of the diseases which at the moment we say it is not worth finding out because they are untreatable and because there are no clinical outcomes there will be as we learn more and more about the disease. Are we pushing the need for clinical translation a bit further than the science allows?

Dr Crolla: There are large-scale studies - the UK Biobank studies and a Western Australia equivalent study - which are really designed to tease out these associations on a populational basis. I think perhaps we need again to wait a little. I think there are two questions that arise about going and screening for 23 disorders. The first is the cost and the second is whether there is an intervention and, if there is an intervention, is it acceptable? I think this point has been made several times. If you just want to know for the sake of knowing at this point because at some time in the future that knowledge may be useful, what are the ethical implications of having that information available for that patient knowing that in the future there may be repercussions and implications about which you know absolutely nothing at this point? As a clinical scientist I am driven by the imperative of being asked to do a test based on its clinical utility, based on its diagnostic impact and based on potential therapeutic interventions. I think by moving into this very, very broad area of genomic association studies we are in danger of perhaps going too far at this point - although I am not saying it is not going to be true soon - and I think the seminar that this Committee organised a few weeks ago underlined that point time and time again because not only do we not have the data on which to make these definitive prognostic judgments but we also at the moment do not have the bioinformatic resources in place to do these, except within a pure research milieu. Perhaps what we are talking about here is how you would translate that into a diagnostic setting and I think we need more time.

Professor Furness: I think your point is well made but, again, I would come back to the differences that there are in different areas and the complexity and the vast number of questions. I have already given one example of a molecular method for distinguishing two different groups in what we thought was one type of lymphoma where if you know the difference you know whether the treatment is going to work or not, and this is a very nasty toxic treatment. At the other end of the spectrum, you have heard the example of genetic screening for bipolar disorder, manic depression, on which the current opinion is that it is not worth doing. That has not stopped commercial companies from marketing it direct to the public over the Internet. The underlying problem is that we do not have the system for evaluating when we have stood back for long enough and evaluated the evidence; there is no co-ordinated evaluation system. You get this discrepancy: people leaping in on inadequate evidence at one end of the spectrum and not acting on good evidence at the other end of the spectrum.

Q192 Baroness O'Neill of Bengarve: I found the distinction in the Royal College of Pathologists' submission between clinical utility and clinical validity very useful. Am I right that what we are now discussing is how you take a second step, having established clinical validity, in order to establish the utility of a given test or possibly the use of a test as a screen? You have just pointed to an example of the disorganised and helter-skelter nature of the response with some of the commercial organisations jumping and others holding back. I think one of the things that is proving pretty hard, at least for me, to get my mind around is what structures do we have and what structures should we have in order to make that transition. We have a lot of bodies here with a lot of different, and sometimes perhaps overlapping competencies, and it seems to me that we do need to gain some understanding of who could fund research into the utility - it is I think clinical research that is needed here - and is such funding now going on? Is NIHR able to fund it; if not they, who?

Dr Crolla: That is to the nub of the problem that I think that Joint Committee's submission also underlined. In terms of pure research I think there are adequate funding streams through the MRC, Wellcome and charities with specific interests. The problem comes in the translation between the research funding and being able to demonstrate its clinical utility in a clinical setting. Historically, laboratories were able to access Culyer funding in order to underpin some of that R&D within the laboratory structure but that funding has been withdrawn. I do not think we have any problems with a much tighter and a much more peer-reviewed process replacing the Culyer top-sliced funding stream through NIHR, but NIHR excludes laboratory-based research from its current calls. The Joint Committee has tried to enter into a discussion with NIHR because several members have reported that there is a funding gap, and I think that NIHR would be the place that we would look to to create specific funding streams. The MRC has recently announced a call for translational research and I am not quite sure how that is going to map out. It is a new call and we need to look at it and evaluate it and see how successful it is, but NIHR from the evidence that I have to hand and from my personal submissions, they simply do not get past triage, they do not go out to peer review because they do not fit the current calls. I think that is a serious issue and if the Select Committee could in some way influence the NIHR funding streams so that area could be addressed, I think that would be very valuable for the scientific community.

Mr O'Rahilly: I have recently been asked to chair the MRC's translational research overview group which gives me a seat on the strategy committee so we can discuss these things. It is certainly true that the new £120 million of Government money to the MRC to do translational research includes the evaluation of diagnostics and not just therapeutics and so there should be new money from the MRC specifically with the goal of translation, and of course translation of diagnostics is exactly what we are talking about there. I do agree that it is a gap in NIHR's funding criteria. I think NIHR has done a fantastic job in the last year or two

under Sally Davies to really be imaginative and to work together under OSCHR to try and get all this right. I had not realised that they had specifically excluded laboratory-based research. They obviously do not do that in their bio-medical research centres because within the bio-medical research centre funding umbrella NIHR very much emphasises laboratory research, but they are in limited geographical centres and they may not be co-terminous with the centres of genetic excellence. That could be a problem and I agree, John, that NIHR should perhaps look at that and see that these tests are just as an important part of the patient management experience as treatments or interventions.

Professor Furness: Those two responses concentrated on doing the translational research to work out whether something has clinical utility. The next step of course is making the decision on when is the evidence good enough to spend the money. There have been some new developments since we submitted our written proposals in that area. They are new proposals and not physical developments that I think I should mention in that the Department of Health in Connecting for Health has recognised that it needs to have a catalogue of all the pathology tests that we do, all the laboratory tests that we do, which is itself proving somewhat challenging. As part of that, and I think I can say partly because of the arguments we have been putting forward, they have now very recently recognised that there will be a need for a mechanism to keep that list up-to-date. They have also tentatively recognised the need to have information about all these tests that will guide when they should and should not be used for commissioners and also potentially for the development of expert systems to guide doctors in appropriate laboratory testing. We are in the next few weeks having some exploratory meetings with the Department of Health to discuss how their rather static pathology catalogue list might be expanded into mechanisms to cover all this. Inevitably, funding remains a problem. A small amount of money has been identified which we hope will allow a sort of seed-corn development of trying to work out how to do it - and there is no

promise of anything long term. I am very hopeful that that approach to making decisions for the whole NHS will go forward because otherwise decisions on how to interpret the research will be left to local accountability and we will have different areas taking decisions on very limited expertise and coming to completely different conclusions.

Q193 Baroness O'Neill of Bengarve: That has been very, very helpful but I think beyond that there is a level of decision-making that has to address the question of clinical effectiveness and cost effectiveness, some analogue if you wish of NICE. Could you envisage such a body? It clearly does not exist but is there a need for such a body?

Professor Furness: There is a huge need for such a body. The problem with NICE, as I have suggested, and indeed with all the various government bodies that have an interest in this is that they decide which questions to answer and they pick up a few small, as they put it, “big ticket” issues rather than addressing this vast number of questions, and their model will not work. The organisation which I think has done splendid work to address this problem is the UK Genetic Testing Network in its gene dossier system which has, I think, established a paradigm for doing proportionate evaluations in order to make decisions where a large amount of the Exchequer’s money does not necessarily hang on it but patient care could benefit. We need to expand that sort of system to be able to cope with taking large numbers of decisions, which include how much evidence do you need in this particular case to make a decision. The UKGTN, I think John would agree, is vastly too small to take on this task but it has developed a good model.

Q194 Baroness Perry of Southwark: I would like to turn to the subject of training and education for health care professionals. A lot of the evidence that we have had suggests that they are going to be a central component to understanding and interpreting genetic tests. Given that the number of such tests coming into clinical practice is increasing, what is being

done to plug the gap in genetic and genomic education in the existing workforce and indeed what is being done about the initial training of medical students?

Dr Rafi: From the perspective of general practice, there is some preparatory work that has been on-going. The National Genetics Education Centre have been working with the Royal College of General Practitioners and they have now devised a curriculum for specialty training which is part of the general curriculum for new trainees going through general practice, so they will be tested on genetics in their final examination and, more importantly, to learn about the important facets of genetics and how to get basic genetic knowledge but also to consider all the ethical, social and legal implications of genetics as well. Out of the White Paper in 2003 there were ten GPs that were funded nationally to work within their PCTs and a lot of the work that these GPs did was to promote education and raise awareness of the value of primary care genetics. Most, if not all, of those projects were very successful in doing that. I think they are the two main drivers that have happened. I think there is a realisation now that GP trainers who are involved in training GPs locally need to gain genetic knowledge. For example, the London Deanery realised this and are setting up courses for genetics, so I think general practice is taking up the mantle.

Q195 Baroness Perry of Southwark: What would your estimate be of the proportion of the existing force of general practitioners that understands enough to be able to counsel and interpret?

Dr Rafi: There have been research papers in general practice that have looked at this and the overall consensus is that confidence is low. That may be a generational gap and it may be that as new trainees come through and they pick up genetic knowledge through the undergraduate curriculum that they will naturally get a better expertise of genetics but, similarly, you cannot ignore the rest of the workforce, and so I think it is really important that

the RCGP work with the deaneries who in turn work with local GP trainers to disseminate genetic knowledge.

Q196 Baroness Perry of Southwark: Last week in America we were told some pretty startling commercial companies' conclusions where people can send off their baby's genetic material and they will tell you whether your child is going to be a star athlete. It will not be long (because it is all on the Internet) before people are turning up at their GP surgeries with this sort of rubbish and asking for interpretation, and it is very important that they are able to reply and to counsel people.

Dr Rafi: Exactly and being able to recognise from these printouts which patients are at high risk and which can be relatively reassured in general practice without the need for further referral. An anecdote I heard recently was that a patient came to their GP with this printout of their genome and they had 40 tests done of various aspects looking at various diseases. They were referred on to the geneticist who in turn had to contact the company to find out what tests were actually done and then had to counsel the patient for those diseases. It is going to be a time-consuming affair and there are going to have to be service models set up to look at what is the most effective way of being able to provide patients with the necessary support that they need.

Mr O'Rahilly: One concern I would have about the direction of travel of both undergraduate and postgraduate medical education is that the role of science in the training of doctors has been rather downplayed. With the necessary increase on the emphasis on communication, et cetera, that has sometimes been to the detriment of a basic grounding in hard science, if you like, and that is concerning with the greatly expanded number of graduates, including new medical schools et cetera, if we are creating a new cadre of doctors which is going to be less capable of having a deep understanding of what the science is about; that is a concern.

Q197 Chairman: We have had this issue about education which we will probably explore with the Colleges too, about wider education (i) about public education in genomics and genetics and (ii) about the education of all health professionals, and particularly the availability of genetic experts and also then to be able to communicate as the science develops and not teach something today and then two years later the world has moved on but they have not caught up. How do you impart continuing education and what should the professional organisations be doing about this?

Professor Furness: We have structures for continuing professional education and development which are intended to cope with the continuing problems. Whether they are adequate to the rate of change in this field is debatable. John, you are probably the best person to talk about the training of specialist professionals in genetics.

Dr Crolla: Yes, I would just predicate that first by saying that the National Genetics Education and Development Centre, which is run by Peter Farndon, is also developing core curricula for medical undergraduates. I am not quite sure how far that curriculum has been developed but hopefully that will be rolled out and cascade genetic information and knowledge through a whole range of different health professionals and it does it, I think, in some very imaginative ways.

Q198 Chairman: So do you think there should be, as a view has been expressed to us, a centralised responsibility for somebody to impart genetics-based education to all health professionals as the knowledge increases?

Dr Crolla: This was one of the primary remits of the National Genetics Education and Development Centre. It comes up for a funding review later this year.

Q199 Chairman: Who funds it just now?

Dr Crolla: The Department of Health - Diana Paine is sitting behind me - so that is being rereviewed this year. I think that is one mechanism that needs to be looked at and strengthened if necessary. I think through the Joint Committee we have certainly seen submissions where they have done some really quite excellent work in cascading genetic knowledge. Can I just take your Lordships then to the question of specialist training for our current workforce. What is happening now is a curious mix of initiatives. Currently clinical scientists who aspire to become, like myself, Fellows of the Royal College of Pathologists (it is the only Royal College that admits non-medical graduates) undergo training which currently involves four years of pre-registration training which will be specialist training either in cytogenetics (chromosomes essentially) or molecular genetics (that is DNA). At the end of those four years the Health Profession Council will then register that person as a state-registered clinical scientist and then they either stay at that stage or they enter into higher specialist training which largely is completely unstructured and unfunded. I think this has been an issue for many, many years but has never been adequately addressed. What is now coming up is that an initiative called Modernising Science Careers is being initiated by the Chief Scientist ---

Q200 Chairman: I hope it does not have the same fate as Modernising Medical Careers!

Professor Furness: It is worryingly similar.

Dr Crolla: It is worryingly similar and it is some of the same personnel but, anyway, I will not divert there. The current plan, although none of this is actually written in stone, is that the pre-registration scientist training will be dismantled and be replaced by a generic training, so this will have a flexible workforce, so one day you will be in a biochemist lab, the next day you will be in a haematology lab, then histopathology, and then you can rotate into genetics. All the professional groups have reported back that this does not make sense. It only seems to make sense to the Modernising Science Careers framework. The bit that we do 100 per cent

agree with is the post-registration part of the training which will be tenure-tracked, it will be linked to the number of available consultant posts, where it will be fully funded right through the MRC Path or FRC Path through the examination system of the Royal College of Pathologists, fully accredited, et cetera. Thus we have a real problem there. What is actually happening of course is that emerging technologies have blurred completely the distinction between the cytology, the chromosome and the DNA. The primary analate will be DNA and it is effectively already DNA, so if we are going to do a genome-wide test, we will do it on a DNA-based test, be it an array looking for copy number change or an array looking for expression profiling. This has really happened so fast that I do not think we have got the structures in place in order to accommodate this, but I think the professions have really got to get together. The Clinical Molecular Genetics Society and the ACC in collaboration with the RCPATH can get this sorted and get it sorted fairly soon. The other important point I really want to make to this Committee is that we have now regulated ourselves to a stand-still. This is so important and it was brought home to me when my PhD student graduated this year. She had done three years work in my laboratory on array CGH applied to constitutional chromosome abnormalities. She was highly skilled, she was trained at the Sanger as well as in my laboratory, and she decided to go to Italy and she has now got a job setting up a diagnostic process in Italy. I could not have offered her a job in the UK except as a technologist.

Q201 Chairman: Why?

Dr Crolla: Because in order to undergo the regulatory training she would have to go back to supernumery grade A training, do four years, learn how to read chromosomes, and then go into higher specialist training, so she would enter into a training programme which actually is going to not make her fit for purpose.

Q202 Chairman: I see why you say “worryingly similar”; there is no flexibility at all.

Dr Crolla: That is an important point.

Q203 Baroness O’Neill of Bengarve: I wanted to put in a small and slightly provocative supplementary at this point. How far should the NHS take responsibility - and I think this is particularly a question for Dr Rafi - for interpreting tests that people have got over the Internet? Might it not be better to say, “You got this; you paid for it; I am not even going to advise you on whether your money was well-spent. You come to me with a symptom or no symptom.”

Dr Rafi: I think most GPs would want to try and support their patients and if ---

Q204 Chairman: They are not your patients at that stage, they might be on your books.

Dr Rafi: They are still your patients and it is in the same way that they come to you with the results of a general health screening that they might have had done privately. I think most general practitioners would be happy to help but it is really having the competency to be able to deal with the information that you have got. In terms of competency, the RCGP are providing a competency framework for practitioners who want to specialise in genetics within their PCTs and that has largely arisen out of the work that the National Genetics Education Centre did with the GPs with the specialist interest. The whole point of education is to be competent to be able to deal with the questions that you have framed.

Mr O’Rahilly: When you mentioned the patient there it struck me that there was an anomaly there with the fact that patients with cancer, for example, who go off-piste and buy drugs essentially are banned from having continuing NHS care. It is a disgrace but clearly we are treating therapeutics in the NHS rather different from diagnostics; in other words, you can go out into the private sector and get diagnostics and generate cost and income for the NHS. I agree that it is an anomaly and we certainly do not treat the two the same.

Dr Rafi: The likelihood is that a lot of these print-outs are going to generate low relative risks for these diseases and there are going to be one or two that are going to be particularly high risk, and it is being able to identify those and being able to help the patient through the NHS system if they need that help.

Professor Furness: Could I make a lateral link at that point because part of the problem with direct-to-the-consumer testing is that the consumer has no idea what he or she is buying. If we had an established system whereby all the tests that the NHS regards as being clinically justified, and maybe a few that it does not, are on a database where information about them is available to general practitioners and to the public, then you would have a resource first of all for the GPs to answer those questions relatively straightforwardly: “Here’s what the official answer is about that test,” and you would have also have a resource for members of the public to look up and decide whether or not this is worth doing or not. That is even without going down the route of legislation to control what may or may not be offered to the public, which I think in some circumstances there is quite a strong case for, but even without that if you provided the information, if the information is there and accessible you have removed a lot of the problem.

Q205 Lord Colwyn: I think in the States taking a test of course included an interpretation of the test. They have got it down out there to a \$1,000 a test now but of course the quality of the interpretation varied dramatically between the different laboratories.

Professor Furness: And the commercial pressure to avoid saying, “Here’s something we have picked up but it does not make any difference.”

Q206 Baroness Perry of Southwark: I want to turn to the question of commissioning but just before I do that could I press Dr Crolla, the Joint Committee says in their evidence that

more genetic counsellors are needed. Are people not coming forward in sufficient numbers to do the training or is there not enough training being provided?

Dr Crolla: I think for genetic counsellors it has been a great success story, and certainly under the White Paper initiative there were a number - I cannot remember the exact number - of new genetic counsellors that were recruited and trained, but I think the demand for genetic counsellors is growing at the rate of the number of tests and scenarios which require interpretation of diagnostic tests, so I think that was part of the submission. Yes, it has been a great success but we need to expand that.

Q207 Baroness Perry of Southwark: We need to expand the provision; people are coming forward willing to be trained? That is my question.

Dr Crolla: Absolutely, yes.

Q208 Baroness Perry of Southwark: Turning to the question of commissioning, the Joint Committee on Medical Genetics say in their submission that commissioning is not structured to react to the rapid change that is happening and as a result the introduction of genetic testing is patchy and inconsistent across the country. Given that commissioners have very limited understanding of the details about genetic testing, does the existing policy framework for example enshrined in the NHS Genetics Team, need strengthening and if so how?

Dr Crolla: I think the take-home message here, as Peter has alluded to, is that the UKGTN as currently structured is very focused on dealing with disorders with DNA as a primary analate and developing gene dossiers which have the correct level of clinical utility and interpretation built into them, so that is a recommendation that then goes to GENCAG for acceptance, and specialist commissioners sit on GENCAG (I sit on GENCAG) and that mechanism works very well. What does not work is that there is then very patchy uptake of the recommendations of GENCAG for the uptake of tests which have been approved by the

UKGTN Gene Dossier Committee. There are all sorts of different reasons for this. It is very low on the list of priorities of Health Service managers; the PCTs are too low a level for the commissioning of this service; there is not the knowledge base there to really understand it; and real health need is defined as the “ability to benefit”, which in turn is a function of the prevalence and the effectiveness of interventions. These are complex issues which cascade down to PCTs who are under enormous pressure for a whole range of other interventions. I think the recommendation from the Joint Committee would be that this specialist commissioning should go back to a national level so that when agreed nationally there should be provision for the rolling out of these tests. Again, I will stress I am really talking about rare mendelian disorders. Also where the UKGTN needs to be strengthened is that it needs to expand its gene dossier remit and it is beginning to do that by taking on board cytogenetics and looking at ways in which it could develop gene dossier-type recommendations to commissioners for the commissioning of new technologies like comparative array CGH, both dosage and genomics.

Q209 Baroness Perry of Southwark: And you would want that ring-fenced funding to remain national?

Dr Crolla: That would be the ideal because what is happening now when it cascades to the PCTs is it is very patchy so it is postcode. I think it needs to be ring-fenced and national.

Mr O’Rahilly: Let me just give an example by Jenny Taylor who has drafted the document that the Academy will send you in response to these questions. She was involved in Oxford in the development of a service whereby people who died young and suddenly of sudden cardiac death, of which there are a number of genetic causes, would have their post mortem DNA analysed and family members would be screened and then those individuals who carried the risk factors were given implant defibrillators, et cetera, to prevent sudden cardiac death. That was accepted pretty much everywhere in the UK apart from the Oxford Thames,

region and it could not be implemented there because of financial pressures on the PCT, so there you had an example of the very place that was developing and leading internationally in the area of development was unable to fund. There are numerous such anomalies within the Health Service but that is a good example of how patchy commissioning can lead to strange anomalies.

Professor Furness: I think in terms of Health Service commissioning it is important to recognise that what we are talking about here at the moment is small numbers, which makes the model of the National Commissioning Group for Specialist Services an appropriate one. But if, as we anticipate, this sort of methodology and approach becomes relevant to more and more and more people, then it will rapidly move out of the realm in which that group has been accustomed to operating. It will not necessarily get that much simpler for primary care trusts to understand, even if a lot of people within one PCT might justify participating in a particular investigation. The issues will still be very complex and unfamiliar and the number of questions that are being asked will become very large, so there really is a conflict here with the policy of local decision-making in the Government because it will inevitably drive postcode diagnostics.

Q210 Earl of Northesk: At the risk of stating the obvious, genomic data makes huge demands on information technology and it is acknowledged that existing IT systems, not least with respect to band width, the speed of transfer and expertise, are likely to be insufficient for future needs. In your view, where is the investment needed and where should the balance be struck between investment in IT in reference labs, secondary care and primary care? Who is best placed to develop and establish the increased infrastructure and expertise?

Professor Furness: Could I suggest an answer from the specialist labs and from general practice.

Dr Crolla: I have had some inter-activity with Connecting for Health when we were first establishing array CGH in our reference laboratory. The problem was that through the NHS N3, the band width out to the Internet was 250 kilobits speed width for the whole of the NHS, for all 1.2 million users. I am not sure it was anything to do with the pressure that we put on but they were in negotiation with BT to increase that band width to one megabit per second, which it currently is as I understand. It urgently needs upgrading to much faster, ten or 20, or as the French are now installing in Paris 100 megabits per second as a standard broadband band width. That is one point. The second point is that in terms of data storage and data analysis there is a real training issue as well where clinical scientists are beginning to wake up to the real bioinformatic resources that are required in order to do interpretation, be it genome-wide association studies, sequence analysis or array analysis. I am not sure that I would be able to give the Committee a particular steer on where the resources need to be put but where we are finding, and I find other colleagues are finding it particularly frustrating is that we constantly are battling with our local trust IT departments who work under very strict clinical governance rules, appropriately, and also they have huge political drivers like Choose and Book and the implementation of PIMS and other initiatives, and so our requirements are relatively small-scale. I do not think that this technology infrastructure improvement should only be in the reference laboratories. I think it should be in all laboratories which are accessing genomic information. I think the final point I would like to make is that we have in the UK at the Sanger Centre one of the leading genome campuses in the world, and within the Sanger Centre there is the Ensembl Genome Browser with all the bioinformatic resources, and they have a suite of servers there which is the size literally of an aircraft hanger, and they have bioinformaticians who I think would be approachable and who should really be collaborating with NHS Connecting for Health. There are other initiatives that are on-going where genetics laboratories are currently developing new laboratory information management systems on a

consortium basis, again highlighting the rather clunky nature of trust IT systems against what we need, which is fast, unrestricted access to the Internet and genome analysis.

Q211 Lord Winston: I am surprised you mention the band width and do not mention security. Is not security rather more important?

Dr Crolla: The conflict is security and so clearly we have to conform to all the acceptable use of IT, but there has got to be a way of having parallel access which does not impinge on or affect security. Clearly if you are going to be sending large wads of data across the Internet it has to be anonymised before you can do that, but what I am talking about here is not transferring data but access to bioinformatic tools, and the current structure is really too clunky to do that in an effective way. I do not think it has any issues in terms of patient confidentiality. We would not want to in any way impinge or breach acceptable use policies under the NHS clinical governance.

Q212 Chairman: Do you get the feeling that the current IT development in the NHS as it progresses is going to be adequate for genomics information?

Professor Furness: I think if you asked that question omitting the words “for genomics information” you would probably get a no; it will not be adequate.

Mr O’Rahilly: I would be pleased if it could get me an Electronic Patient Record in the next ten years. It will have to be bespoke developments, as Peter and John say, because the nature of the questions that you are asking with information is totally different. You need detailed bioinformatic information about the likely effect, for example, of a particular mutation on a protein. You need to be able to access whether something is likely to be disease-causing or not. There is a whole range of information that is needed that is different from what we usually think of with a simple transferring of patient records or simple numbers with a normal range. This information is very dense and deep and I think there will need to be bespoke and

focused investment, particularly on bioinformatics within the NHS, if we are going to take genetics to the next level. I think that has to be not just the regional labs but the specialist labs too.

Dr Rafi: In terms of primary care, generally IT within primary care has been pretty good and probably in some places a lot better than secondary care. There are certain needs, though, that I think we are going to need for the future including how we record family histories and pedigrees. There are no such systems up and running at the moment within primary care, although there are people looking at computer-aided packages that can give family pedigree information and also risk assessments. That is one thing that I think would be useful. The way that we record data in primary care, particularly applicable to genetics, is going to be important and as we get new classifications of diseases, disease coding is going to be particularly important. I asked Simon Delucion(?), who is Director of Bioinformatics at St George's about this, and he is a GP with a real expertise in bioinformatics, and his feeling was that what we need is a informatician in primary care who can deal with psuedo-anonymised databases where you look at the coding that goes into these databases, which may change over to time so trying to look at archived data from the past may be difficult in the future when your queries change, when your coding systems change. I think this is really important. The other aspect of care is obviously surveillance, and with people for example with colorectal cancer or with breast cancer, who need to have regular surveillance over time, we need to have good methods in primary care to be able to ensure that these people get the relevant procedure that they need at the time, and so we need good registers in primary care to be able to deal with that situation.

Q213 Earl of Northesk: Back to your observation, Dr Crolla, that the existing NHS IT systems are clunky. This may be a little provocative but it does provoke the thought to what

extent therefore are existing NHS IT systems a potential barrier to active transfer of genomic data?

Dr Crolla: I used the word clunky - it is a relative term - and obviously people who are accessing the data warehouse for PIMS applications would find the download speeds perfectly acceptable. Where colleagues are trying to download gigabytes of sequence information in order to blast sequences, that is a very different scenario, and that is where it is clunky, it is too slow. What often happens is that colleagues will go home and use their own broadband connectivity and do the work and then email it back to work, which is an unacceptable situation. There are ways around it, and Lord Winston highlighted the security issues, and you can have parallel broadband access within hospitals providing it is within the acceptable use provisions but which does not impinge on the security issues for patient confidentiality. Where I think the parallel should be drawn is between what is available within university IT systems compared to the NHS. I wear two hats, I have a university position and an NHS position, and because of our physical separation from the university I cannot have access to the library resources in the university via the NHS. The systems do not talk so I cannot instantly access data or on-line journals and things like that on my desktop when I need to see them, so there is a delay in there. Really if we are going to develop and utilise these resources we need to have those resources available at the desktop through the NHS IT system.

Q214 Earl of Northesk: So another part of your wish-list is a much more federated IT architecture?

Dr Crolla: Yes.

Mr O'Rahilly: The problem is not unique to separate sites. Even on one site at Addenbrooke's in Cambridge our NHS colleagues cannot access journals, et cetera, through

their IT system, so it is not just a physical separation, it happens in most institutions even when the university and the hospital are in the same place.

Q215 Chairman: But have we not had a recent directive about information about individuals and how it can be taken out and there are strict rules now that have to be applied? If you are familiar with that is that not going to make difficult what you suggest where people are taking information away from the NHS environment so that they can work on it?

Dr Crolla: That is a very good point, Lord Chairman, yes, indeed. Again, this would be accessing pseudo-anonymised data or genomic data which is not personalised, so that was the example I was giving. There are initiatives to encrypt all NHS computers which I think will make life impossible.

Q216 Chairman: That is the direction given just now?

Dr Crolla: Yes and our local trust is looking at ways of implementing this encryption, but most of what we are doing is in international collaboration and so we do need to have access and be able to share anonymised data across international boundaries. If it goes outside the NHS it is gobbledegook unless they have the encryption software. It is a big problem.

Q217 Chairman: Including your Blackberry emails?

Dr Crolla: Yes, especially your Blackberry emails!

Q218 Baroness O'Neill of Bengarve: In the last section of the Royal College of Pathologists' report you suggest a new policy framework and in particular the establishment of a new UK-wide body, or the reorganisation of one of the existing bodies to provide a single comprehensive function of horizon scanning and for taking and evaluating new laboratory investigations. I have several questions about that proposal of which the sharpest is: which bodies would you abolish? There is a constant tendency to recommend multiplication of

bodies and then to complain that there are overlaps and gaps and things that are difficult to deal with. If you were being really quite surgical about this, what would you abolish? Could, for example, the UK Genetic Testing Network be enough or what else would you do? This body has got to do a number of different things but just adding a body does not strike me as perhaps the whole or best remedy.

Professor Furness: Those are my words so if I could at least start the answer to that one. This is a new task which could be taken as a justification for a new body. I have listed the various bodies that do something similar on a small selective scale. Obviously one would not abolish the whole of NICE but that is an organisation that could potentially be reformed and expanded to cover this function if it was able to alter its working practices radically in this field. At the moment I gather it has a charter which means that it could not do that. I do not know enough about the other bodies to say whether they could actually be abolished or not, but I suggest that their role in evaluating diagnostic investigations could be abolished. The trouble is they all have other roles as well, so one could readily extract those roles from those various bodies and thereby reduce them a little in size and either expand one of them to cover what is necessary or set up another body. I would not wish to prejudge which would necessarily be the best way of doing that as long as there is an organisation that can speak with a single authoritative voice on all these topics.

Baroness O'Neill of Bengarve: Thank you very much.

Chairman: Does anybody else have any comments about that? Lord Colwyn?

Q219 Lord Colwyn: At our Genomic Seminar, which I know you came to and I am not sure if any of the others came as well, it was suggested in evidence from the Academy of Medical Sciences that in future pathology services might be reorganised with a molecular pathology lab acting as the hub of molecular tests in clinical genetics, cytology, haematology and

pathology. What is your view on the benefits of organising pathology services in this way? What do you think the costs might be and the desired timescale?

Professor Furness: That was an Academy point and could I answer it, please, because it has been discussed a good deal within the Royal College of Pathologists, and indeed it is a topic that arises from Lord Carter's work on the provision of pathology services. There are aspects of providing molecular biology systems that are very expensive and nowadays rely on very large expensive machines where you only have look at the economics and it is absolutely obvious that it is more efficiently done with a small number of those machines analysing samples from all over the country, if that is the sort of thing that you are talking about. However, on the other hand, the people who actually interact with patients who need to decide what investigations are needed for individual patients and to help interpret those tests for the benefit of individual patients have to be aware of where the patients are. To that extent you are potentially talking about a hub and spoke arrangement to make it most efficient. How many hubs you have around the country is a difficult question and will probably depend on the tests that you are talking about. If it is an investigation that needs some massive high throughput machine and the country really only needs one, then you are talking about one hub for that investigation; for others you will more efficiently have lots of hubs with spokes. I think the idea of the different specialities of pathology collaborating to have one hub almost per hospital to cover microbiology, clinical chemistry, histopathology - the existing specialties - is one which is being discussed repeatedly and is of value in terms of generating local hubs to make things more efficient. The barrier to that is, first of all, the need for capital investment to do it and, secondly, the current structure of NHS funding where we have silo funding where this amount of money goes to this service to keep doing what it has been doing year in year out irrespective largely of new demands and new developments, and it is very difficult to get agreement to change that pattern. The expense of that sort of reorganisation

would be there, I personally suspect it would not be enormous and I think the savings could be greater than the expense if it is done logically, but we have this hump, this barrier of organisational inertia to get over to make it happening. I am very keen to see that sort of development happening but it is the politics that get in the way at the moment, I think. John, you have had particular discussions within the UK Genetic Testing Network.

Dr Crolla: We have not actually discussed this specific issue within the Joint Committee but when I saw the question I canvassed the opinion of the Joint Committee on this. My personal view was “if it ain’t bust don’t fix it” in the sense that regional genetics laboratories and collaborations with clinical geneticists have really served the population pretty well since the inception of the regional genetics system, but most of my colleagues responded by saying, “Hang on, there is a critical mass issue here,” and that really as the technologies are evolving - high throughput sequencing, various new generation sequencing technologies, the arrays - as Peter was saying, the capital investment is so large and the capacity of that equipment is also very large, it really does make sense to centralise some of these testing scenarios. What we must not lose is this link between the interpretation and the clinical use of the data that is generated by these hub and spoke models, but I totally agree, as did most of the respondents from the Joint Committee, that we cannot be ostriches and stick our heads in the sand and say things will remain the same because the technology will drive change.

Professor Furness: It has training implications as well of course. If you are splitting the doing of the tests from the interpreting of the tests, how you train the people and how you make the jobs attractive could be difficult, but I think those are issues we will have to address.

Q220 Lord Colwyn: Are some of the simpler tests computerised now? Do you actually need a pathologist to do the test? I am thinking of haematology for instance when you are just looking at ---

Professor Furness: You can get do-it-yourself at-home testing kits but the quality thereof is debatable, and I for one would rather have someone who actually understands what is going on inside that test to at least oversee what is going on and then come on to the interpretation. Even if doing the test is frightfully easy, which I suppose may increasingly be the case in some tests, the interpretation is often very complicated. At one extreme is the good old pregnancy test where you are either positive or negative hopefully but most of the tests we are talking about have very complex interpretation problems.

Mr O'Rahilly: I just wanted to confirm and support that. The pathological disciplines contain an analytical component which is obviously critical and the quality of that is critical, but also grossly underestimated, I think, when it comes to certainly economic evaluations of pathology is the quality of the interpretative service that is provided to primary care and other colleagues in secondary care where the deep experience within those departments and the knowledge of what to do with the test is really a crucial part of the functions of those departments. You are right, it is relatively trivial to do, clinical biochemistry, you just get the agents from a company, stick them in a machine, and the machine comes out and gives you a result, but it is the knowledge base within that department of what they mean under certain circumstances, what the interferon substances might be and how to interpret an odd rogue result. All of that requires extensive training and experience, et cetera, so you need to make sure that that is maintained. The idea of a lab factory that could be somewhere off-site and just generating results back is a slightly worrying one.

Q221 Chairman: Is it not a fact that genomic medicine as it advances will get more embedded into clinical practice and, if you believe that is going to happen, is this not an opportunity to look at the whole of pathological services and on the one hand to do what you said in terms of diagnostics and genomics to have a more centralised approach (and we can debate whether interpretation needs to be local and it cannot be centralised) and at the same

time look at the way the current services are delivered in pathology and biochemistry and microbiology and unify them and stop this decentralisation and thereby every trust will then want every laboratory including genomics?

Professor Furness: From a professional viewpoint that is going to be part of my job for the next three years. We have already seen cytogenetics and molecular genetics coming together in a discipline that is almost indistinguishable. At the moment there is an enormous gulf between histopathologists (which is how I was trained) who look at shapes down microscopes, and molecular biologists who look at shapes of DNA, and I think that is going to merge and we will see that happening. The speed at which it should happen is difficult to foresee. Making it happen on the ground clearly has political and inter-professional problems that we must seek to overcome. I think starting now and say, "Right, let's re-organise everything," would be inappropriate. An incremental approach would be needed to go in exactly the direction that you suggest.

Q222 Chairman: But if there was some central push to that happening, that would help?

Professor Furness: The development of central facilities will force people from different disciplines to work together more and I think will facilitate that trend.

Q223 Chairman: If there was a central push from the government side or the Department of Health side, would that not help?

Professor Furness: I do not think we currently have a major problem that requires a government push in terms of the professions re-organising themselves. I think that may become more of a problem in the future. I would not really like to see that happen at the moment. I think changed patterns of working are currently being driven by the Carter process and Lord Carter's report - at least I hope. I would be cautious about recommending such a central initiative at present but maybe we should keep talking about that.

Q224 Chairman: What about when it comes to RNA and DNA-based diagnostic tests?

Professor Furness: Diagnostic tests based on RNA and DNA is this vast spectrum which we have been talking about and in cancer diagnostics, histopathologists and microbiologists will be working together.

Q225 Chairman: But you also mentioned that some of these will require expensive equipment. Is there a need to have a push from the Department of Health for that to happen or is there not?

Professor Furness: The organisation and funding of the laboratories and equipment is a problem where I think a central push would be a good idea, yes. If the organisations to that extent are remodelled logically on the basis of need I hope that the professions will gladly follow and adapt. We have done quite well so far I think.

Q226 Lord Winston: You have partly answered my last question. My experience may be a bit out of date but certainly with cytogenetics there have been sometimes horrendous delays in getting results in from centralised services. Is that just under-resourcing at the moment? My impression is that it is pretty patchy across the country.

Dr Crolla: You are absolutely right, Lord Winston, part of it is under-resourcing; part of it has been a reluctance to change practice, so that quicker tests would have been available had certain practices been changed earlier. I think you are alluding really to prenatal diagnosis results primarily and for carrier-type results from chorionic villus and amniotic fluid. Part of that has now been superseded by molecular testing for aneuploidies and sex chromosome abnormalities, but I think you are absolutely right, you put your finger on one of the difficulties, which is how to radically shake up what is actually quite a conservative profession. I think there are going to be two drivers. Firstly, the White Paper capital investment (and I think this is a slightly later question but if I could use an example now)

investment for equipment, which is driving the introduction of novel technologies, is really coming to an end and it was a one-off payment, and it may be the opportunity to look at reconfiguring and re-financing the next generation of very expensive technology for central testing. That is just one idea. I do not know the answer to the way in which you drive professions to do things in a quicker way except for example in America you would go out of business if your test result took 14 days and the lab in the next state's took eight days. You would go out of business and those pressures do not happen here.

Q227 Lord Winston: I am all for my Lord Chairman's suggestion that this should be centralised but once you are centralised of course you are divorced from the clinical need to some degree and that perhaps represents a problem?

Dr Crolla: Yes, had there been universal uptake of molecular testing for the aneuploidies clearly that would have been a testing scenario had commissioners driven that forward. It has only happened in Yorkshire and London but had that gone right across the commissioning spectrum then clearly it would have been a complete nonsense to set up QFPCR and FISH right across the laboratories. That would have been a driver for centralising those tests. The difficulty, as you absolutely point out, is that you are then divorced from the obstetrician who is getting the test. I think Peter has alluded to that and how important if we do centralise technology because it is an economic driver and we do need to maintain that interpretative link between the analyst and the patient at the other end.

Q228 Lord Winston: Dr Crolla has largely answered my last question but can I ask a supplementary. It is this question of the Genetic White Paper and the funding and then the Royal Colleges' funding which we need to keep up-to-date. I wondered where you felt the investment was really needed. I presume if we are going to be screening then it is going to be with robotics and I imagine it is going to be with more automation particularly with

cytogenetics. Do you want to comment on that and how far short are we of those sorts of targets and are there plans for getting that sort of funding in place?

Dr Crolla: On the first part of your question in terms of cytogenetics specifically and rolling out array technologies, I think the White Paper investment did a pretty comprehensive job of putting that in place. We are right at the beginning of the roll-out phase of that technology, and so I think where the investment needs to go is really in the restructuring of the workforce and the retraining of the workforce because people will no longer be looking down microscopes primarily. We must not get rid of that skill, we must hold on to that skill, but they will not be looking down microscopes, they will be sitting in front of PCs doing bioinformatic interpretation and generating other tests as a result of the results that they are getting. That is where I think the investment very much needs to go at this particular point in time. If you do some blue-skies thinking in looking at high through-put, high volume, fast sequencing, I am not really the right person to ask, but I could ask appropriate people to submit written evidence to your Lordships if you felt that would be particularly helpful. We do have experts in my laboratory whose remit is looking at next generation sequencing and how it will impact on the delivery of genetic services. I could provide that.

Lord Winston: I think that would be very helpful.

Q229 Chairman: If you have any further information that will help to amplify and answer the questions please feel free all of you to do so.

Professor Furness: It might be helpful to chip in a specific example on this point of funding for large equipment. It was anticipated that when the White Paper introduced new developments and new equipment that commissioners would have arrangements to replace that equipment in due course. My understanding is that in some areas a lifetime of five years has been agreed in the budgets over which such equipment will be written off, and that is probably too long, but there are certainly other areas where commissioners have made no

provision whatsoever for writing off and replacing the equipment, so we are getting differences of funding in different parts of the country which I think is regrettable.

Q230 Chairman: Thank you very much. We have appreciated it very much you coming and giving us evidence. It has been a most interesting and informative session. If you have any further submissions you would like to send, please do so. Finally, whilst it came out in your evidence session the areas where you might like to see the Committee focus or even make recommendations, feel free if you want to tell us about two or three recommendations that you would like to see. It does not mean that we will make promises that it will be there but at least we will listen. Do you have any comments to make about that? What recommendations would you like to see?

Dr Crolla: Put on the spot!

Q231 Lord Winston: The Chairman is asking you to do our work for him.

Dr Crolla: I think to address the funding gap as I identified in NIHR; to perhaps look in some depth at the provision of training for clinical scientists within the context of what is actually happening under the Professor Hill initiative, Modernising Scientific Careers. I think we are at a critical point and if we do not get it right now we are going to be regretting it for some time.

Q232 Chairman: I hope you will do a better job than my profession in making sure that it does get it right.

Dr Crolla: We will certainly try. Those would be my two principal recommendations.

Professor Furness: As you probably guess, my principal wish would be for an authoritative national system for the evaluation of new developments and to also provide recommendations

on how they will be implemented. I think all my other wishes would be so expensive that they are probably not realistic.

Q233 Chairman: Professor O'Rahilly, did you want to say something?

Mr O'Rahilly: I suppose a more high level, almost philosophical emphasis, I think what genomic medicine is revealing to us is that human disease is not as simple as we would like to think and that an approach towards medicine which involves ticking box and following algorithms in a rather thoughtless way is likely to lead to poor patient care, and that doctors need to be very sophisticated biologists and they need to be trained appropriately. Any push towards the more rapid training of less-trained doctors is likely to have adverse consequences in the future. I think that this is one area of medicine and one area of current discovery which is really exposing the great need for the biologically sophisticated doctor of the future.

Q234 Chairman: Thank you. Dr Rafi?

Dr Rafi: Two points really. One is education and training, picking up on the last theme. It is really important to provide money for educational input into primary care. The role of the National Genetics Education Centre has been excellent but it would be nice to see spin-offs from there in each region so that you have local genetics education centres that can help train the workforce or educate the workforce in primary care. The other is to have a local resource available within primary care trusts, and there are various models for this - GPs with a specialist interest, perhaps community geneticists or perhaps genetic nurse counsellors - an identifiable resource that is available both for practitioners but also for the primary care trusts as well.

Chairman: Thank you very much indeed all of you; we appreciate it greatly.