Regulation of regenerative medicine in the UK

1. We all want to see research continue to thrive in the UK. To ensure this, as regulators we must facilitate high quality research, manufacture and clinical use. Effective regulation provides essential safeguards for ensuring quality and safety, and supports good practice and high quality science – which in turn leads to improved healthcare. There is no doubt that some of the regulation in this area is demanding, reflecting the nature of the technologies and their risks, but this should not mean that the regulatory demands are unnecessary, excessively complex or burdensome. A key role of regulators is to provide clarity and support to organisations working to the regulations.

2. We are fully supportive of close scrutiny of regulation to ensure that any unnecessary obstacles are removed. As regulators we should be vigilant to ensure that we are supporting innovation. Our track record of collaboration and working with the sector demonstrates how we are committed to this; we work in partnership to maximise clarity and minimise burdens on the sector.

3. This document sets out the roles of the regulators in regenerative medicine, how our legislation aligns, and how we work to reduce the regulatory burden on researchers through collaboration and other initiatives.

Our roles in regenerative medicine

4. We each have a clear remit and regulate distinct areas of the regenerative medicine process. However, there is adjoining legislation and we work closely together to provide effective advice and guidance to support establishments through these regulations. Each regulator has a core set of standards that apply depending on where you are in the process. We are focused on ensuring that the standards that are applied at one stage of the process do not act as a barrier at another. The role of each of the regulators in regenerative medicine is set out below:
a. Human Fertilisation and Embryology Authority (HFEA) – The HFEA regulates treatment in hospitals and clinics using eggs and sperm. It licenses 4 establishments in the regenerative medicine sector out of a total of 132 licensed Clinics. In the context of regenerative medicine, it regulates the use of human embryos or human admixed (human-animal) embryos to derive stem cells for use in the treatment of patients.

b. Health Research Authority (HRA) – The HRA protects and promotes the interests of patients and the public in health research, to ensure the UK is seen as a place to do high quality research. Specifically it has a remit to approve the ethical aspects of clinical trials involving stem cells and other regenerative medicines through the Gene Therapy Advisory Committee (GTAC). It also provides a system (IRAS) through which applications and approvals from GTAC and MHRA for clinical trials involving regenerative medicines can be made.

c. Human Tissue Authority (HTA) – The HTA works to ensure that human tissue and organs are used safely and ethically, with proper consent. It licenses 800 establishments, 15 of which are in the regenerative medicine sector. In the area of regenerative medicine, its remit relates to the use of human tissue or cells as starting materials for advanced therapy medicinal products (ATMPs). Under the European Union Tissues and Cells Directives, it licenses establishments that remove, test, process, store, and distribute tissues or cells that will (or may) be used to treat patients.

d. Medicines and Healthcare products Regulatory Agency (MHRA) – The MHRA’s mission is to protect and improve public health through the effective regulation of medicines and medical devices, underpinned by science and research. In the area of regenerative medicine, its remit includes responsibility for granting the appropriate authorisation ATMPs which are prepared and used under the hospital exemption, and for ATMPs made and supplied under the specials scheme under the relevant provisions in medicines legislation. In the area of clinical trials, MHRA’s remit includes assessment of applications for clinical trial authorisation and the associated manufacturer’s licence for investigational ATMPs. By way of comparison of scale, MHRA’s wider responsibilities include responsibility for inspection and supervision of 830 medicinal product manufacturing and import sites and 3500 medicines wholesale distribution sites. On 1 April 2013 the National
Institute for Biological Standards and Control (NIBSC), which houses the UK National Stem Cell bank, will officially become a new part of the MHRA.

**Simplified regulatory route from embryos to medicines**

5. Because of the stepwise process of developing regenerative medicines, only a small number of establishments (less than 12) will hold a licence from two regulators at any one time. When this does occur, each regulator is responsible for different aspects of the development of regenerative medicines, under different pieces of legislation.

6. For example, in the case of the derivation of stem cell lines from embryos, the HFEA will regulate the early stage of procurement. Once the embryo is dissociated, the HTA regulates the derivation process in preparation for banking for later manufacturing. MHRA will grant a licence at this stage for an Investigational Medicinal Product (IMP) which may be used in a clinical trial.

Diagram 1.
<table>
<thead>
<tr>
<th>Regulator</th>
<th>Licensed establishments in regenerative medicine</th>
<th>Approve clinical trials</th>
<th>Approve research projects involving stem cells</th>
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</thead>
<tbody>
<tr>
<td>HFEA</td>
<td>Yes – 4 in regenerative medicine out of a total of 132 licensed clinics [under Human Fertilisation and Embryology Act 1990 (as amended)]</td>
<td>No</td>
<td>Yes – only those involving human embryos or human admixed embryos. [under Human Fertilisation and Embryology Act 1990 (as amended)]</td>
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<tr>
<td>HRA</td>
<td>No</td>
<td>Yes – ethical review through the GTAC [under the UK Clinical Trials Regulations 2004]</td>
<td>Yes – ethical review through Research Ethics Committees (RECs) [under the UK Clinical Trials Regulations 2004]</td>
</tr>
<tr>
<td>HTA</td>
<td>Yes – 12 in regenerative medicine out of 260 establishments [regulated under the European Union Tissues and Cells Directives]</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>MHRA</td>
<td>Yes – approx 20 sites across three sectors (gene therapy, somatic cell therapy and tissue engineered products) of ATMPs. Not all of these sites hold HTA or HFEA authorisations.</td>
<td>Yes – responsible for authorising all clinical trials of IMPs [under the Clinical Trials Directive (2001/20/EC)]</td>
<td>Yes – authorising all clinical trials of IMPs including investigational ATMPs [under the Clinical Trials Directive (2001/20/EC)]</td>
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Key areas of collaborative working in regenerative medicine

Joint inspections

7. Over the last two years, collaborative regulatory work that aims to reduce the burden on establishments has expanded significantly. For example, the HTA and MHRA both license 12 establishments involved in the manufacture of ATMPs, and have been conducting joint inspections of these since 2010. In particular, establishments have appreciated the consistent and joined-up advice provided during joint HTA / MHRA inspections to ensure the pathway from one regulatory remit to another is seamless. In practice, this means that all of these establishments are offered a joint MHRA / HTA inspection, and four to five joint inspections take place every year. The HTA and HFEA both license four establishments involved in embryonic stem cell research and are committed to information sharing about licensed establishments.

UK stem cell took kit

8. The regulators in this area have worked closely together to provide clarity about regulatory requirements to guide establishments through the advice and guidance. For example, the UK Stem Cell Tool Kit has been jointly developed to provide clear guidance on the regulatory pathways that must be followed in developing a regenerative product derived from stem cells.

New arrangements for GTAC

9. In November 2012, the HRA as the Appointing Authority for the GTAC made a number of changes in the review of applications to GTAC. These changes, which clarified the respective roles for the MHRA and RECs, are already improving the service offered to researchers who wish to carry out clinical trials involving stem cells, ATMPs, and gene therapies. The approval times for ethical review have been significantly reduced, with all studies reviewed within the legal requirement of 90 days. The most recent study was approved in 38 days, surpassing the new HRA 60 day target, and approaching the average approval time for RECs in general. Options for meeting dates and locations have also improved for researchers.

Key work to reduce regulatory burden in regenerative medicine

MHRA Innovation Office

10. To help organisations developing innovative medicines, medical devices or using novel manufacturing processes to navigate the regulatory processes, the MHRA launched an Innovation Office in 2013. The
Innovation Office aims to promote early dialogue between organisations and the MHRA to support their understanding of the regulatory requirements. This is built on many years of engagement with such organisations where the MHRA typically have approximately 25 such (Regulatory Advice) meetings per year.

**IRAS**

11. The Integrated Research Application System (IRAS) hosted by the HRA on behalf of a number of bodies, streamlines the research application process and allows researchers to provide the information needed to gain approvals – from MHRA, RECs including GTAC, and others as required – for research projects, including multicentre clinical trials. For regenerative therapies, the approvals come from the MHRA and GTAC. The HRA is leading a fundamental review of IRAS to streamline the information requirements. In future IRAS will become an application and approvals system.

**HRA assessment pilot**

12. The HRA is currently conducting a feasibility study of the potential benefits of a streamlined HRA assessment for all research in the NHS which would combine and replace aspects of the current review by NHS Research and Development (R&D) and RECs. Scoping work suggests that it could potentially improve both study set-up times and the quality and consistency of review for all research projects, including multicentre trials of regenerative medicines.

**Summary**

13. The HFEA, HRA, HTA and MHRA are committed to working together to streamline regulation and reduce burden on establishments. Our aim is to provide effective advice and guidance to support establishments through the regulations.

14. Our collaboration is demonstrated by a number of initiatives – including joint working agreements and Memorandums of Understanding – that have a positive impact on reducing the burden of regulation. We are always looking for suggestions about how we can work together even more effectively, from those we regulate, and the research community more broadly.

15. Whilst we believe the regenerative medicine community is largely aware of all this information, this summary document might still be useful, and we
plan to share the document with them. Feedback on this document is welcome.

For further information contact Dr Shaun Griffin, HTA Director of Communications and Public Affairs, Tel 020 7269 1905, Mob 07917 551 609, Email Shaun.Griffin@hta.gov.uk