

# Regenerative medicine in the United Kingdom

Policy Briefing 2015

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## Overview

- This Policy Briefing is the first of a regular series of reports by the ESRC's REGenableMED project
- Policy initiatives and new resources for regenerative medicine are growing rapidly across the UK and elsewhere
- The field is marked by specific challenges which in combination require bespoke policy responses
- Different innovation paths for regenerative medicine characterise economic activity in the field
- Understanding the institutional context within which regenerative medicine is likely to be adopted is key to its future success

## Background

REGenableMed (2014-2017) is an ESRC-funded social science project examining the ways in which institutions and agencies are interacting and 'readying' themselves for regenerative medicine (RM)', focusing mainly on the UK. It identifies the various institutional, legal, social and political factors that enable and hinder the development of new RM/stem cell therapies. The aims of the project are to:

1. To provide an overview of the current RM landscape in the UK, and also in the EU and US.
2. To explore how actors navigate logistical, legal, regulatory and reimbursement challenges.
3. To identify the challenges associated with the upscaling, and the implementation and dissemination of RM products in clinical settings.
4. To identify and explore the roles various stakeholders play in enabling the development and potential adoption of RM.
5. Identify common business models and their relationship to regulatory, social and political factors.

6. To predict how RM is likely to evolve, and provide recommendations aimed at supporting responsible research and innovation within RM

## Current Key Developments

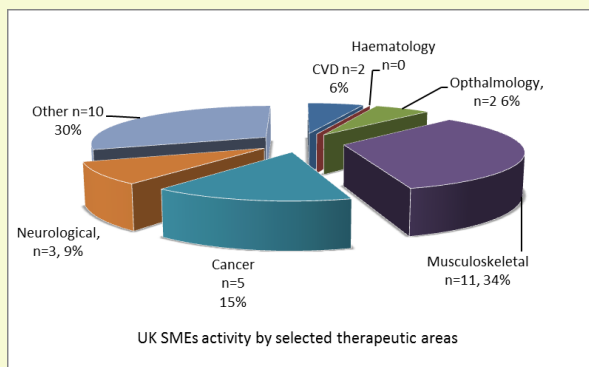
The policy context within which RM is located is fast-moving and includes a number of key developments. Innovation is being fostered via initiatives relating to cell manufacturing, notably the Cell Therapy Catalyst's new £55m centre for scale-up being established in Stevenage, as well as a growth in the number of GMP licensed centres for cell and gene therapy (n=18). In regard to regulation, the UK's Department of Health is now working to incorporate the new European Directives on importing and coding tissues and cells into UK law; and moves towards consideration of more flexible 'adaptive licensing' for RM products are underway within the European Medicines Agency (EMA), with a joint meeting to be planned between Member States authorities for tissues and cells and medicinal products (Advanced Therapy Medicinal Products [ATMP] in particular) in 2015.

The EMA has also recently published a revised Reflection paper on classification of ATMPs and the UK regulatory agency (the MHRA) is now aiming to future-proof the guidelines because of constant developments in the field. Another major development is the new European Bank for Induced Pluripotent Stem Cells (EBiSC). Its principal facility will be at the Babraham Research Campus (Cambridge, UK) and will undertake cell expansion, quality control and characterisation. The European Cell Culture Collection (ECACC) of Public Health England (Department of Health, UK) will coordinate cell line distribution.

Finally, the NICE Board has approved the establishment of the Office for Market Access which is to be operational from the Autumn of 2015. This development along with the outcomes of the ongoing Accelerated Access Review could support faster access to promising RM in the future.

In terms of economic activity, there are currently 37 UK-based SMEs active in the field, though not

all have products on the market. Some provide services to the field including cell expansion [bioreactors], assays, reagents, or techniques for cell differentiation; a smaller number offer actual therapies. Of the 51 clinical trials currently taking place in the UK, 11 are sponsored by UK companies (e.g. Reneuron, Cell Medica). A recent report by REGenableMED members to the ESRC and InnovateUK explores the different business models and funding landscape in the field.<sup>ii</sup>



[Notes:

1. UK SMEs currently active in selected therapeutic areas n=33. Some companies active in more than one area.
2. Figures exclude SMEs active in 'Services' category n=20 (n=15 plus n=5 also active in product development).
3. 'Other' includes all other therapeutic areas (e.g. wound products, autoimmune diseases etc.)]

Reflecting a worldwide trend, nearly all trials and projects are based upon progenitor cells, such as mesenchymal, haematopoietic, endothelial or neural stem cells. Progenitor stem cell-based therapies are emerging relatively quickly as clinicians and researchers have been able to draw upon existing infrastructure and expertise to translate research findings into products, especially those intended to treat various forms of immune disorders, such as Graft-versus-host disease, inflammatory bowel disease, rheumatoid arthritis and diabetes. There is also a major interest in immunotherapies and gene engineering approaches (in the UK, for example, Adaptimmune are developing an autologous engineered T-cells approach to cancer treatment; GSK have recently submitted a marketing application to the EMA for a gene therapy to treat patients with a rare disease (ADA-SCID).

Looking more widely, in the US the main centres of RM activity can be found in four states, California, Texas, Maryland and New York. An

analysis of Clinicaltrials.gov indicates that California has the highest number of clinical trials at 442, sponsored roughly 50/50 between industry and the public sector, with a third of these in the leukaemia area.

## Challenges

The main challenges identified by the project to date are summarised in the Box below.

Accessibility of tissues & cells
Lack of standardisation (protocols, safety criteria)
Uncertainty over translational pathway
Inflexible clinical trials framework
Scale-up and logistical difficulties
Inadequate health technology appraisal methods
Potentially reluctant clinical environment
Securing IP
Despite recent increase, risk of insufficient investment

A recently published paper<sup>iii</sup> from the REGenableMED project (Gardner et al, 2015), discusses the degree to which these challenges are specific to RM, compared with other emerging biomedical technologies. It found that RM shares many of these challenges with biomedical developments elsewhere but that there are three which, combined, feedback on each other and produce especial difficulties for RM. These are:

- the production, stabilisation and use of live cells and tissues,
- their complex and often uncertain regulatory definition,
- their manufacturing/scale-up.

## Responses

Some of the key policy-related responses to these challenges have focused in particular on strengthening the science base and on regulation. The government established the Regenerative Medicine Expert Group (RMEG) in 2014 following the House of Lords (2013) Report on the field. The RMEG established three subgroups to examine Delivery; Evaluation and Commissioning; and Regulation and Licensing. Members of the REGenableMED project are members of the second of these. One of its principal tasks has been to commission a review

of NICE methodology and whether any adjustments need to be made to it in appraising RM products. In regard to the science base and clinical links, the UKRM platform was underway in 2014 with various ‘hubs’ focused on a number of key challenges such as safety and efficacy, cell behaviour and the immune response.

## Clinical Adoption of RM

Extensive fieldwork completed in the first year of the REGenableMED project indicates that the adoption of RM therapies will require major, long-term infrastructural commitment and systems alongside responsive ad hoc clinical demand-dependent product supply. At present, adoption has been most rapid involving clinician-led surgical procedures whose development may require only minor adjustments to existing clinical practices, such as in limbal stem cell transplantation to restore corneal function. A key issue is how the administration of cell therapies aligns with *existing* clinical treatment pathways in specific therapeutic areas.

More generally, the emergence of complex advanced therapies and combination and borderline products (including medical devices and diagnostics), which do not have a clear regulatory and commercial route to clinic, highlights the need for progressively adaptive regulation that can evolve with emerging scientific knowledge and new technologies.

## Future REGenableMED Reports

This first Policy Briefing from the REGenableMED project has highlighted a number of issues currently being examined by the project team.<sup>iv</sup> There will be two summative Policy Briefings, in 2016, and 2017 paralleled by a series of shorter reviews on specific issues. Included within these will be findings related to the project as a whole. Among these will be results relating to:

- the provision of social science-informed metrics on how quickly adoption is occurring in particular contexts, and why this is so.
- how the project results can build scenarios that will be of value to the current NHS 5 Year Forward View, especially in regard to its interest in ‘combinatorial innovation’.
- how innovation pathways are being pursued by SMEs and how this might be influenced by moves towards new supply chain

systems, such as ‘re-distributed manufacturing’.

- how patient engagement and the role of patient groups are shaping the field.
- how UK regulatory and reimbursement systems for RM compare with those found in Europe, Japan and the US.
- how we need to understand not just technological readiness for RM, but what can be called “institutional readiness” and system readiness.

<sup>i</sup> Advanced Therapy Medicinal Products, including gene therapy medicinal products, somatic cell therapy medicinal products, combined products incorporating a medical device and tissue engineered products to restore or regenerate functionality

<sup>ii</sup> Omidvar, O., de Grijns, M., Castle, D., Mittra, J., Rosiello, A. and Tait, J. (2014) *Regenerative Medicine: Business Models, Venture Capital and the Funding Gap*. Report to ESRC and InnovateUK, 30<sup>th</sup> Oct, 2014.

<sup>iii</sup> Gardner, J. *et al* (2015) Are there specific translational challenges in regenerative medicine? Lessons from other fields. *Regenerative Medicine*, vol 10.

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