

WEDNESDAY 24 JUNE 2009

Present

Arran, E
Brooke of Alverthorpe, L (Chairman)
Caithness, E
Cameron of Dillington, L
Dundee, E
Livsey of Talgarth, L
Palmer, L
Sharp of Guildford, B

Memorandum submitted by the Bioscience Sector

Examination of Witnesses

Witnesses: **Sir Mark Walport**, Director, Wellcome Trust; **Sir Leszek Borysiewicz**, Chief Executive, Medical Research Council; and **Professor Max Headley**, University of Bristol, representing the UK Bioscience Federation, examined.

Q208 Chairman: Good morning, gentlemen. Thank you for your joint evidence which you submitted to us in advance. The session has been arranged to take formal evidence for the Committee's inquiry into the proposed revision of the Directive on the protection of animals used for scientific purposes. A transcript of the evidence will be taken and you will have an opportunity within a few days to look at it and to make any corrections, if any are necessary. I should also mention that the session will be webcast, but not broadcast on television. I wonder if you would like to start by introducing yourselves and also if there is any additional statement you might wish to make, supplementing the written evidence you have put in before we get to the questions.

Sir Leszek Borysiewicz: My name is Sir Leszek Borysiewicz and I am Chief Executive of the Medical Research Council. I am here wearing three hats, I believe. The first of these is as Chief Executive of the MRC, where we spend about £600 million a year on biomedical

science and about 20 per cent of the projects involve the use of animals. We therefore have a real interest in this particular issue. Secondly, I house and am charged with financially supporting NC3Rs, as the organisation that sits within the MRC Head Office, supported in large part by the MRC. We also scrutinise the performance of that organisation and ensure that its findings are brought into good scientific practice within the projects that the MRC itself supports. The third element that I am involved in is that I am Vice-President of EUROHORCs, an organisation you may not be aware of but it is the organisation in Europe that represents all of the national funding agencies that are publicly funded, which in essence accounts for 85 per cent of all European science funding, as opposed to the nine per cent that is funded through the Commission. This is therefore an international organisation. I am also the United Kingdom representative on the Council of the European Science Foundation and the European Council of Medical Research Councils; as well as coupling that as the representative for the international and European agendas on behalf of all research councils in the UK. It is this last aspect that I would particularly like to address. First, we are all supportive that the Directive needs to be reconsidered, because of the period of time that has passed. I am particularly pleased, as I think are virtually all the organisations, with the higher prominence given to the 3Rs in this activity. However, the point that I would like to make from the heads of European research councils – it is available on the website and I can furnish additional information – is that I was mandated as Vice-President of that organisation to seek the advice of all the major member countries in Europe as to their national funding bodies' opinions in relationship to this particular documentation. There are 36 organisations enshrined within EUROHORCs from 24 countries. We received responses to our suggestions in relation to 19 out of the 36 organisations, representing 15 countries. The major concerns that we identified as an organisation were in relationship to non-human primates; the severity levels; the restrictions on re-use; the extension of scope to invertebrates; and particularly the

care and accommodation issues that are there. In summary – again, I can provide further detail – 19 out of 19 respondents agreed that there were significant problems in relationship to security, to severity levels, the extension of scope to invertebrates, and particularly the care and accommodation standards. In other words, there was no agreement with the proposal as it was placed before the European Parliament. Eighteen out of 19 wanted to distance themselves entirely from the proposals around non-human primates, in view of the impact it would make on the science programmes in Europe, and 17 out of 19 were opposed to the issues on restrictions proposed on re-use. In addition, eight out of 15 countries were convinced that their governments would follow the line that these organisations are proposing directly to their governments. In France, Germany, Poland and Sweden, the views of the relevant councils would be the views expressed by those member countries in considering this documentation. The point that I would therefore like to make to the Committee is that the views we expressed in our joint statement are views that are supremely and very widely held by all research organisations that utilise animals right across the European Union, and the UK's position is not an isolated one in this context.

Sir Mark Walport: My name is Mark Walport. I am the Director of the Wellcome Trust and have been so since 2003. The Wellcome Trust funds approximately £600 million of medical research each year. To put that in context, approximately 30 per cent of the grants that we award involve some animal research. The vast majority of that animal research is in small rodents, particularly mice. Overall, as I am sure you will have heard from others, non-human primates account for less than 0.2 per cent of animal research, though an extremely important component of that – as I am sure we will come back to later. I agree entirely with what Sir Les Borysiewicz has said; in particular, I would like to emphasise that the response to this Directive has been very consistent, not only from the nationally funded research councils but also from the charity sector and also the industry sector. We all support conducting animal

research to the highest possible standard. Indeed, again as you will have heard from others, the UK has the highest standards of animal research. I think that we all recognise that the Directive is out of date and does need to be brought up to date. However, my final comment at this stage is to say that more bureaucracy does not equate to better standards of animal care, and I think that there is considerable confusion between the two in the way this Directive has been put together.

Professor Headley: My name is Professor Max Headley. I am a veterinary surgeon by training and a professor of physiology at the University of Bristol. Over my career, I have held all the different roles that are required under the Animals (Scientific Procedures) Act, except that of being a Home Office inspector; so I come as a doer across the board. I am here representing the Bioscience Federation, which increasingly is representing all the different sectors of bioscience across the UK, from academia through to the funding agencies, patient groups and, increasingly, industry. I would like to support what Mark Walport has just said: that there is a remarkable degree of unanimity across the sector in terms of our approach to the legislation that has been put in front of us.

Q209 Chairman: You say 19 out of 36 organisations or representative bodies were approached. Could you give some indication of what kind of bodies did not respond and what kind of countries they represent?

Sir Leszek Borysiewicz: I will group them in two and I will certainly make the specific evidence available to you. They fell into two groups: those research bodies which primarily funded physical sciences, like CNRS in France. In some countries, particularly France, one body, Inserm, is charged with responding on behalf of all French funding agencies, therefore the others did not respond. There are one or two smaller countries like Slovenia, Slovakia and others, which did not respond to our request for information around this area; but the responses covered countries as diverse as Hungary through to Portugal at the other extreme of

Europe, in terms of the views that were expressed. As I said, I could make available to you the complete list or I could read that list out, if you would like me to.

Q210 Chairman: You have covered your concerns there on the non-human primates, on the alleged growth of bureaucracy and the severity of definitions as well, I think.

Sir Leszek Borysiewicz: Yes.

Q211 Chairman: What about data-sharing? It is an issue that has been drawn to our attention.

Sir Mark Walport: The first thing to say is that research funders as a whole are very strong supporters of the fact that research is not completed until it is published. We have a grant condition that says that, within six months of publication of papers from the research we fund, all publications must be made available on the internet to anyone who wants them; so the scientific community works on the basis of sharing data. Again, the issue is proportionality. Just because data is shared, it does not mean that it is necessarily useful data. What we support, therefore, is data to be shared of properly completed research. The idea that every piece of data about every animal experiment should be made available would neither improve animal welfare nor would it realistically increase transparency. I think that one has to get behind the issues around data-sharing. One of the allegations that has been made is that there is a great deal of duplication of work. The reality is that that is not the case. When we make funding decisions, part of the peer review process actually says whether there is any evidence that the work has been duplicated or not. We do not fund duplicated work. The costs of research are high and therefore it is not in the interests of researchers to do it. Equally, it is not in the interests of industry to duplicate the work needlessly. I think that this is therefore trying to crack a problem that does not really exist. The other thing to say is that some duplication is appropriate. Science advances on the basis that people make observations that

can be verified; so from time to time things are repeated. That is deliberate and it is either to confirm or refute important findings. The answer, therefore, is that the general principle of data-sharing is one that we support, but we do not support data-sharing as an unalloyed good, as it were. One has to recognise that there is work that is done in industry which is competitive, which has to be finished properly and the intellectual property protected, before it is made public.

Q212 Chairman: There is also the argument, from people who are concerned about the numbers of animals used in experiments, that there are many experiments that take place which never reach the point where there is any published report on what has happened because there is no outturn which is of public value, and these do not surface in any way, to be counted in terms of the number of animals involved.

Sir Mark Walport: That is not really the case as far as research funders are concerned. When we make a grant to someone which involves animal research, that is expensive research. It would be a very disappointing outcome if there were no published outcome. It would not be good for scientists in terms of their future prospects of getting grants. People do work very carefully with the aim to get it published. I therefore think that there is a minority of animal work, as it were, that is not published because it does not reach any useful conclusion.

Q213 Chairman: To what extent have differences in the way the 1986 Directive has been applied across Europe had an impact on the academic research sector?

Professor Headley: There have been and continue to be significant problems with the implementation of ASPA, as it is referred to colloquially – the Animals (Scientific Procedures) Act. It is very restrictive and that causes enormous frustration. If you are doing an experiment today as an innovative scientist, you want to be able to modify in the light of today's experiment what you do tomorrow. Not to be able to do so without having to go

through the application procedure for amendments and obtaining appropriate approval to do so causes enormous delays. It is one of the reasons why people are increasingly going abroad, to collaborate and do their animal-based research abroad rather than in this country. That is largely because of the level of stipulation of detail that has been required since the 1986 Act came in, although that has increased progressively over the first ten years of the operation of the Act. I am happy to say that, over the last year or two, the Home Office has started to reverse that trend and is now tending to reduce the amount of information that is required in licences, which allows the scientists a little more flexibility. That has not gone far enough, however, and there is still a great reluctance to engage in risk-based assessment, the controls should be greater for those procedures that are more likely to cause an animal suffering than those procedures that are not likely to. To take the example of a so-called non-recovery experiment – one that is undertaken exclusively under anaesthesia with no recovery at the end – it seems inappropriate to demand the same level of bureaucratic control for that situation as for more serious procedures that will cause significant welfare deficit. We therefore do still need to have a greater degree of proportionality in the system than we have currently. So, yes, I would argue that there have been and continue to be significant problems with the implementation of the 1986 Act.

Q214 Chairman: Could you say something about the German position of academia? As I understood it – and I asked some questions of the Commission about this and they were not themselves able to give us an immediate example – we had been led to believe that the 1986 Directive did not apply to German academic research.

Sir Leszek Borysiewicz: That is the position as I understand it in Germany at the present time, but the DFG, the *Deutsche Forschungsgemeinschaft* organisation, has engaged with us as EUROHORCs, and part of the evidence that it has provided is the impact that this would have

on research in Germany as well; so they are engaged with the process. However, as I understand it, formerly the 1986 Directive did not apply to academic research in Germany.

Professor Headley: I think it is true that they all have controls; the difficulty in understanding it is that it is based on the *Länder*, the states. They vary very considerably according to, in simple terms, the balance of political parties in the local parliament. The political influence on the decision-making process on animal research is therefore quite heavy.

Sir Leszek Borysiewicz: We should not run away with the view here that the standards therefore applied in Germany are any the less stringent. I think it is true to say that many of the *Länder* have far more stringent requirements than the 1986 Directive. It is very important therefore that this is not counted as a negative against those investigators working in Germany, who work to very high standards by and large. That is very clear in the responses that we have received from DFG and the Max Planck Society.

Q215 Earl of Caithness: Professor Headley, you have made it clear that the Home Office have gold-plated the European Directive of 1986, and what you have said about Germany is interesting. There are two countries that have ratcheted it up above the EU level. What about the other countries? Have the other major players, or are we facing huge discrepancies across Europe?

Professor Headley: Yes, we are facing considerable discrepancies and therefore there is considerable export of animal research, not just to non-EU countries but also to Europe. There is much more flexibility in quite a number of EU countries, including some states in Germany, than there is in the UK. So, yes, we do not have a level playing-field at the moment, and that is one of the advantages that we see in terms of the potential revision of the Directive.

Sir Leszek Borysiewicz: This is precisely the view across all of the funders in Europe. While we all agree that a revision of the Directive is necessary, we have had new Member States

coming into the European Union, some of which perhaps do not have as stringent requirements in this area. Ensuring that they are up to speed, to ensure that we have uniformity of view, is considered to be generally a good. What is important is that that is reached through appropriate debate and discussion over a period of time, to ensure that this very important area is covered right across the board. However, there is no disagreement between any of the countries that this does need revision at this point.

Chairman: Professor Headley has just referred to considerable export of animal experimentation, so I think that we will move on to talk with Lord Livsey about international competition.

Q216 Lord Livsey of Talgarth: On 10 June, Professor Hammond told us that the UK's academic base is "as good as anywhere in the world" but he also said, "It is under threat – we are seeing migration of skills out of the UK". Your written submission stresses the need to ensure that the UK's and the EU's "brightest and best scientists have sufficient incentives to remain within the EU". What evidence is there of a brain drain out of the UK to other parts of the world?

Sir Mark Walport: I can comment on that in relation to non-human primate work, where a combination of costs and regulation has meant that there is a significant decrease in the amount of neuroscience that involves non-human primates. I think that, increasingly, youngsters who are looking to a career in neuroscience will look to the States as the place that can provide that. In the context of rodent research, there is no doubt that the UK is in the world forefront of research involving rodents. None of us dispute the fact that this work has to be done to the highest standards across the board, and I think that we have a model that works very well. One of the benefits of the EU Directive if got right, and it is far from right at the moment, would be, for example, the incorporation of ethical review. The issue is much more that people make judgments about the quality, appropriateness and the standards of

research, rather than trying to write down the precise letter of what is and is not allowed; because then you get into enormous bureaucratic knots. The issue for the UK is to make sure that the processes run smoothly and rapidly. That is the issue. I do not think that researchers mind the fact – in fact they applaud the fact – that research is well done and well judged; but there is a duty on the bureaucracy to work efficiently, and I think that has been one of the challenges. We are less qualified to speak for industry; they can speak for themselves. However, as regards the decisions about where industry locates its R&D – which are absolutely crucial to the economy of the UK since the pharmaceutical industry is one of the major economic platforms in the UK – they look at the bureaucracy around animal research and they make judgments, which could be harmful to the UK. In terms of an academic brain drain, this is not happening on a large scale but there is no doubt that people are making decisions, particularly if they want to work on primates. However, there are very significant threats in the Directive about imposing time lines and bureaucracy, which actually will not improve animal welfare.

Sir Leszek Borysiewicz: Regarding the issues here in relation to species other than primates, I think the evidence is very patchy and there is very little evidence that regulation is playing a significant part. In relation to primates, a very eminent journal has already quoted the issues about people emigrating to the United States. I had the privilege recently of being in Shanghai and having some discussions, probably with the very centre that was mentioned in the evidence previously provided. There are issues that some countries are using their position in relation to primate research as a way of attracting industry away from the UK. However, as my colleague Mark has said, the real issue here is that all investigators want to work to the highest possible standards. It is not about dropping standards; it is about making sure that the bureaucracy is appropriate to the work that is being done. Clearly, in some parts of the world where high standards are also in place, it is easier to conduct some of this work

than it is in the UK. I am very concerned that, for example, the expertise we are likely to lose particularly in the primate area. Young staff numbers training in these disciplines in the United Kingdom is falling, as is the use of primates for particular procedures in the UK; whereas the evidence from the United States is that it is static or growing slightly. This is very important to maintaining the UK's competitiveness for the future.

Professor Headley: We should be mindful that we are talking about two different things. One is migration of people, lock, stock and barrel. The other is people based in the UK but doing their animal-based research, or some of it, abroad. From my perspective, I see that as the bigger problem or, shall we say, the more extensive problem; because it then starts to lose the skills base which the ABPI and others have emphasised in recent years is severely lacking in this country. If we start to export the work, we will simply fall further behind on that score. Getting evidence of that is quite tricky. That is because few of the people who do this are willing to stand up and be counted, because they still have animal operations in the UK. They are nervous about the way that the Home Office inspectorate would respond to the fact that they are starting to do some work abroad. I have asked repeatedly, through the Bioscience Federation, for people to stand up and be counted and to give us examples. Although I know of many cases ad hoc, it is quite difficult to collect the evidence.

Q217 Chairman: So in a sense it is being outsourced?

Professor Headley: It is being done by collaboration. It depends what you call outsourcing. It is not so much that you say, "Go and do this for me" but "Let's do it together, but I'll do it in your lab rather than you doing it in my lab".

Q218 Lord Livsey of Talgarth: Clearly this is a very big subject. If one factored into this an article in *Nature* published in October which says "Made in China?" it goes on to say that the companies see opportunities abroad and that "The combination of desperation outside

China and promise within has convinced almost every big pharmaceutical player, including Roche, Novartis, GlaxoSmithKline, Eli Lilly and Pfizer, to collectively invest hundreds of millions of US dollars into research operations there....” That clearly must be a factor which we cannot ignore. You have given a lot of causes of migration. We are very interested in what evidence there is that controls over the use of animals in scientific procedures are at all a significant factor. In particular, are there scientific procedures which cannot be done in the UK now, or which could not be done under the revised Directive, which UK scientists would take abroad?

Sir Leszek Borysiewicz: I think that there are several issues here. What is very difficult is to tease out the various incentives that countries like China and India are now putting to scientists in order to recruit them to work in China. The attractiveness of China certainly to academics is that they are providing facilities that are second to none. Many of those are being built at cost, with very little cost to utilise the facilities; so there is widespread subsidy in order to attract that kind of business into China. The animals are very often treated to very high standards in many parts of that country, certainly the ones that I visited, but clearly it is just one part of a major incentive to attract that research to China. In order to maintain our competitive edge, it is very important to retain this activity in the United Kingdom. While we are talking about non-human primates, I would have to stress that, as currently formulated, the withdrawal from the capacity to study non-human primates for primary biology in order to understand the very basic processes that can lead to future discovery, as highlighted by the article yesterday by Lord Rees in *The Times*, is something that is a very real threat. Certainly all the countries with which I have corresponded and engaged see this as an absolutely unacceptable part of the proposed Directive that non-human primates should only be used in very specified areas. I also have some views about the restrictions on great apes, because again it is trying to predict what is required when it is impossible to make that prediction in

our current state of knowledge. I do not accept that we have yet reached the point on replacement where we could replace non-human primates adequately with alternatives. That is a very real anxiety and the fundamental worry that underlies the problems in the Directive around non-human primates.

Sir Mark Walport: May I add three things to that answer? The first thing is to make absolutely clear that research funders would not agree to something being done overseas that was considered unethical to do in the UK. That is a very important principle. The second thing to say is that if the Directive was implemented as is proposed at the moment, then for primates the specification is that research could only be done if it related to life-threatening or debilitating clinical conditions. Frankly, that would impose restrictions that would make no sense. For example, the use of deep brain stimulation in Parkinson's disease, which is helping many people worldwide, depended on fundamental research on the rate of neuron-firing in the brain. Again, it comes back to my point earlier that we have a system in the UK which, if used well, means that people use judgment when they are considering whether experiments on primates are justified or not. Trying to define whether a condition is life-threatening or debilitating is not something that can be readily done by statute. The third thing which I think would cause major problems is that some of the proposals – and you may wish to ask questions specifically about this – that specify, for example, the precise cage sizes would, in a non evidence-based way, add approximately 25 per cent to the costs of mouse research. That in itself would make it uneconomic for the research funders in the United Kingdom. There are some very major threats here, therefore.

Q219 Earl of Arran: How much, if any, is the remuneration package a draw to researchers working out of the UK?

Sir Leszek Borysiewicz: At the moment, I think there is very little evidence that for UK-based researchers this is a major consideration. China has a very favourable remuneration package

to attract back Chinese workers who were particularly based in the United States, and they are given very special consideration within the Chinese system. However, there is no evidence that, outside that grouping, this is a major factor. We have done several studies to try to look into this in our trainees. It is the availability of facilities, the ability to undertake work and, frankly, the availability of money from the academic sector in order to conduct that research through funding agencies in those countries. There are other incentives obviously for industry and other sectors that would have to be taken into account, including tax breaks, facilities and aggregates on large science parks. All of these have played very well into the scale of developments taking place in China, India and Singapore.

Q220 Lord Palmer: I was going to ask the same question as Lord Arran but, just going to the other end of the scale, are you worried about the number of undergraduates who are going into the medical research aspect, or might this be a worry in, say, five or ten years' time – that there will not be enough of the likes of you, with your expertise?

Sir Mark Walport: This is something on which we are working very hard. The problem starts in schools and probably goes far beyond this Directive. I think that there is quite clear evidence that there are fewer youngsters going into university to read the pure natural sciences – so physics, chemistry, mathematics – and these are all absolutely key skills for the biosciences in the future. We are working very hard to remedy those problems. I would have said that this is a relatively small part of that particular puzzle about people going into research and medical research in particular.

Sir Leszek Borysiewicz: We have looked at this area in particular and the real anxiety here is people who have specific expertise in physiological models, which is of particular importance to the pharmaceutical industry and elsewhere. There does appear to have been a trend that fewer and fewer of the young scientists who come in at university level and then want to take on a professional career want to do so in the context of animal research. There are a variety

of factors, not least among which are the climate in which animal research takes place. However, we have instituted special measures, alongside the industry, in order to train more people in these aspects and creating specific units that focus on these areas, because we do consider research in this area as an absolutely critical part of future advances in biomedicine. Whatever we say, animal research is an absolutely integral part of all biological research moving forward, both in gaining a better understanding and in being able to alleviate disease.

Sir Mark Walport: Perhaps I may add to that. This is an important point. When we were undergraduates, part of the training of a medical student did involve undertaking physiological experiments using animals. That hardly happens now. If these regulations were to be put in place, students would not even be able to do experiments on some decapod species. Shrimps and other species are used in undergraduate experiments. This would make that extremely difficult. It is a continuation of a long trend, which I think would be very damaging.

Professor Headley: It is certainly true that if you want to have the next generation, you have to engage interest at a relatively early stage of people's careers. It is not something you can bolt on at post-university level. However, it has become increasingly difficult to expose undergraduate students to this sort of work, for a combination of reasons. Part of that is cost; part of it is the absurdity, for instance, that the annual licensing fee for personal licences does not match the academic session. You therefore end up having to buy two licences in order to expose your undergraduate students to one year's worth of training. Significant are the cost of animals and also the restrictions that there have certainly been – which I am happy to say are slightly relieved now – about getting a project licence through the Home Office in order to allow you to undertake relatively small numbers of demonstration-type experiments with undergraduates. That has been a major difficulty. It is becoming somewhat better. Indeed,

there is a workshop taking place in September with the Home Office in order to try to promote that operation of licences involving teaching – but it has been a major problem.

Q221 Baroness Sharp of Guildford: Your final remarks pick up the question I wanted to raise with you. It is clear from the evidence you have given that from your point of view it is the implementation of ASPA and the directives by the Home Office that is the crucial issue, and you do not feel that the bureaucracy that they have in place is as helpful as it could be. I was going to ask you if you could give us some examples and whether there was hope that, in discussions with the Home Office – you were indicating that it has got easier in the last two years – one might be able to get procedures that were more friendly towards research in this sense.

Professor Headley: It is certainly true that ASPA has been one of the major difficulties in this area since 1986. That has waxed and waned with the level of risk aversion within the Home Office, in terms of the threat of dissent by antivivisectionist groups, et cetera. We are in a slightly more positive environment now and, as I intimated just now, we hope that that will improve things. That is not a complete solution as yet. At my University, for instance, we have just had to renew our project licence for undergraduate training. We still had to have three circuits round, about addressing the aims and objectives, making sure they were sufficiently precise, and so on; none of which has the slightest impact on welfare, particularly since most of the experiments that we are undertaking are mostly non-recovery. Even with the renewal of a licence with virtually no extension, therefore, there were still many hours of academic time being put in to make this work. That seems quite unnecessary. We have to try to move to a system which is related to the welfare impact of procedures, rather than dotting Is and crossing Ts in the way that the Home Office has felt obliged to do under the current Act.

Sir Leszek Borysiewicz: There is a big concern among investigators about an issue underlying this Directive, which is that the imposition of additional bureaucratic steps – over and above the ones that we already have, on which we are negotiating and working very hard together with the Home Office – will add an additional burden. There are statements, requirements, authorities and authorisations in here that do cause a lot of anxiety in academic investigators that this will just make it bigger without actually improving the animal welfare side, as my colleague pointed out in his opening statement. We are very concerned that a linkage is being made that bureaucracy in some way reflects animal welfare. We absolutely refute that there is any association between these two. Bureaucracy has to be appropriate to the level of animal welfare that you want and not be overwhelming.

Chairman: I think that you are getting your message through! Can we go back to non-human primates, with a question from Lord Cameron.

Q222 Lord Cameron of Dillington: Perhaps I could first say that I am a farmer and so I understand that any representative body always resists change like mad, particularly if it is being foisted upon us by our political masters, shall we say. I wonder if I could start by asking if you accepted that minimising – and you can interpret that word in whatever way you like – the use of non-human primates must be part of the acceptability by the general public of all the work you do, not least in connection with the question being asked by Lord Palmer.

Sir Mark Walport: I think that we would agree with that completely, and we would go further and say that minimising the use of all animals has to be the goal. One then has to recognise that one needs to make judgments and it is actually about proportionality and deciding on a case-by-case basis whether the experimentation is justified or not. In parenthesis, it is worth noting that research on agricultural animals is something that would become almost impossible under these regulations. The housing conditions that are required would make agricultural work almost impossible. You would not be able to release animals back into your

farm afterwards. There seems a slight paradox that this, which has come from a committee that ought to know about agriculture, has completely neglected it in terms of the regulations.

Sir Leszek Borysiewicz: Could I add that every funder from the Association of Medical Research Charities as well as the public bodies, as part of the application form where there is a request for “use of animals”, stipulates that there has to be a specific justification, which is tested by peer review as to why those experiments are to be conducted in animals. The numbers are strictly tested, both for the ethical considerations in relationship to the use of the animals as well as to the numbers actually required in order to achieve the end goals of the proposed studies. It is not just something that we aspire to, therefore; it is something that we have inherently in our funding practices that is tested grant by grant, application by application, as it comes to every funder.

Q223 Lord Cameron of Dillington: This is an area that obviously divides the two sides pretty thoroughly, but even the RSPCA last week were saying that they do not want to ban experiments on non-human primates; they are just looking for ways of minimising them. Clearly, as you said, the draft Directive restricts [non-human primate] research to life-threatening and debilitating clinical conditions, although that was broadened by the Commission, when they gave evidence to us, to include conditions such as infertility, diabetes, Parkinson’s and so on. On the other hand, two weeks ago Professor Hammond, who perhaps more represents your position, was saying that they wanted to “protect basic research that generates knowledge”, which is pretty well a free-for-all as far as we were concerned. How would you minimise the use of non-human primates?

Sir Mark Walport: I think the short answer is that it is not a free-for-all, because we review this extremely rigorously. We have scientific review, which asks the question “Will this fundamentally add to knowledge?” In the case of primates we also add an additional level of peer review in that the MRC, the Wellcome Trust and other funders send the applications to

the National Centre for the 3Rs for an additional layer of peer review; so we are therefore extremely careful. Let me give you another example that has recently been discovered. There are these neurons called “mirror neurons”. If you are looking at someone moving, there are neurons that respond to that. That is relevant to the understanding of autism, which is an extremely important condition; but I do not necessarily think that the researchers doing that research at the time would know what the clinical implications of the research are. A fundamental understanding of the brain is therefore absolutely crucial to the understanding of neurological conditions, which are a huge burden of ill health. We are very careful that, when a research question is asked, it is an important question. In other words, if it is answered it will tell us something which we did not know that is important about how the nervous system works. That is not a free-for-all by any means at all. It is very tough to get the money; it is very expensive for us, actually.

Q224 Lord Cameron of Dillington: Where would you draw your line? How would you reduce the use of non-human primates?

Sir Mark Walport: We would reduce it by the use of the judgments that are done at the moment. In other words, the UK system, which has peer review, it has ethical review and, in the case of non-human primates research, it has a further review of animal husbandry. We would still believe that asking wise people to make judgments on a case-by-case basis is the best way to do this.

Sir Leszek Borysiewicz: There would be two elements that I would like to add to that. First and foremost, please do not underestimate the potential ingenuity of applicants for grant applications. If you put in stipulations such as proposed in this legislation, you can begin to contort and convert any sort of basic research that you wish to undertake to having some downstream benefit. We all believe that there should be absolute transparency as to the purpose of an investigation, which is clearly outlined in the grant application, rather than

creating a fantasy in order to fulfil rules. That transparency is tested in the UK system very clearly and very rigorously, particularly as it applies to primates, as my colleague has outlined. It is therefore very important to do that. Secondly, the numbers of primates in use in experiments in the United Kingdom has fallen, for a variety of reasons. Therefore, the trends in terms of utilising alternative models are already there and reasonably well established within the community. I would therefore say that we are already on a trajectory whereby we are seeing that minimisation, through the processes that my colleague has already identified.

Q225 Lord Cameron of Dillington: Can I touch on the F2 question, where the problem lies and how we cannot work towards a date whereby we are using only captive-bred animals?

Sir Mark Walport: The first thing to say is that there is actually no evidence that suggests that animal welfare is any better by using F2; in other words, entirely captive-bred animals compared with others. The second thing to say is that in principle it does seem a sensible direction in which to move; but we are a long way from having the capacity to do that and, frankly, it remains enormously expensive. The question therefore is, in a world where there are other economies, if it turns out that F2 animals are very much more expensive than animals bred elsewhere, then I think the community will vote with its feet – particularly the pharmaceutical industry. So I think that this could be dangerous to the pharmaceutical industry. As I say, we do support it in principle, but I think that there are questions. In particular, there is the question as to what the evidence is that it is necessarily any better for animal welfare to be dealing entirely with captive-bred populations. We do not know that.

Professor Headley: Could I add that, from a veterinary perspective, there are potential problems that are beginning to surface in some colonies about having rather small groups, and the genetic inbreeding that is likely to result from those, that may have problems as you start to get through the generations. That is beginning to surface. We really do need to have, as

was proposed by the EU Parliament, a clear scientific review of that situation before there is any enforced implementation. It is notable that the Commission itself commissioned a report, the SCHER report that was released only in January this year, which does delve into a number of these issues in quite some detail and is rather antithetic to the position that was taken by the Commission in the original November draft. That is a mistiming that is somewhat unfortunate, because one would have hoped that the content of that SCHER report would have been reflected rather more in the draft Directive.

Q226 Chairman: Could we stay on the subject a little longer, on breeding? We have a later paper in evidence from the Medical Research Council and the Wellcome Trust, “Principles of appropriate levels of scrutiny, checks and balances for the use of animals...”, which has come to the Committee this morning. In paragraph 13 you say, “If the grant contains rhesus macaques, the main funders of non-human primate research in the UK stipulate that researchers must source animals from the UK-based Centre for Macaques (CFM)”. Presumably this is something that you run yourselves?

Sir Mark Walport: Yes, that is correct.

Sir Leszek Borysiewicz: Yes. It is a centre that we look after. For obvious reasons, I am not going to disclose locations and so on – but, yes, we do. We support that centre.

Q227 Chairman: You do have the fullest opportunities then to explore some of these issues?

Sir Mark Walport: Yes, we do. Indeed, one of the challenges of that is that the costs of macaques being produced by that centre are enormously high. They are at present in excess of £20,000 per animal, and that does raise quite important questions about the long-term viability of that as a simple solution.

Q228 Chairman: Do you have second-generation?

Sir Leszek Borysiewicz: There are numbers of second-generation animals, but at the present time the numbers produced by that centre would in no way be able to provide the supply that is required in totality within the UK, not just in the academic sector but in the wider CRO sector.

Professor Headley: Could I make one extra point in relation to the NHPs? Something like 70 per cent of the NHPs used in this country are for regulatory purposes. The numbers that we are talking about that are discretionary, if you like, in terms of fundamental research or applied research, are really very small. Whilst there is therefore this stipulation from the major funders that the CFM should be used for the supply of NHPs in that fundamental work, it cannot apply to the majority use, which is in industry; because the supply is not there and the costs would be prohibitive.

Chairman: This is an important area.

Q229 Earl of Arran: We have been touching on this for much of the morning, on authorisation. This terrifying set of procedures here on page 27, which has secured the criticisms from many organisations as “pedantic”, “bureaucratic”, “slow-moving”, to put it politely. I do not want to put words into your mouth, but how much of a problem is this at the present time? Do you at all see the existing consultation process currently going on as a way of improving this, of simplifying this? Would the proposals for the revised Directive make matters worse or, on the other side, might they help by standardising procedures across the EU?

Professor Headley: As I hinted earlier on, I think we do have an over-regulated system in the UK that is not sufficiently proportional to the welfare costs involved. In terms of what is being proposed now, we have this, as you say, very complicated mechanism that would make that situation significantly worse. That said, we do see the introduction of a new Directive, and the implementation into the UK legislation subsequently, as an opportunity to get it right.

We would very much like that to take place and have been working hard with the Parliament, and now the Home Office which acts through the Council of Ministers to try to get our views across. The issues are, on the one hand, harmonisation; so, yes, we would like there to be a level playing-field across Europe of both animal welfare standards and the ethical review process and support for the 3Rs. There is no attempt at any stage by our sector to try to dilute the welfare standards that should be applied to animal research. What is sadly lacking in our view from the draft Directive, is any sense of proper proportionality – the point I was trying to make earlier on – whereby the level of regulation should be proportional to the welfare impact of the procedures that are taking place. That is what we would like to see and what is singularly lacking. We have therefore been trying to make the point that we have to have that. One of the aspects that our sector proposed to the European Parliament – and that the Parliament in our view happily adopted as one of its amendments – was the notion of “notification” of the least welfare-costly procedures. That is part of this argument about proportionality. Nobody is suggesting that any research worker can do anything just because it happens to fall within the notification that is submitted. We still have the local ethical review process that would be undertaken. We still have a licence that needs to be prepared. We still have the issue of funding, and animal research is not cheap. So the idea that notification would somehow immediately permit huge numbers of irrelevant experiments to be undertaken is rather fanciful. What it would mean is that those experiments that are of zero or minimal welfare impact would simply be more adaptable. The other point that I would like to emphasise there is that we have always argued for advance notification, not for retrospective notification. What we are basically saying is that you go to the local institutional ethical review group; you write your application; you send it in to the competent authority – in our case the Home Office – and you say, “I intend to start this in a week’s time”. You therefore have your advance notification. That still allows the competent

authority to come back and say, “Hang on a minute. I think you have got your severity classification wrong. We need to look at this a little bit more”. I think that check is still something that would be very important to have, for public confidence, and to make sure that individual institutions do not drift too far sideways from what is permitted. We are still in favour of that, therefore. What we are trying to achieve, however, is the flexibility for research to move and adapt rapidly, in order not to hinder the advance of research in the way that we have currently.

Q230 Earl of Arran: Much of the criticism is levelled against the Home Office. Who advises the Home Office? Where do they get their advice from? It would not be from your good selves, would it?

Professor Headley: Over the last four years or so, we have had a lot more input. That started with the Government’s Better Regulation agenda, to which we made a formal submission as a sector, and also the Davidson Review on the implementation of EU legislation, where we also made a submission. Since then, we have had much more of a dialogue with the Home Office than was possible beforehand.

Q231 Earl of Arran: Where are they getting these ideas from?

Professor Headley: I suspect a lot of it is the lawyers. It is the threat of challenge from antivivisection groups and the way in which that can lead, as we have seen, to judicial reviews – which are hugely time-consuming in terms of Home Office staff time and disruption to research on the ground. We have seen that taking place and it is the concern over that happening again, which means that the lawyers say that they have to close things up all the time.

Q232 Earl of Arran: Do you think they regret that decision at the Home Office at times, and they blame those down the corridor? Is there any sign of that?

Professor Headley: I think the fact that we now have, I would not say killed the antivivisectionist problem, but we at least have it in far greater control than we did up to about five years ago – that has made a huge difference to the ability of the Home Office to take a slightly more risk-based approach and to relax the controls a little bit. However, there is still the looking over the shoulder and the concern that the way in which ASPA was worded does not allow for adequate risk base. Can I exemplify that? There is one word in ASPA that has caused more problems than just about the rest of the Act put together. That word is “*may* cause pain, suffering, distress and lasting harm”. Not “is likely to” or “is expected to” or “will”, but “may”. “May” can be interpreted as being a one per cent chance, a 0.1 per cent chance, somewhere, some time, something will happen. It leaves one open to having to close all the possibilities of something going wrong, in a way which is extremely pedantic. Indeed, some of the changes we successfully encouraged Neil Parish to adopt in the amendments to the draft were to substitute “may” with “is likely to” or “is expected to”. That would be hugely helpful in terms of promoting the intent of the legislation.

Sir Leszek Borysiewicz: Maybe I should add that the Home Office seeks guidance and advice through a number of advisory committees. In order to get that advice, we are consulted in specific areas and I know that the Trust is consulted in specific areas.

Q233 Earl of Arran: And presumably it has served on them as well?

Sir Leszek Borysiewicz: Absolutely. Particularly on non-human primates, we are actually providing advice and guidance and it does seek that advice and guidance very widely. I think that at the top level of the Home Office a lot of this is taken on board. What is important here is that the relationship between the guidance and the investigators and the Home Office allows for a to-and-fro, in order to get to a position which is both equitable with the legal

requirements that are there, and rightly there, to protect suffering in animals and the ability to carry out and conduct scientific experiments effectively and well. That is a particular area of importance. The concern most investigators have is that the imposition of the additional directives on top of that will add a significant second tier of activity, which will then be very counterproductive towards retaining Britain's competitive position, both commercially and also in terms of scientific competitiveness, to be able to maintain our pre-eminent position in life sciences internationally.

Q234 Earl of Caithness: That is the very point.

Professor Headley: We should also acknowledge the role of the Animal Procedures Committee, which is advisory to the Home Office in this respect and has given some very useful advice over the years; admittedly not always with great alacrity, so a lot of the reports from the APC can take a year or two to come back. That in itself has caused problems, and continues to do so.

Q235 Lord Palmer: I want to talk about data-sharing, but you have already answered my first question earlier on about duplication; so I have only two questions left. Do you believe that there are opportunities for more data-sharing, particularly within the field of negative data? What would the impact of a mandatory data-sharing approach be on academic intellectual property?

Sir Mark Walport: As I have already said, as funders of research we do encourage the sharing of data. I think that the scientific community is increasingly responsive to this, and I will give you one practical example. There are two very large international consortia which are basically trying to delete a number of important genes in mice, so that one can understand the function of these genes. Those are working at the level of international collaboration; so instead of individual groups trying to knock out genes – and occasionally that does result in

duplication – this is now a co-ordinated universe; there is sharing of results; there is sharing of both positive and negative results. We are therefore encouraging the creation of databases where the results of animal experiments can be put. In general terms, therefore, we think that the sharing of data is something that should be encouraged and we work hard to increase it. However, one can also share data in a mindless fashion. The danger of what is proposed here is that the sharing would be the end in itself. Very large databases could be created at both very large opportunity cost and financial cost, which would then add very little value. Ensuring that sharing adds value is in itself a highly technical thing, which the Wellcome Trust strongly supports. For example, we and the MRC fund the European Bioinformatics Institute. In terms of the sharing of negative results, that has been an issue particularly in the clinical trials area; but, again, I think that great progress has been made and, increasingly, there are clinical trial registration processes, which means that both positive and negative clinical trials results are accessible. The idea that, as it were, every single animal experiment would appear on a database somewhere does not really make sense. We have to be sure that the data that is shared means something and can be interpreted. What we are concerned about here, therefore, is a blanket diktat to do it but not actually to do it well.

Q236 Lord Palmer: Which would have nothing to do with the protection of animals?

Sir Mark Walport: It would have nothing to do with the welfare of animals at all, no.

Sir Leszek Borysiewicz: Could I deal with the issue you raised on intellectual property, my Lord? I am afraid that this is often used as a red herring. Intellectual property is intellectual property, whether it is commercial or academic. In terms of the normal restraints that universities applied, from my previous experience as Deputy Rector of Imperial College, even when we entered into commercial contracts as an academic institution, there was a delay put in place in terms of publication and making data available, in order to allow protection of intellectual property by that institution. Therefore, as funders of research we certainly would

allow a reasonable delay in order to allow intellectual property to be registered, but it cannot be an end in itself that you can delay indefinitely in order just to claim “This is protecting intellectual property”. Beyond that reasonable time limit, academics are free to publish. There is a time factor here that is often not considered when that question is asked.

Professor Headley: Could I add that one should remember that it is the nature of academics to sing from the rooftops the wonderful results that they are achieving. That is deep in the psyche of the people who go in to do this sort of research. One has a whole industry of international conferences to which scientists go, in order to broadcast their latest results. That then spawns a network of informal contacts between the scientists working in cognate areas; so that you can pick up the phone and say, “Have you ever tried this?” and get the information that is supposedly, if one read the draft Directive rightly, not available to anybody. It is available through this informal networking, which is actually quite effective in the way that it operates.

Q237 Chairman: I think that there is a concern, though, that there are many experiments that take place where people do not achieve successful results, so that they do not want to broadcast it, for very obvious reasons. There is a fear that these take place on animals which are subject to experimentation. I take your point that to try to record every one would be difficult. This is a concern, though.

Sir Mark Walport: I understand that it is a concern, but it is also a concern for the people who fund research. We worry if we fund a grant and no results appear. The pressure on investigators to make sure that the results do appear is actually very high, and we do look into grants where nothing happens.

Professor Headley: There is a serious scientific difficulty with negative results, in knowing whether they are meaningful negatives or whether they are negative simply because the experiment did not work – in which case one learns nothing from broadcasting the

information. It can be very difficult to know which of those two is the case when something has not worked out properly. That is one of the reasons why people are reluctant to broadcast; they just are not sure. They might discuss it informally but they will not put it down on paper, because they do not know to what extent it was simply a failure of the techniques in some way or whether it genuinely meant that that is not the way the system operates.

Q238 Chairman: Professor Headley, you originally intimated that you may want to leave around 12 o'clock. Are you staying with us?

Professor Headley: I am afraid that I do need to catch a train and I need to leave in ten minutes.

Q239 Chairman: In which case, is there anything before you leave that you particularly wanted to draw to our attention which you have not had an opportunity so far of expressing?

Professor Headley: Perhaps we could touch on the severity classification a little more?

Chairman: Which is the next set of questions.

Q240 Earl of Caithness: The Commission gave us a very good exposition as to why their severity classifications were right and justified. Sir Leszek said this morning that 19 out of 19 of his reporters said they were ghastly and horrible and needed to be changed. What is the true situation?

Professor Max Headley: There are two different things. One is whether the number of bands and the names that one gives them are appropriate; the second is the definition of what falls into those different bands. The names that the Directive gave us were reasonable, but what it did not do at all was to describe where the boundaries between those bands are. That causes major problems for the interpretation of the rest of the Directive. If you do not know when you are designing the rest of it [the Directive] what is a mild procedure and what is a

moderate procedure, then how can you start to design and interpret those articles that refer to this terminology and make sense of it? The argument that has come from the sector, therefore, is that it is crucial to the design of the rest of the Directive that we have a well-designed and described set of procedures that fit into each of those severity bands. In the sense that the Parliament's amendment gave us the beginnings of that description, we supported it. In the sense that it did not include non-recovery as a category and did not separate out humane killing as a category, we did not approve of it. It was a step in the right direction of descriptions but it did not get it right. I emphasise that it is very important that we have non-recovery and humane killing as separate categories to serve the 3Rs function; because if you do not have the lesser welfare impact procedure separated out, you remove part of the incentive to refine from a more vigorous procedure to a less vigorous one. We therefore consider it hugely important in terms of animal welfare to ensure that we have non-recovery and humane kill as identifiable bands that are separate from the "mild" category, but that was not separated out by the amendment. In that sense, we support to a greater extent the Directive's wording but we feel that there must be a description of that wording within the Directive, so that the terms of the other articles can be interpreted appropriately.

Sir Leszek Borysiewicz: Perhaps I may come back, My Lord Chairman. It was said that it was ghastly, but actually the proposition that we discussed and considered was that it was critical that the definition of the severity band was included in the main body of the Directive. What is particularly disliked by the group is that in some way there will be a Directive and, somewhere downstream, there will be a few committee meetings that will then put in those definitions, which can then be gerrymandered and moved around as required. The lack of clarity as to what those boundaries are, if it is not in the Directive, then makes the definition of when can re-use of animals be reasonable extremely difficult. The re-use issue was one of particular concern to the member organisations that I referred to.

Q241 Earl of Caithness: I will come on to re-use, but are you taking part in the EU working groups and is the Commission listening to you and your concerns?

Professor Max Headley: I do not think we know the answer to the latter question but, yes, we are all contributing to the meeting that is taking place in July. We are restricted in the numbers of members that can take part, but we have one member of the Bioscience Federation who is contributing and Roger Lemon, who is unable to be here this morning, is contributing as a representative of the European Science Federation. There is no restriction on the number of NGOs across Europe that can contribute to this discussion, but there is a limit on the national representatives that can go. We are restricted to one member from our sector, therefore.

Sir Leszek Borysiewicz: The representation, both through the European Science Foundation and elsewhere, is well established on these committees. However, your second point is valid because this is one of the major concerns that certainly European members have expressed, as well as a real concern to us in the United Kingdom. We had a Directive drafted from the Commission. That was very carefully considered by the European Parliament. Statements emanating from the Commission are that they will tacitly ignore everything that the Parliament has suggested or that has been debated; they will be going back to their original submission and are just going to drive it through willy-nilly. Therefore, while we thought that a great deal of debate had happened around the consideration of this Directive by the European Parliament, it transpires from statements currently emanating from Brussels that actually they are just ignoring all of that particular discussion. That is causing a great deal of disquiet, because it seems that we have to go through the process all over again at the second reading, when that comes forward to the European Parliament. We do not feel that that is an appropriate way for the Commission to behave, in something as important as this Directive.

Q242 Earl of Caithness: Could you tell the Committee what your thoughts are on the proposals for the limitations on the re-use of animals?

Sir Mark Walport: I think that there is a fairly general agreement that these may be counterproductive to animal welfare. A very good example is that, in order to study a drug that may alter blood pressure, telemetry devices can be implanted that will measure blood pressure. The idea that, rather than re-using an animal that has had a device implanted, a new animal would have to be used each time is actually deleterious to animal welfare. We basically support the position that examples of re-use need to be looked at carefully, but there are many cases where re-use will improve rather than harm animal welfare, and I think that is one area where the evidence has been fairly uniform from all the communities that have responded. Again, it is a question much more of using judgment rather than trying to have a blanket rule that says that re-use is not sensible; you have to look at it on a case-by-case basis. There was some criticism of the Home Office before, but I think, actually, we have a system that the Home Office is operating and is responsive to the scientific community which actually depends on proper review where people form judgments, and there is nothing like a group of wise people looking at something and determining, on a case-by-case basis, whether it is the right approach or not.

Q243 Chairman: Presumably, there is a case against re-use.

Sir Mark Walport: There is a case against re-use under some circumstances. So it is on a case-by-case basis. There should neither be a blanket ban on re-use or a blanket permission that says that re-use is OK. One has got to look at it on a case-by-case basis.

Q244 Chairman: Should there not be an attempt to define the circumstances in which ----

Sir Mark Walport: Very difficult to define because the second you try and do that you run into all kinds of knots; it is much better to think about whether re-use is appropriate or not and make a judgment on a case-by-case basis.

Professor Headley: That is, to our mind, the function of the ethical review process that takes place, which every study is subjected to. There somehow seems to be a view that re-use would bypass that ethical review and authorisation process, which is not our intention in any way at all.

Q245 Earl of Dundee: You express concern about the Directive's intention to include immature forms of vertebrates and certain live invertebrate animals. If such proposals should remain unamended what impact will they have on the research community?

Sir Leszek Borysiewicz: I think this is quite an important area and there are two distinct areas that we have to consider: one is larval and embryonic forms of animals, which are very important, for example, for studies of development and other conditions; and then there are the invertebrates themselves that are actually employed in experimentation. The argument seems to come down to two areas. One is whether this should be recorded. In practical terms, it can be extremely difficult for free-swimming larval forms in a variety of tests to estimate how many larval forms are exposed to particular conditions. So there is a practicality that is extremely difficult to pertain here. Secondly, the question of whether there is sentience within some of these lower forms of life is inherent as to why they should actually come under this particular Directive. The evidence base on which that is based is very limited indeed, and is, in fact, very difficult to prove one way or the other, in some of these animals. The problem is that many of these animals will also form the basis on which we can eventually look for substitutions of non-human primates and other species, so that if you begin to restrict their potential use and investigation in this area it does cause major problems for reasonable movement in the 3Rs direction. That is the main reason why I, in

particular, find that extremely difficult to engage with. These are the major areas that I would identify as to why this is not a practical proposition as enshrined in the Directive, and these issues have to be considered in far more detail than has actually been conveyed in this Directive.

Q246 Earl of Dundee: On scientific evidence relating to sentience, which you point out is very thin – there is not much to go on – would you forecast that that will – if there are no signs in the next five or ten years of such elements, following on from the nature of certain experiments that may be ongoing - improve or would it be very unlikely?

Sir Leszek Borysiewicz: If I had to make a guess, and it can be no more than that, I would think it is going to be extremely difficult in some of these forms to actually prove sentience. What is important is that we are aware of the evidence that comes forward and that you have a series of directives which are able to be flexible enough that it can be assumed and that changes can be brought in pretty rapidly if such evidence exists, rather than trying to take the other position which is to say: “Let’s consider all forms potentially sentient until you prove the negative. So, from my point of view, it is about remaining open to the possibility of sentience; if it is observed and if it is seen and the evidence becomes firm then you take action at that point, and bring it in. The Directive seeks to be a blanket cover with a whole series of assumptions for which the scientific evidence is very limited indeed.

Q247 Earl of Dundee: A moment ago you warned us that the record, so far, in the Commission may not be terribly good in paying attention to the European Parliament. Nevertheless, to protect your concerns in this case, which amendments would you like to see being introduced?

Sir Leszek Borysiewicz: I can provide you with the detail of that. I have not got the specific numbers but it is where the definitions are in terms of decapods, in particular, that this is seen,

because the evidence for sentience in that group of animals is extremely thin. There are some arguments one way or the other around cephalopods and there is some evidence of rudimentary sentience in some of these animals; so it is a matter, again, of not trying to provide a blanket definition and a blanket ban, if you like, on particular groups of invertebrate but being aware of evidence as it arises, and taking note of it when it is actually there and available.

Q248 Chairman: There is a list in Annex 1 of those that you mentioned. Would you remove this or would you amend it?

Sir Leszek Borysiewicz: I would look towards amending it; I would certainly look towards the removal of the decapods. I think the issue should be open; it should rather be provided as guidance to countries so that they can begin to take a view on, for example, cephalopods, since, as I say, there is a reasonable case that we may need to look quite carefully at some of the higher level cephalopods.

Q249 Chairman: Have you put these views to the Commission?

Sir Leszek Borysiewicz: We have put these views to the Commission; we have put them to the rapporteur and to the European Parliament as well.

Q250 Baroness Sharp of Guildford: Earlier on you have indicated that the proposals for the minimum standards of care and accommodation were going to cause difficulties. I wonder whether you could spell out for us some of those difficulties. Secondly, how far were you consulted about these standards? Again, we gather that they were agreed by the Council of Europe expert working groups that included representatives of industry, scientists, academia and animal welfare organisations. How far did you play a part in consultations

earlier and how far do you feel that your views were in any sense listened to when these standards came out?

Sir Mark Walport: The first thing to say is that a lot of this was based on a document called, I think, ETS123, and there were expert advisers who participated in that. I think that they all acknowledged, as part of the work, that the scientific basis for making these decisions was virtually absent. In light of that, their view was that these should be recommendations. Of course, what has happened is that they have been changed from recommendations into absolute standards. In some cases, it is absolutely clear that for some of the larger animals the cage sizes specified were actually much too small. In other cases, particularly in examples of cage sizes for rodents, the cage sizes would be larger than those used, at the moment; they would be weight-adjusted, really, on the basis of very little evidence in terms of animal welfare and, indeed, some evidence that suggests that, actually, rodents prefer to be at high-density in relatively small spaces in terms of free living rodents. The issue here is that the scientific expert group which produced the document said: “This is the best we can do but we believe it should be recommendation and not statute,” but this has been transposed into a set of rigid cage sizes, where, as I say, in some cases, welfare would be reduced and in other cases costs would be added with absolutely no welfare benefit whatsoever.

Q251 Baroness Sharp of Guildford: Picking up another issue which we have already touched on, do you endorse the assurances given by the ABPI’s representatives on 10 June that the UK-based researchers (whether commercial or academic) would require standards of care and accommodation to be maintained at UK levels, even if the work were conducted overseas? As, again, we touched on earlier, there is a lot of collaboration taking place now, and within those collaborations the experiments might take place ----

Sir Mark Walport: I can speak for my own organisation, which is a research funder, and it is one of our grant conditions that we would only award a grant if it was going to be conducted

at the standard which was considered to be acceptable by UK standards. Equally, industry is dependent on the results of their research being sufficiently good for drug development meeting the regulatory standards, and therefore it is in no one's interests, actually, to conduct work at low standards.

Sir Leszek Borysiewicz: We have entirely the same procedures within the Medical Research Council that they have to be at the standards that are required in the UK. We actually fund very little animal research overseas; we try to ensure that much of it is conducted within the UK. However, there is something else that we have to be really clear about here: that good animal welfare and paying attention to good animal welfare does give the best and most credible scientific results at the end of the day. Therefore, when you challenge most animal investigators, it is extremely important – cost is just one factor – that you conduct the experiments on the minimal number of animals, with the minimum amount of suffering that is required in the best possible conditions to ensure that the results that you get are as valid as possible. I think it is extremely important to remember that the debate that we are engaged in around the issue of the Animals Directive is not about, in any way, reducing the welfare standards not least because it is not in investigators' interests to reduce the welfare standards; it is around other aspects.

Q252 Baroness Sharp of Guildford: I have one further question, if I might, which is actually off this particular subject but which I am quite interested in. You mentioned the NC3R centre, which is a UK-based centre which, as I understand it, is funded by the Research Council.

Sir Leszek Borysiewicz: Through the Medical Research Council, yes.

Q253 Baroness Sharp of Guildford: Is there anything equivalent at a European level?

Sir Leszek Borysiewicz: There are some centres which are becoming involved at a European level in terms of the 3Rs. What I would say is that I believe this is an area where the United Kingdom is providing enormous leadership. This is an extremely important organisation; it funds a lot of research; it is helped by a large number of very eminent scientists who have served on panels of both the Wellcome Trust and elsewhere. What is more important is that its work is open and open to scrutiny so that they ensure that the research that is conducted in the 3Rs area is conducted, also, to the highest possible scientific standards, so that makes its application all the more important. The research boards within the Medical Research Council certainly use evidence coming from the NC3Rs when we consider any applications which utilise animals, as to whether it is, in fact, the best involved. In relation to higher animals, particularly non-human primates, as my colleague has already pointed out, we utilise and provide advice that it is, in fact, the best and only way in which this research could be conducted. So it is Britain's leadership here that is important, and all I can say is that I think they are doing a fantastic job. One of the important things about this Directive is that it does support the 3Rs, and if we broaden that activity around the European Union I would just say "Amen".

Baroness Sharp of Guildford: I was going to ask whether it provided something of a precedent that actually could be extended across the EU.

Q254 Chairman: Are you content with the proposals in the Directive or do you think they should go further?

Sir Leszek Borysiewicz: I am reasonably content with them. It is important for two reasons: firstly, it is about highlighting to the academic community that there is real research to be done in this area, and that research is vital in order to progress the goals of the 3Rs. In some areas of the Union (I am glad to say that is not part of the United Kingdom), that is still, if you like, a missionary activity – to actually say: "This work really matters because it then tells us

what is the best work to do with animals”. There is, however, an increasing tendency to propose national laboratories in this kind of activity. Now, I do not believe that that necessarily is the best way to go forward. One of the things that we have seen through the 3Rs programme in the United Kingdom is that what is important is to engage scientists who really understand the area that they are working in, so that they understand both the deficits of animal models in particular conditions and, also, could then be able to start looking at how best to replace them. So it is the scientists who work in a particular condition or in a particular field or a particular physiological system who are often best placed to advise and consider what are the best experiments to be done to consider replacement, rather than an arbitrary creation of a national physical centre which brings in experts who may not be expert in the specific field that you are trying to replace. I am not in favour of these sort of big, national laboratories in this area; I would like to try to promote the way in which this is conducted in the UK which, of course, you may say: “I would say that, wouldn’t I?” but I do think it is a particularly good example of where the UK has led.

Q255 Chairman: How does one translate that into not just an exhortation on a European-wide basis but a practical reality? Could that be achieved to a degree by having time limit targets?

Sir Leszek Borysiewicz: I think the best way that a lot of these issues can be dealt with in the Directive is, firstly, not to put rigid timelines on when the Directive is imposed. This Directive is an important one; it is recognised by the community as being important, but adequate time should be given for debate around many important issues that this raises, and not to set arbitrary timelines in the way that appears to be happening at the present time. There is a huge amount of debate, and I believe that one can convert many of the ideas that are coming from national bodies, national agencies, governments and other bodies into a real discussion, and then, if you like, to translate it into Euro-speak in a way which allows

guidance and recommendation rather than directed initiatives which, I think, could be counterproductive in many of the areas where the proposal is seeking to obtain real benefit.

Q256 Chairman: Surely, was that not a failing of the 1986 Directive – that it was written precisely in those terms?

Sir Mark Walport: My Lord Chairman, you cannot put timelines on discovery. Of course, we would all like to live in a world where it was possible to discover new drugs and cures for diseases without the use of animals, but the practicalities are that we cannot prescribe a timeline for the discoveries that are needed to make that happen.

Sir Leszek Borysiewicz: Nor in discoveries in 3Rs with which we will be able to replace some elements. If you take it at its extreme, the understanding of the human and mammalian brain, particularly neurosciences, where so much disease is affecting our communities, I would frankly have to say I would be very hard-pressed to see in any of those disorders any situation that will arise where we will be able, in my lifetime, to see a reduction in the use of non-human primates, which remain the only species that are capable, in some areas, of utilisation in this area. I wish it were not so, but, nonetheless, we have to be realistic as to where the priority has to reside, and that priority has to be tested application by application, not by directive and diktat from a centralised position.

Q257 Chairman: Could I go back to where we started? You mentioned that you chaired a group of state researchers on a European-wide basis. Is there an international grouping?

Sir Leszek Borysiewicz: We conduct and discuss this at meetings of the Heads of International Research Organisations - HROs. They tend to be rather more selected, in the European Union. Here we virtually have every single country, including countries outside the European Union (such as Turkey and Switzerland) that engage with this wider grouping. Internationally; HROs it is more of a mixed bag; it includes many countries of the former

Commonwealth, the United States and other countries like China and India who are engaged in these discussions. So, yes, these debates do happen at that level but there is not an international consensus building up in this area. We have raised this particular issue for discussion, and we have considered, within that organisation, this Animals Directive and how far it impacts on other countries, but, at the moment, I do not think there is any consensus emerging on the wider international stage.

Q258 Lord Cameron of Dillington: You have, basically, said that you approve of efforts to harmonise procedures and authorisation procedures across Europe, and so on. However, you have not really touched on the whole question of harmonising of enforcement and policing in different Member States. I was wondering whether you would like to comment on that area.

Sir Mark Walport: The issue is whether it is true harmonisation or whether there is the opportunity for gold-plating, because, of course, if different EU countries gold-plate in different ways then that destroys harmonisation. Equally, I believe there is the possibility that Member States can set their own penalties. So I think it all depends on what one means by “harmonisation”.

Q259 Lord Cameron of Dillington: I was thinking more of bringing the minimum up to the current average, rather than the other way round.

Sir Mark Walport: Of course we would support that, and I think that that is the strongest argument for there being a new Directive – that, actually, it is a long while since the Directive was first introduced and there does need to be greater harmonisation.

Q260 Lord Cameron of Dillington: Is it a problem with the different enforcement in different countries at the moment, would you say?

Sir Mark Walport: I think it is difficult to comment from a UK perspective. We operate within the UK system, largely, which does work very well.

Q261 Lord Cameron of Dillington: I was thinking from the European experience.

Sir Leszek Borysiewicz: From the European experience, I think it is a patchwork. In different countries there are different levels of inspection, regulation and enforcement. There is going to be a very real European issue here, under that awful word subsidiarity, as to at what point does a recommendation actually require the country itself to enshrine the requirements of a Directive within the legal structure of that country. I would argue that the United Kingdom, I think, has, by and large, reached a position where there is a good inspectorate service that looks after animal welfare well. In some European countries, I think, one would have to say that may not reach the standards that we have in the United Kingdom.

Q262 Lord Cameron of Dillington: Would you like to highlight a particular problem country?

Sir Leszek Borysiewicz: No, I would not, at this point.

Q263 Chairman: Could you explore the possibility of suggesting ways in which the policing could be improved to make sure that they do raise the standards without having to identify any individual countries?

Sir Leszek Borysiewicz: I think the answer is yes that can be done, but I think it is best done by consultation with those countries as to the areas they accept from such a Directive. It stresses the need for the Directive to be clearly and carefully thought through, such that it is acceptable to the widest possible community in Europe, and the best way, I believe, within Europe that you achieve that level of agreement is by getting that to the position of consensus, instead of what we have, at the moment, which is basically camps that are in very different

positions as a result of this Directive. If we can get to that position of consensus then I believe the implementation would follow downstream, because I cannot believe that any country that is a member of the European Union would want to be far away from the standards that are recommended within such a Directive as being appropriate in terms of its own internal structures. So I do think you have got to rely on those countries to uphold a Directive which is virtually universally seen as being of benefit in this area, which is why we support the need to revise the 1986 Directive.

Q264 Chairman: Some people could argue that can lead to the lowest common denominator, though, and, indeed, that this is being used as an opportunity by the industry in this country – to some extent supported by academia – that we should reduce standards to a degree.

Sir Leszek Borysiewicz: No, I would not accept that. I think, for the reasons that I have already said, particularly in the academic sector, which I can speak for best, it is extremely important that the value of the experiments that you conduct are conducted in the best possible circumstances and tested in those situations. There is very little advantage in the competitive world of science to be conducting experiments that are subsequently shown to be erroneous or wrong, which often could result. So scientists, by and large, will always move to very high quality standards, which we uphold and the Home Office upholds in the United Kingdom. Could I be certain that that is happening in 27 countries of the European Union? The answer is no, I cannot be, but I do believe the only way we are going to get that to happen within the jurisdiction of individual countries is to ensure that you have a Directive that is bought into by the widest possible community in Europe. Then you can begin to have the debate and discussion to ensure that appropriate levels of scrutiny are in those countries, and then you can hold out bad practice and put the searchlight on bad practice quite openly in relationship to such an agreed Directive.

Q265 Chairman: Do you not think that, in examining the appropriate levels of application, we should be ensuring that is in the Directive, in the first instance, once you have reached the consensus?

Sir Mark Walport: We clearly do not want the lowest common denominator. I do not think anyone would argue for that.

Q266 Chairman: It has been alleged that ----

Sir Mark Walport: I think we would say that is not what we are arguing for. I think what we are arguing for is the best regulation, and that should not be equated with the most regulation.

Sir Leszek Borysiewicz: We also have to be very careful as to how far a Directive of this sort should, for example, interfere with the internal governance of Malta or Cyprus or other countries. What we have to then do is examine what practice is put in place in those countries, and it is reasonable for the Commission to ask for guidance as to how far an agreed Directive has actually been implemented in those countries, but not to be directive in how a country actually polices it. Every major country in the European Union has its own structures in place. I believe the ones in the United Kingdom are very good and might serve as a model for other countries in the European Union.

Q267 Chairman: I think the suggestion is that it should be reviewed every five years. Do you think that is appropriate? I know you have unhappiness about timescales.

Sir Leszek Borysiewicz: I have unhappiness about timescales because I think some countries may take a lot longer to achieve the sorts of standards that we would want, from my own knowledge of the system.

Q268 Chairman: As we have seen from 1986.

Sir Leszek Borysiewicz: However, we also must remember that since 1986 we have had a large number of countries who have joined the European Union, and we do have to ensure that they are brought into the discussions that are currently taking place.

Sir Mark Walport: In ensuring that, we should be constantly alert, so it is not a question of saying there will be a review in five years because if something arises in one year which resulted in an improvement in animal welfare it should be implemented. I think it is a question of a constant awareness rather than, again, a rule-based system. There is a certain irony that we have been discussing the welfare, for example, of decapods, when, of course, the biggest harm to decapods comes from the millions of them that are consumed across the restaurants of Europe, where welfare standards do not really form part of the discussion at all.

Q269 Chairman: There are still a few contradictions around.

Sir Mark Walport: There are indeed.

Q270 Chairman: Gentlemen, you have been very helpful indeed. Are there any final comments or points you may wish to bring to us?

Sir Leszek Borysiewicz: From my perspective, my Lord Chairman, I think the most important issue to remember is that, by and large, we are all agreed – and the point I have made across the countries – that actually there is a need for a revised Directive. This one still falls well short of where we believe it should be; that we should give adequate time in order to have the debate and discussion around the very important issues that this Directive has, and I believe that that this process, eventually, will give the best opportunity for full implementation right across the European Union. So engaging in that discussion and engaging in that debate is extremely important. What I am more concerned about are the diktats that are enshrined in this Directive, as currently drafted, and the failure of the Commission to take on board the very real discussions that took place in the Agriculture Committee of the European Parliament

and others with a large number of amendments accepted through those committees and, indeed, some of the statements coming from the Commission, basically, just saying: “We will carry on as if that debate had never happened.”

Sir Mark Walport: The only thing I would like to add – because I think it has not really come up in much in the discussion – is that it seems curious that this is a Directive that has come from Environment DG rather than from DG Research. One thing that it would be helpful for you to enquire more into is to what the extent of the involvement of DG Research was in the formulation of this Directive.

Q271 Chairman: We are going to Brussels fairly soon, so we will raise precisely that question.

Sir Leszek Borysiewicz: Anecdote suggests that there was very little involvement of DG Research in any consideration of this, in the first instance.

Chairman: Nothing more from the Committee? Thank you very much indeed.