Government Response to the House of Lords Science and Technology Committee Inquiry into Regenerative Medicine

Presented to Parliament by the Secretary of State for Health by command of Her Majesty

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Introduction

This document sets out the Government's response to the House of Lords Science and Technology Committee report on Regenerative Medicine, chaired by Lord Krebs. Detailed responses to each of the 24 recommendations contained in the Committee's report can be found from page 4 onwards.

The Government remains committed to the field of regenerative medicine, which is recognised as one of the UK's Eight Great Technologies[1], given its huge opportunities for technological advance and the economic benefits we believe it can bring to the UK economy. As established by the *Taking Stock of Regenerative Medicine in the UK*[2] report, the UK retains a strong position in Europe and globally in the science and commercial translation of regenerative medicine. The quality of our work in research and academia is world class, supported by a strict but enabling legislative and regulatory framework that is helping innovation to flourish.

The Government is already demonstrating its commitment to the translation of innovative research, including regenerative medicine, through the following:

- The £180 million Biomedical Catalyst is an integrated translational funding programme jointly operated by the Medical Research Council (MRC) and the Technology Strategy Board (TSB) to support academics and UK SMEs to develop innovative solutions to healthcare challenges. Regenerative medicine is within the scope of the Biomedical Catalyst programme and a number of regenerative medicine projects have been awarded funding.

- The Department of Health's National Institute for Health Research (NIHR) funds infrastructure in the NHS for translational research in regenerative medicine, in particular through Biomedical Research Centres (BRCs) and Units (BRUs). These are established in leading NHS and university partnerships to drive progress on innovation and translational research in biomedicine into NHS practice. In 2011, the Government announced £800 million NIHR funding for five years from April 2012 for 11 BRCs and 20 BRUs. As part of this, the BRCs and BRUs are currently undertaking £9 million per annum of world-leading translational research in regenerative medicine across a range of disease areas.

[1] http://www.policyexchange.org.uk/images/publications/eight%20great%20technologies.pdf
[2] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32459/11-1056-taking-stock-of-regenerative-medicine.pdf

complementary research hubs have been established, which together provide a world-leading programme to promote the development of regenerative therapies.

- The Cell Therapy Catapult is a centre of translational excellence for regenerative medicine. Its vision is for the UK to be a global leader in the development, delivery and commercialisation of cell therapy, making it a location for business start-up and growth. The Catapult has already initiated several projects advancing the translational agenda including assisting industry or academic groups to develop key manufacturing processes, design and execute clinical trials and give regulatory advice. In addition the TSB supports Regenerative Medicine themed R&D competitions and in 2013 has already committed a further £8m to a competition in this area.

As a result of recommendations made by the Committee, we will include a central place on the UK Regenerative Medicine Platform which provides information on these funding schemes.

The Government is pleased that the Committee recognised the potential resource that the UK has in the National Health Service (NHS), providing access to patients in one system. For new innovative therapies, such as regenerative medicines, we are implementing recommendations from the *Innovation Health and Wealth*[3] report to spread innovation quickly and at a scale throughout the NHS to improve outcomes and quality for patients and the NHS. The establishment of 15 Academic Health Science Networks will provide a unique opportunity to align education, clinical research, informatics, innovation, training and education and health care delivery. They will improve patient and population health outcomes by translating research into practice, and developing and implementing integrated healthcare services.

We agree with the Committee that a clear pathway from development to delivery of regenerative medicines in the NHS will aid the growth of this sector, so that effective regenerative medicines become readily available and provide benefits to patients. This is why we are establishing a Regenerative Medicine Expert Group to develop an NHS regenerative medicine delivery readiness strategy and action plan. This group will draw on existing initiatives mentioned above and elsewhere in this response and will build on these so that the NHS is fully prepared to deliver these innovative treatments. The group will be supported by the Department of Health and members of the group will include NHS England, National Institute for Health and Care Excellence, regulators, industry, researchers, patient representatives, NHS Blood and Transplant, Scottish National Blood Transfusion Service and the Cell Therapy Catapult.

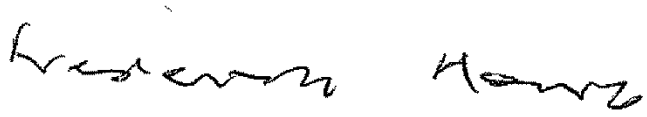
The Regenerative Medicine Expert Group will also include in its remit a role to monitor the effect of regulation on the development of regenerative medicines in the UK. Bringing together the regulators with those developing regenerative medicines from academia and industry through the membership of the group will allow any regulatory concerns to be

[3] http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_134597.pdf

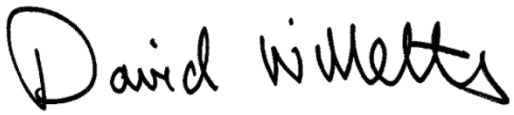
raised with the group and addressed. The UK has benefited from strong support for the development of regenerative medicines with a robust, but facilitating, regulatory system for stem cell research, recognised as leading the world on regulation of embryonic stem cells. The Government is committed to ensuring that the regulatory system remains proportionate and risk-based, whilst also operating within the context of EU level regulatory harmonisation of advanced therapy medicinal products.

The Government is also taking forward an "Adaptive Licensing" pilot programme, with the objective of accelerating the availability of new and innovative medicines using existing medicines licensing processes. As set out in the Prime Minister's 2011 *Strategy for UK Life Sciences*[4], the MHRA has brought together an expert group on innovation in the regulation of healthcare to agree a programme to drive the adaptive licensing agenda forward. This group has endorsed the UK progress on adaptive licensing and early access.

Regenerative medicine has the potential to play an increasingly vital role in delivering the next generation of healthcare, offering treatments or possible cures for areas of unmet medical need. The Government welcomes the Committee's report which makes a number of helpful recommendations aimed at translating regenerative medicines to improve the quality of peoples' lives and drive economic benefits for the UK. The Government hopes that this response is clear in establishing how we will achieve those aims.



Earl Howe, Parliamentary Under Secretary of State for Quality (Lords)



David Willetts, Minister of State for Universities and Science

[4] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32457/11-1429-strategy-for-uk-life-sciences.pdf

1. **We recommend that, as a matter of urgency, the HRA establish a regulatory advice service. This would build on the expertise of the Office for Life Science toolkit, the newly established MHRA Innovation Office and the experience of regulators. Researchers and companies require more than a web-based service. They should be assigned a single point of contact to support them in navigating the regulatory system, directing their queries to others where appropriate, but retaining ownership and oversight of the advice process. Such a service would be of short-term value to this (and the broad healthcare) sector until such a time as the regulatory environment is rationalised (paragraph 71).**

The Government recognises the need to provide regulatory support and guidance to assist those working in the area of regenerative medicine. The regulators with functions which extend to regenerative medicine carry out a range of ongoing initiatives to provide regulatory support. The regulators also collaborate in providing guidance, for example in developing the Department of Health and the MRC's UK Stem Cell Tool Kit[5], referenced in the Committee's report.

The Health Research Authority (HRA) provides guidance, advice and resources for applicants and the research community through its website, the Integrated Research Application System (IRAS), the National Research Ethics Service (NRES), the HRA's email queries line and online decision tools. The HRA is committed to developing, improving and building upon these existing tools and will work with research regulators and other organisations providing guidance and advice to improve consistency and reduce unnecessary duplication in information provided by regulators. This will include developing a single queries line, and redevelopment of the HRA website to provide a source of consolidated information on requirements for research, and make information easier to find. The HRA are also testing whether the early provision of advice to applicants improves rate and time to Research Ethics Committee (REC) approval. Health Research Wales has also recently been established to provide information and support with clinical research in Wales.

As mentioned by the Committee, the Medicines and Healthcare products Regulatory Agency (MHRA) opened an Innovation Office in March 2013 to foster and support innovation in the development and manufacture of medicines and the development of medical devices. The Innovation Office is in addition to the existing services the MHRA offers to support innovation through regulatory advice meetings, scientific advice, workshops and guidance. To date, while the number of enquiries received has been relatively low, some of them have been related to Advanced Therapy Medicinal Products (ATMPs). Enquiries have come from a wide range of organisations; the largest category was SMEs, followed by consultants, academics and pharmaceutical companies. The MHRA will be following up with those who have made enquiries to seek feedback about their experience and extent of satisfaction with the Innovation Office.

2. **The Health Research Authority (HRA) has made some positive first steps and it must now demonstrate its effectiveness by streamlining the macro regulatory environment. We recommend that the HRA commission an independent advisory**

[5] http://www.sc-toolkit.ac.uk/home.cfm

group, made up of national and international experts in regulation, to develop a designed-for-purpose regulatory system. The UK rightly has a good reputation for its robust regulatory system; it is vital that this reputation be maintained. Similarly, we acknowledge there is significant value in the expertise of some regulators. But patients, business and the taxpayer deserve a modern, designed-for-purpose, efficient regulatory system rather than one that has evolved in a haphazard, piecemeal way. An independent advisory group supporting the HRA will give it the necessary support to focus and clarify the functions of regulators. This group should give special consideration to reducing the overall number of regulators. We recommend that the group make proposals 18 months from its establishment. We will revisit this aspect of the inquiry to ensure that progress has been made. The HRA must simplify the regulatory route so that the development of regenerative medicine, and other innovative therapies, is not hindered (paragraph 73).

The Government's *Plan for Growth*[6], published in March 2011, recognised that health research regulation and governance had become increasingly complex and committed to setting up the HRA to streamline regulation and improve the cost effectiveness of clinical trials. The Government is committed to embedding the principles of proportionate, risk-based regulation across all regulated sectors. This includes cutting bureaucracy and unnecessary 'red tape' to deliver greater accountability and better focused, better targeted and more effective protections.

The Regenerative Medicine Expert Group that we will be establishing (see recommendation 10) will include in its remit a role to monitor the effect of regulation on the development of regenerative medicines in the UK. Bringing together the regulators with those developing regenerative medicines from academia and industry through the membership of the group will allow any regulatory concerns to be raised and addressed. This role for the group, as well as work already ongoing to streamline the regulation in this area and the recent reviews of the regulators, means that the Government does not believe there is a need for an additional advisory group on regulation.

We agree on the importance of streamlining the regulatory pathway as far as possible. The Government made a commitment to cut the number of health arm's-length bodies and to significantly reduce bureaucracy. The Government commissioned an independent review[7] of the work of the Human Fertilisation and Embryology Authority (HFEA) and the Human Tissue Authority (HTA) earlier this year. This included looking at the regulation of activities aimed at developing cell based therapies. The Government accepted the recommendation made in the McCracken report for the regulation of tissue for applications aimed at developing regenerative medicine products to be transferred from the HTA to the MHRA in order to simplify the regulatory pathway for those involved in such developments. The HTA and MHRA are working closely to implement this recommendation.

[6] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/31584/2011budget_growth.pdf

[7] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216947/Justin_McCracken_report_of_review_of_HFEA_and_HTA.pdf

The HRA is one of a number of bodies with responsibility for the regulation and governance of research in the UK and it is taking a leadership role in promoting consistent and proportionate standards for compliance and inspection. The HRA has a number of projects underway to improve the health research process in collaboration with NIHR, the MHRA and the National Institute for Social Care and Health Research (NISCHR). The HRA's Collaboration and Development Steering Group is overseeing a set of projects to improve the environment for research in the UK. The Committee heard about the HRA's study to test the feasibility of a streamlined HRA assessment for the approval of research in the NHS. This would combine and replace aspects of current reviews by NHS R&D and Research Ethics Committees (RECs). This Group found that both study-wide and local R&D assessments can be integrated into an HRA assessment, which itself includes Research Ethics Committee approvals, and would reduce the complexity of the approvals process for researchers and industry significantly. The Department of Health has asked the HRA to develop a business case with costed options on implementing the integrated assessment.

3. We recommend that the NIHR establish a regenerative medicine stream of its clinical research network. Such a move would support researchers in addressing the specific needs of regenerative medicine clinical trial design, help overcome difficulties in identifying patients and ensure that doctors interested in such trials could be easily identified. The network could also facilitate dialogue with regulators on future regulatory needs and issues encountered with regulation. The regenerative medicine stream of the network should employ a hub and spoke model for allogeneic treatments, whereby it has one or two co-ordinating centres and regional operations. Given the need for clinical trials of a certain size, this network should span across the UK and build on existing developed infrastructures like NHS Research Scotland (paragraph 89).

The Government agrees with the Committee's support for conducting clinical trials in the NHS and the benefits this provides to the NHS. The Government is also pleased to see that the majority of respondents to the Committee were in support of the work of the NIHR.

There will be further development of the NIHR Clinical Research Network (CRN) that allows high quality clinical research to take place in the NHS. During the 2013/14 financial year, the NIHR CRN is implementing changes to its organisational structure and with effect from 1 April 2014, there will be 15 local clinical research networks to cover the whole of England. These networks will be responsible for delivering clinical research studies in their patch, across the full breadth of specialties.

In relation to research delivery, the NIHR CRN will structure around divisions. At both national and local level there will be six research delivery divisions, each covering a set of related specialties. The six research delivery divisions are:

- Cancer;
- Diabetes, stroke, cardiovascular disease, metabolic and endocrine disorders, renal;
- Children, genetics, haematology, paediatrics, reproductive health and childbirth;
- Dementias and neurodegenerative diseases, mental health and neurology;

- Primary Care, age and ageing, dentistry, HSR, public health, musculoskeletal, dermatology;
- Anaesthesia/peri-operative medicine and pain management, critical care, injuries/emergencies, surgery, ENT, infectious diseases/microbiology, ophthalmology, respiratory, gastroenterology, hepatology.

Studies in regenerative medicine will be supported within the relevant specialties above.

The NIHR CRN will continue to be part of the UK Clinical Research Network, which comprises the research networks funded by the UK Health Departments.

The NIHR also funds infrastructure within our world- class NHS and university partnerships to support experimental medicine and translate lab-based discoveries into new cutting edge treatments, technologies and diagnostics and other interventions in clinical settings, e.g. the NIHR Biomedical Research Centres, mentioned elsewhere in the Committee's report. The NIHR Office for Clinical Research Infrastructure (NOCRI) helps public, charity and industry-funded researchers to work in partnership with this infrastructure by supporting them to navigate the clinical research environment and find expert researcher collaborators, with the expertise, technologies and patient cohorts to meet their research needs. NOCRI also plays an important role in facilitating NIHR-supported Centres, Units, Facilities and Networks to work together to help drive the flow of innovative research for patient benefit. Case studies produced by NOCRI include examples of collaboration in regenerative medicine[8].

As highlighted in the Committee's report, the NIHR Research Design Service (RDS) supports researchers to develop and design high quality research proposals for submission to NIHR and other national, peer-reviewed funding competitions for applied health or social care research. The RDS provides expert advice to researchers on all aspects of preparing grant applications including clinical trial design and governance.

NISCHR supports the development of high quality health and social care research and clinical trial design across Wales by funding Registered Research Groups (RRGs) Infrastructure Support Groups (ISGs) and Trial Units. RRGs provide the research infrastructure in priority themed areas by bringing together researchers to develop a portfolio of high quality research projects. Regenerative Medicine research is supported within the relevant RRGs.

4. We recommend increased dialogue between regulators and researchers in the form of regular regenerative medicine workshops, and that the MHRA produce a series of guidance notes (to be updated bi-annually) setting out clinical trial endpoint requirements for regenerative medicine, in consultation with the industry and academic researchers. UK regulators should learn from the example of FDA-CIRM workshops and similar efforts in other countries (paragraph 91).

The regulators in this area work closely together and they will continue to engage with those involved in the development of ATMPs, including researchers and the Cell Therapy

[8] http://www.nocri.nihr.ac.uk/resources/case-studies/

Catapult, to help clarify the regulatory requirements that apply. The HRA recently held a regenerative medicine event hosted by the Cell Therapy Catapult to look at changes and discuss issues with the sector, regulators and representative bodies. The MHRA is currently organising a further cell therapy seminar to follow up one previously run in May 2010 and is aimed at academic investigators and SMEs.

The Committee will be aware that the legislative framework for conducting clinical trials of medicines, including ATMPs, is set at EU level. In view of this and in the interests of achieving consistency in guidance at EU level, the Government considers that it would be preferable to raise the specific recommendation about developing clinical trial endpoints with the European Medicines Agency (EMA) in the first instance. The MHRA will do this via the EMA's Committee for Advanced Therapies (CAT).

5. We recommend that the phase II disease teams of the TSB regenerative medicine platform, and other regenerative medicine funding programmes, specifically require researchers to involve manufacturing and scale-up experts in their development process to ensure that translational work is scalable and therefore deliverable to a large number of patients (where the disease area requires this) (paragraph 98).

The Government agrees with the Committee that the scaling up of regenerative medicine treatments is an important element for the successful delivery of these therapies to patients. This is why the role of manufacturing and scale-up of regenerative medicines is included within the UK Regenerative Medicine Platform. This was established by the BBSRC, EPSRC and MRC to address the technical and scientific challenges associated with translating promising scientific discoveries towards clinical impact.

The TSB and Research Councils will respond further to this recommendation.

6. Recognising the importance of capacity to deliver therapies at scale, both for trials and wider patients populations, and the fast-moving pace of the manufacturing and scale-up field, we recommend that the TSB and EPSRC undertake an annual stock-take of regenerative medicine manufacturing capacity and make recommendations to BIS about future needs, with the first survey informing the Government's review of infrastructure investment. The Cell Therapy Catapult has begun work on such a survey so we recommend that this work is taken as a starting point. BIS must then act to ensure that appropriate infrastructure investment is made to support the field. At the very least, investment should be made in facilities to support the scale-up of treatments in mid to late stage clinical development. Money for this, and other recommendations, should be found by the re-prioritisation of budgets and innovative funding methods (paragraph 100).

The TSB and Research Councils will respond to the recommendation for an annual stock-take of regenerative medicine manufacturing capacity.

The Cell Therapy Catapult have presented the results of their current survey to BIS who will consider the evidence and its implications through a partnership project being run with the pharmaceutical industry on medicines manufacturing. Project findings will be presented to

the Ministerial Industry Strategy Group[9] at their November 2013 meeting and recommendations will then be considered by Ministers. The Cell Therapy Catapult has confirmed that it will continue to survey manufacturing capacity and capability in the UK along with forecasting demand based upon the pipeline of clinical trials activity and in market supply requirements.

7. UK capacity to manufacture at scale could be attractive to companies considering investing in or expanding operations to this country. We recommend that the UKTI Life Science Investment Organisation use the results of this survey to advise foreign companies on UK capacity to manufacture regenerative products (paragraph 101).

UKTI, through its Life Science Investment Organisation (LSIO), will work with the UK academic, business and clinical community to produce a set of externally facing marketing materials that articulates the UK regenerative medicine offer. This will include the funding environment, government support, basic science, clinical development, manufacturing, regulatory and product launch. The UKTI LSIO will promote this material through targeted business development activity using internationally recognised conferences to engage targeted regenerative medicine companies.

8. We recommend that the NHS develop a training programme for technical staff to support the development of cell therapies and other regenerative therapies at scale (paragraph 103).

The Government is committed to ensuring that the NHS workforce has access to high quality education and training and that is why we have established Health Education England to be the national leadership body for education, training and development of the health workforce.

Health Education England have advised that they will work with the medical Royal Colleges to ensure cell therapies and other regenerative therapies are included in the relevant training curricula, through discussion with Colleges and the General Medical Council about addition to the curriculum during the next round of revision.

9. We recommend that the MHRA canvas views from industry on the suitability of current GMP requirements and, if there is significant discontent, take these problems to the European Commission to seek agreement on overcoming them through amendments to the GMP Directive and associated guidance (paragraph 105).

Within the European Economic Area (EEA) Good Manufacturing Practice (GMP) is harmonised at a community level and the responsibility for maintaining its currency rests with the GMP/GDP (Good Distribution Practice) Inspectors Working Group (IWG). This Group is hosted by the EMA and its members are representatives from across Europe and to ensure harmonisation includes observers from across the world. EU GMP is revised on an on-going basis in response to triggers raised by IWG members, the Commission and

[9] https://www.gov.uk/government/policy-advisory-groups/ministerial-industry-strategy-group

industry. Information on revisions are publicly available via IWG's work plan and on the Commission's website, with the revision process for each GMP element involving at least two public consultation phases.

There are three parts to EU GMP and Annexes providing more detailed guidance on specific topics. The specific annex for biological, biotechnology and ATMP products for human medicinal product is Annex 2, which was recently revised with the UK being the rapporteur for this work. The revised annex came into effect on 31 January 2013.

In light of the very recent revision of the specific GMP guidance on ATMPs, industry's involvement in the revision process and ongoing changes elsewhere in GMP it is not considered necessary to take further action on this recommendation at this time. We do agree with the need to keep regulatory requirements under review and the MHRA will continue to monitor the impact of GMP requirements in the UK, raising any issues with the IWG where appropriate.

10. We recommend that the Department of Health establish a regenerative medicine expert working group to develop an NHS regenerative medicine delivery readiness strategy and action plan by December 2014. This group should report to the Secretary of State for Health directly and have the support of a high-profile, independent chair. The group must also contain NHS England officials, NHSBTS and devolved blood and transfusion services, regulators, researchers and industry representatives. We consider the role of the chair further in Chapter 5 (paragraph 110).

The Government agrees with the Committee that different types of regenerative medicine treatments will require different delivery models. Some of which, such as bone marrow transplantation procedures, already have a well-established delivery route in the NHS.

To bring together those working in this area of delivering regenerative medicine treatments to patients in the NHS, the Government will establish a Regenerative Medicine Expert Group to deliver an NHS regenerative medicine delivery readiness strategy and action plan, as recommended by the Committee.

The Expert Group will be supported by the Department of Health and will include those involved in the commissioning and assessment of products such as NHS England and the National Institute for Health and Care Excellence (NICE), researchers and companies developing regenerative medicines, the regulators and patient representatives. Organisations such as NHS Blood and Transplant (NHSBT) and the Scottish National Blood Transfusion Service (SNBTS) will also be important members of the group as they already deliver regenerative medicines and have a key role in establishing delivery routes for future treatments. The Cell Therapy Catapult will also be a key member of the Expert Group and has already started to build networks to provide the linkage, communication and coordination to make the UK the preferred location for cell therapy development.

As shown through the implementation of the recommendations from the *Innovation Health and Wealth*[10] report, the Government is committed to spreading innovation quickly and at scale throughout the NHS to improve outcomes and quality for patients and the NHS. NHS England directly commissions specialised services which allows consistent national clinical policies to be developed and implemented. The direct commissioning approach includes a process of Commissioning through Evaluation (CtE) and the piloting of an innovation fund. These approaches enable newer treatments to be delivered by a limited number of centres whilst expertise is developed and the clinical benefits to be evaluated in a controlled way.

CtE has been developed by NHS England as an innovative approach to the commissioning of prescribed specialised services for which there is currently insufficient evidence of relative clinical and/or cost effectiveness to warrant routine commissioning, but nonetheless have been identified by clinicians and patient representatives as having significant 'promise' as a potential treatment option. CtE is particularly pertinent to specialised and other lower volume procedures or services, where randomised controlled trial evidence is less prevalent, and where an alternative approach to evaluation therefore needs to be available to support commissioning policy decisions. NICE is supporting the design and evaluation of each CtE programme.

11. The Cell Therapy Catapult was only set up in May 2012 and we recognise that there is significant potential in the venture. However, we are concerned that it is seeking to achieve too much, too quickly, given the level of funding. We recommend that the TSB and Cell Therapy Catapult prioritise its activities to enable the Cell Therapy Catapult to focus on taking high growth potential projects through clinical trial to be phase III trial ready and developing links with the regenerative medicine community (paragraph 124).

The Cell Therapy Catapult has already initiated several projects advancing the translational agenda for regenerative medicine. The area of focus highlighted by the Committee is included as a key activity on the Cell Therapy Catapult business plan which was recently approved by the TSB Board.

The TSB and the Cell Therapy Catapult will respond further to this recommendation.

12. Furthermore, given the large number of potential funders, the TSB, research councils and NIHR should produce an online funding guide, regularly updated, to help researchers and SMEs know where they should apply at each stage of research and development in regenerative medicine (paragraph 125).

The Government agrees that a central place for information on the funding schemes available for research and development of regenerative medicines would benefit the sector. This will be included on the UK Regenerative Medicine Platform.

The Research Councils and TSB will respond further to this recommendation.

[10] http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_134597.pdf

13. There is insufficient TRL 6-8 funding available to support this fast-developing field. It would be unrealistic to depend exclusively upon additional funding coming from venture capitalist or "big pharma" investment. A mechanism must be found to fill this gap. Therefore, we recommend that the ESRC and the TSB commission an evaluation of innovative funding models, which spread risk and most likely will contain a degree of government matched funding or be underpinned by government guarantees, and recommend how additional funding could be provided for late stage clinical development in this field. The Government have said that this field has enormous potential and that they will support it. They must "put their money where their mouth is"; BIS and Her Majesty's Treasury must adopt the policy recommendation of the ESRC and TSB study (paragraph 127).

The TSB and Research Councils will respond to the recommendation to evaluate innovative funding models for late stage clinical development in Regenerative Medicine.

The Government is confident that regenerative medicine has enormous potential which is why we invest in the research base through the Research Councils and support commercialisation through the TSB. We cannot commit to adopting policy recommendations on regenerative medicine that might emerge from an Economic and Social Research Council (ESRC) and TSB study (if indeed they choose to fund such a study) although we will consider any recommendations of such a study.

14. There is significant commercial potential in the enabling tools and technologies, and commercial know-how associated with regenerative medicine—the regenerative medicine community must ensure that investors are aware of this potential. UK Trade and Investment has a specific programme to attract inward investment in regenerative medicine and so we recommend that they support the field by informing investors about the economic potential of investment in the field (paragraph 133).

UKTI, through its Life Science Investment Organisation, will share and train Embassy staff in the use of the marketing materials created. This has already been successfully rolled out with other sub-sector propositions such as stratified medicine. Through this engagement the UKTI LSIO will target specific overseas companies that are already investing in regenerative medicine.

The HRA has recently met UKTI and has committed to supporting their work by demonstrating improvements to the UK environment for research, including regenerative medicine.

15. Concern over the cost of patenting, the sufficiency of support available for innovators and questions about the ability of universities to recognise the potential in regenerative medicine patents lead us to conclude that the TSB should set-up a time-limited support fund for regenerative medicine patents. This fund should be open to university researchers who wish to pursue patents beyond the first stage, so that potential income from regenerative medicine products is not lost. Such a fund would help foster this fledgling industry and be a helpful tool until university patent

offices are better placed to deal with the potential value of these products (paragraph 137).

The TSB currently offers funding that can include the cost of patenting. Projects awarded funding through their collaborative R&D competitions can claim for costs associated with new patents generated within the project.

The TSB will respond further to this recommendation.

16. We consider the NICE model for evaluating innovative treatments and cures to be inappropriate. It must devise suitable models that give appropriate consideration to the long-term savings sometimes offered by high up-front cost treatments (paragraph 142).

17. NICE must ensure that its evaluation process recognises the higher initial costs of innovative treatments, without compromising its goal of assessing value-for-money in healthcare. Part of its value-for-money consideration should be that early investment in this field could unlock other treatments with significant economic impact, both in terms of savings to the health system and increased potential work productivity (paragraph 143).

NICE, in consultation with stakeholders, keeps its methodologies under review to ensure that they remain fit for purpose. We expect NICE will continue to do this and this will therefore allow it to take into account recommendations made by the Committee.

The recommendation discusses the evaluation process when there are higher initial costs. NICE's evaluation methods can, and do, assess drugs and treatments with high upfront costs, and they fully reflect all health gains to patients – including lifelong health impacts of curative treatments. A recent example is NICE's recommendation of the bone cancer drug mifamurtide (Mepact)[11] which is relatively costly but which can be curative for some patients.

Another example is NICE's recommendation of Peginterferon[12] for hepatitis C in adults. The treatment costs more than the equivalent of two years of conventional treatment. In its evaluation, NICE recognised the drug's long term cost effectiveness because it prevents liver damage far in the future and the attendant consequences of that damage (cirrhosis, liver transplant, hepatocellular carcinoma).

When considering whether a treatment represents good value for money, NICE considers whether the benefits the treatment provides are enough to justify the losses to patients elsewhere in the NHS that are inevitable when funds are re-allocated from some other use. The "affordability" of a given treatment will therefore depend on the magnitude of the gains

[11] http://www.nice.org.uk/nicemedia/live/13593/56821/56821.pdf
[12] http://publications.nice.org.uk/peginterferon-alfa-and-ribavirin-for-the-treatment-of-chronic-hepatitis-c-ta200

it provides to patients, when compared to the costs it imposes on the NHS – and the magnitude of the losses to patients elsewhere.

A treatment which represents a cure for a condition that substantially shortens life would provide very large health benefits. Importantly, even though such a treatment may be "one-off", it is attributed the full amount of benefits expected over the patient's entire life time. Whether the benefits are achieved through a single intervention or continuous therapy is immaterial. It is therefore not correct to assert that the price at which such a treatment could be recommended would be limited at any particular level, as it would depend entirely on the duration of its impact.

For example, if a one-off treatment were to extend a patient's life by 2 years, it would be attributed the same benefits as 2 years of chronic therapy which had the same result, and would be recommended at the same level of cost to the NHS. However if a one-off treatment were to extend life by longer, for instance by 40 years, it would be attributed all the benefits accruing to 40 years of chronic therapy and could expect to be recommended at a commensurately higher cost to the NHS.

The Committee's report makes reference to value-based pricing for new branded medicines. The intention is that, under value-based pricing, the prices of innovative medicines will be more closely linked to the value of the health gain their innovation provides. Following consultation on Government proposals for assessing the values of medicines, the Department of Health explored in detail whether there should be a weighting for Therapeutic Innovation and Improvement, but found this was not supported by the evidence. The Department of Health believes that innovation in pharmaceuticals is important, and should be valued, inasmuch as it ultimately leads to improvements in treatments and benefits for patients and society. NICE is currently developing the new value assessment system for products covered by value-based pricing, and it is important to note that this assessment will be capable of reflecting the full value to society of the treatment's benefits – including the greater value society places on treating severely ill patients with high "burden of illness", and the "wider societal benefits" gained from treatments which, for example, allow patients to return to work or reduce the burden on carers.

18. We recommend that the Department of Health commit to an evaluation of value-based pricing after the first year of operation. We have no doubt that other Parliamentary committees, such as the House of Commons Health Committee, will keep a watching brief on this area—this is vital as appropriate reimbursement is of great importance to the health of both this emerging industry and the established pharmaceutical industry (paragraph 146).

The value-based pricing system will need time to embed and we think that carrying out an evaluation after just one year of operation would be too soon to meaningfully assess the new arrangements. Moreover, it is doubtful that a regenerative medicine would have been assessed under value-based pricing within this timescale. However, as with all new systems, we will be keeping a watching brief on developments, and will evaluate it at an appropriate time.

19. NICE must ensure that it gives guidance to companies developing novel treatments on how to demonstrate comparability. One mechanism for this may be the seminars, developed as part of the life science strategy, which aim to show innovators how to demonstrate value. NICE's processes must allow for difficulties in demonstrating comparability for innovative treatments (paragraph 148).

NICE already provides a scientific advisory service, 'NICE Scientific Advice'. This is a fee-for-service consultation to pharmaceutical companies. By reviewing companies' early product development plans, NICE can advise companies in order to ensure that they produce relevant evidence for future submissions to NICE. NICE has also begun to offer scientific advice seminars for developers of medical technologies. Initial feedback suggests that developers of regenerative medicine technologies are not yet at the stage where they are seeking this kind of advice, due to the relatively early stages of development of these technologies. Nonetheless, the Committee's report recommendation of seminars is one that we welcome and one that NICE will be taking forward in collaboration with other organisations who offer similar types of advice.

20. The UK Government must ensure that its pricing and reimbursement systems are fit for purpose otherwise companies will base themselves in other countries (paragraph 150).

The Government agrees that the pricing and reimbursement system for branded medicines needs to address a number of important objectives. In particular, it should focus on delivering the best possible outcomes for NHS patients, taking value and affordability into account.

There is no evidence to demonstrate a strong link between domestic pricing and reimbursement systems and companies' decisions on where to locate investments or conduct research. As highlighted in the 2007 NERA study *Key Factors in Attracting Internationally Mobile Investments by the Research-Based Pharmaceutical Industry*[13], pharmaceuticals are a global market, and companies locate where they can find the best science base at reasonable cost, taking into account other factors such as tax, flexible labour markets and economic stability. In recognition of this the Government has taken steps to strengthen the UK as an environment for life sciences. As set out in our *Plan for Growth*[14] and our *Strategy for UK Life Sciences*[15], the Government is committed to ensuring that the UK encourages investment and innovation by the life sciences sector, and creates an environment where the NHS is a world leader in clinical trials.

21. The UK Government must take action to protect its citizens from rogue therapies at home and abroad. The primary tool to combat this is information. Patients must have access to information about the safety and efficacy of these types of

[13] http://www.nera.com/extImage/PUB_MobileInvestments_Sep2007.pdf
[14] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/31584/2011budget_growth.pdf
[15] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/32457/11-1429-strategy-for-uk-life-sciences.pdf

treatments. The Government recommend that patients always consult their physicians about the possibility of travelling for treatment—this is, of course, correct. Furthermore, the NIHR has produced guidance for patients considering travelling abroad for treatment. We recommend that the Foreign and Commonwealth Office (FCO) partner with the Department of Health to develop a website, in the same model as FCO travel advice for countries, which, in the first instance, contains summary assessments of the strength of safety measures in place for innovative therapies abroad. In time, they might develop this further, in partnership with organisations such as the International Society for Stem Cell Research (who have begun work in this area), to identify unproven therapies and those who provide them (paragraph 152).

We have taken careful note of the concerns raised by the Committee on regenerative medicine tourism and the risk this has of causing serious harm to patients and the industry. The Government welcomes the support the Committee has expressed for patients discussing the possibility of travelling for treatment with their physicians and agrees that the availability of information for patients is important.

The Department of Health has already set up a website, through NHS Choices[16], which is the UK's biggest health website and provides a comprehensive health information service to the public. NHS Choices provides advice and guidance for patients who are considering treatment abroad through their travelling abroad webpages, which links to the Foreign and Commonwealth Office travel advice for countries. Specifically on stem cell treatments, NHS Choices have also published *'Hope and hype – An analysis of stem cells in the media'* [17] which includes information on what to consider when assessing stem cell treatments.

We will review and update the information contained on the NHS Choices website to ensure that the content is still applicable to those considering stem cell treatments abroad.

The Government also supports the work of the International Society for Stem Cell Research (ISSCR) in providing advice to patients through their 'Closer Look at Stem Cells Treatments' website, so that patients can evaluate claims of potential stem cell treatment. We will link to the information provided by the ISSCR, through the NHS Choices website, and to the workshop on unproven stem cell treatments being held by the ISSCR and the Institute of Medicine and National Research Council of the National Academies later this year.

22. The current EU ATMP Regulation is unclear. Terminology used such as "preparation on a non-routine basis" leaves too much room for interpretation. There is also uncertainty about whether a hospital exemption is still permissible when a fully validated, centrally approved Advanced Therapy Medicinal Product (ATMP) is available. We recommend that the UK Government, during the review of the ATMP Regulations, make the case at the European Commission level for clarity on these two points in the revised Regulations (paragraph 155).

[16] http://www.nhs.uk/Pages/HomePage.aspx
[17] http://www.nhs.uk/news/2011/11November/Documents/hope_and_hype_1.0.pdf

The Committee has raised concerns that the hospital exemption provision under the ATMP Regulation is unclear and that there is inconsistency in interpretation in different Member States. The hospital exemption was included in the Regulation in recognition of the small scale activity that is carried out in this area in hospitals and reflects the different national arrangements that exist in Member States. Member States are responsible for operating their national schemes under the exemption. The hospital exemption provides an exemption from the usual marketing authorisation requirements but it is tightly drawn. It is also possible to supply ATMPs as unlicensed medicines where the product is supplied under the derogation that applies under the main medicines Directive (Article 5 (1) of Directive 2001/83/EC). Under this latter scheme, an unlicensed medicine may be supplied to meet the special needs of an individual patient under the direct responsibility of a clinician where an equivalent licensed product is not available. The MHRA has published guidance on the hospital exemption, 'preparation on a non-routine basis' and the Article 5 (1) schemes in the UK[18].

The European Commission consulted earlier this year on the operation of the Regulation. The point the Committee has raised about whether it is permissible to operate under the hospital exemption when a centrally authorised ATMP is available was raised by a number of respondents from industry to the Commission's consultation. The Commission will publish a report on the operation of the Regulation by the end of 2013. The Government will continue to monitor the impact of the UK's hospital exemption scheme, although to date only one authorisation has been applied for and granted to operate under the UK's scheme.

23. To realise the full potential of this global industry, and to ensure the UK is an attractive location for regenerative medicine companies to invest in and to undertake their clinical trials in, the UK Government must take the lead in promoting harmonisation of regulatory requirements (paragraph 156).

The Government agrees with the Committee that there is a need for greater harmonisation of regulatory standards and requirements across the world. While the legislative framework for ATMPs is set at European level, the UK plays an active role in drafting and developing EU legislation and the underpinning guidance documents that interpret the legislative requirements. The ATMP Regulation was the first step in regulatory harmonisation at EU level specifically aimed at these products and was an important step in opening up European markets. While the UK's aim is to be active in influencing issues at an international level, harmonisation issues are normally progressed most effectively when the UK is part of a wider initiative. Regular dialogue takes place between regulators at a global level. There is, for example, regular dialogue and exchange of information and views between the EMA's CAT and the US Food and Drug Administration via regular teleconferences.

Negotiations on a new EU Clinical Trials Regulation are currently taking place. This Regulation will replace the current Clinical Trials Directive and will lead to more harmonisation in the EU on the rules for the conduct of clinical trials and will make it easier

[18] http://www.mhra.gov.uk/Howweregulate/Advancedtherapymedicinalproducts/Aboutadvancedtherapymedicinalproducts/#l1

to conduct multi-state clinical trials. The Government expects the negotiations to be finalised in 2014 and we are committed to ensuring that the UK is an attractive location to undertake clinical trials. The HRA is supporting this agenda through its activities to improve the environment for research through the Collaboration and Development Group and the improvement to the GTAC service mentioned in response to recommendation 2.

24. We recommend that the Government also appoint the chair of the independent regenerative medicine delivery expert working group as the UK's regenerative medicine champion. This person would foster links between the many stakeholders (including, but not limited to, investors, basic scientists, clinicians, manufacturing experts, delivery networks, regulators), drive forward the regenerative medicine agenda and represent the UK's interests on the global stage. This champion should have a budget and support from a Government office (paragraph 160).

The Government will be establishing a Regenerative Medicine Expert Group to create an NHS regenerative medicine delivery readiness strategy and action plan. The membership of the Expert Group will provide coordination of the development of the regenerative medicine field in the UK, with a focus on ensuring the delivery of regenerative medicines into the NHS.

The Committee have mentioned the coordinating role that the Cell Therapy Catapult may provide and we are keen for this to be the case, with the Cell Therapy Catapult being key members of the Expert Group. An important part of the Cell Therapy Catapult five year business plan is to put itself at the centre of the industry and provide the linkage, communication and coordination that the industry needs to make the UK the preferred location for cell therapy development.

We will give careful consideration as to whether the Chair of the Regenerative Medicine Expert Group should also be appointed as the UK's Regenerative Medicine Champion. Until the group is established and a Chair appointed it would not be suitable to give them this role at this time.

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