The Regenerative Medicine Expert Group

Minutes of the 1st Meeting

22 January 2014, The Bloomsbury Hotel

In attendance

Sir Michael Rawlins (Chair)
Mr Keith Thompson
Mr James Palmer
Professor Marc Turner
Professor Chris Mason
Mr Michael Hunt
Dr Louise Leong
Dr Ruth McKernan
Professor Fiona Watt
Professor David Williams
Professor Robin Ali
Professor Charles ffrench-Constant
Dr Ian Hudson
Dr Janet Wisely
Dr Alan Clamp
Ms Sharmila Nebhrajani
Dr Ahmed Syed
Dr Huw Williams (on behalf of Lynda Hamlyn)
Ms Anna Rajakumar (on behalf of Peter Thompson)
Dr Nick Crabb (on behalf of Carole Longson)

Apologies

Professor Carole Longson
Ms Lynda Hamlyn
Dr Nick Rijke
Air Marshal Paul Evans
Mr Steve Bates
Mr Peter Thompson
Dr Susan Kohlhaas

Government Department Observers

Dr David Griffiths-Johnson
Dr Mark Bale
Dr Dorian Kennedy
Dr Tom Barlow

Secretariat

Mr Emyr Harries
Ms Nula Clark

1. Welcome

1.1. The Chair welcomed members to the first meeting of the Regenerative Medicine Expert Group (RMEG).

1.2. Members introduced themselves, and the organisation they were representing.

2. House of Lords Science and Technology Committee Inquiry into Regenerative Medicine

2.1. Professor Fiona Watt gave a presentation summarising the House of Lords report and her perspectives of the report findings.

2.2. Professor Watt then summarised the recommendations of the report including the recommendation to set up an expert group.

2.3. The Chair raised a question as to whether gene therapy was considered to be a regenerative medicine, and whether this would be covered in the scope of the work of RMEG. Following a discussion it was agreed that many regenerative medicines may encompass gene therapy and therefore the broad scope of RMEG should

include gene therapy due to the overlapping science and technical regulatory, evaluation and commissioning issues.

3. Terms Of Reference and Membership

3.1. Mr Emyr Harries introduced the Terms of Reference, including the membership, what the work will deliver, who the group will report to and the ability to commission others on behalf of group to undertake work, that had been circulated to members prior to the meeting.

3.2. On the Terms of Reference and membership, a number of comments followed:

i. It was agreed that reimbursement was an important factor to consider to pull regenerative medicines into mainstream use in the NHS and support their commercialisation. The Chair agreed to make this amendment in the Terms of Reference.

ii. It was clarified that the group will report to all UK health Ministers as the report is UK wide and covers issues that are devolved matters, although it was recognised that the differences in the commissioning framework between the NHS in England and the other nations would need to be taken into account. Scotland is represented by the Scottish National Blood Transfusion Service (SNBTS), and the other devolved administrations had been invited to join RMEG.

iii. It was noted that the UK is in a good position to capitalise on regenerative medicine but that medicines need to be exportable. It was suggested that this needs to be considered in the solutions that RMEG should offer.

iv. It was noted that it was important to consider public awareness and patient and wider clinical engagement in the strategy as these would be key influences on the uptake of regenerative medicines in the NHS and it was agreed the Terms of Reference would be amended to reflect this.

3.3. On membership, it was noted by the secretariat that the Medical Research Council have agreed to attend future RMEG meetings with observer status and would represent the UK research councils.

3.4. A suggestion followed to increase the membership to include BUPA who already provide reimbursement for some regenerative medicines in the UK and also a suggestion of having membership from a large NHS trust, as there may need to be consideration of infrastructure changes that could be needed within the NHS to deliver regenerative medicine. The chair agreed that it may be useful to involve wider representation and this could be achieved through invitations to the planned subgroup meetings and workshops that would be discussed later in the agenda.

3.5. It was agreed that alternatives and deputies to attend the meetings would be accepted.

3.6. Members were advised by the secretariat that a web page for RMEG will be created on the Department of Health website that would hold details about the group including the terms of reference, membership and minutes of meetings.

3.7. Members were reminded to fill in their Declarations of Interest form and send these to Mr Emyr Harries.

4. RMEG remit and proposed work plan

4.1. The RMEG remit had been circulated to the members prior to the meeting and is based on the definition for Regenerative Medicine used in the House of Lords inquiry and definitions used in the Advanced Therapy Medicinal Products regulations. The members agreed the remit and reconfirmed that gene therapy would also be included in the group's remit following the earlier discussion.

4.2. The Chair introduced the proposed work plan. It was proposed that the work of RMEG would be taken forward through three subgroups 1) Delivery 2) Evaluation and Commissioning and 3) Regulation and Licensing.

4.3. On the proposed work plan a number of discussions followed, to summarise:

4.4. It was suggested that a route map setting out the process, steps and current barriers, including regulatory approval, reimbursement and logistics to taking a regenerative medicine from its development to delivery to a patient in the NHS would be very useful to develop.

4.5. Suggestions on the form of this piece of work included choosing specific products and mapping their routes to delivery i.e. autologous cells, gene therapy, embryonic/allogeneic cells (bulk production lines). The Cell Therapy Catapult noted that in their work on the manufacturing capacity for cell therapies in the UK, they identified seven core processes for regenerative medicines which they have mapped that could be useful in this process. Although the route map may differ between regenerative medicines depending on their nature, it was agreed that it should be possible to select three or four different therapies that could be reasonable exemplars of the wide range therapies.

4.6. It was agreed that members in consultation with their academic and industry contacts would identify potential exemplars and provide these ideas to the secretariat.

4.7. It was agreed that in order to cover the wide range of issues that need to be considered to fulfil RMEG's remit, the three subgroups should be established but it was important the work of the subgroups was joined up to ensure that issues did not fall through gaps and this cross- sub group piece of work could inform the work that these will carry forward and would be useful in reducing any gaps that could occur between the three subgroups.

4.8. Following a suggestion that the blood services might provide a central role in the supply/distribution of regenerative medicines in the NHS, it was agreed that Marc Turner (SNBTS) would provide a short paper outlining the services that the blood services in the UK cover.

4.9. On the evaluating and commissioning sub group a number of points were raised:

i. It was agreed that it would be good for NICE and/or NHS England to lead the group and that the respective RMEG members from these organisations should be asked to lead on the set up and work of this group.

ii. It was noted that changes to system of measuring cost effectiveness with the introduction of value based pricing (VBP) would have an effect on regenerative medicines and that it would be useful to look at examples of regenerative medicines and how they might be evaluated under VBP and how the costs would be reimbursed.

iii. The House of Lords inquiry highlighted concerns over the application of current evaluative processes for regenerative medicines. The Government response to the inquiry addressed these concerns, providing an explanation of the Evaluation process used by NICE. In addition, The Cell Therapy Catapult was working with NICE on the evaluation of cell therapies. Regenerative medicines may be very expensive, but if the health benefits could accrue over a lifetime they could be cost effective. Therefore, a short term reimbursement mechanism may be needed to cover high initial costs. Pricing could be lowered if there are opportunities for large scale-up.

4.10. It was agreed that the regulation sub-group will feed in to the evaluation and commissioning sub-group as the two are closely allied.

4.11. On the delivery sub-group the set up was generally agreed and it was noted that the delivery depends on the type of product (for example for autologous and allogeneic products), and therefore this is an important factor for this sub-group to consider.

4.12. On the regulation sub-group a number of discussion points followed:

i. A point was raised on current hospital infrastructures and how the characteristics of a centre of excellence in the area of regenerative medicine would look.

ii. There was a discussion on how the efficacy of treatments would be assessed and whether regulation could move from case-by-case valuation to a set of principles.

iii. The Cell Therapy Catapult identified where they have used real examples. It was agreed it would be useful for the group to use a similar approach and look at worked examples. The Cell Therapy Catapult agreed to lead on setting up and running this sub-group.

iv. It was agreed that in order to further develop the work of the three subgroups it would be useful to hold a workshop to consider in more detail the issues that regenerative medicines raise by inviting the developers of, say, four products to describe the pathway they are following and the steps they are following and the barriers. This would allow possible solutions and better pathways to be considered and development of the route map; it would be important to establish a set of principles that could be applied to aid the delivery and commercialisation of regenerative medicines.

5. UK Regenerative Medicine product/therapy development pipeline

5.1. Mr Keith Thompson presented on behalf of the Cell Therapy Catapult outlining the four strategic goals of the Catapult which are 1) increasing the UK pipeline of cell

therapies 2) Creating investible propositions 3) Increasing the attractiveness of the UK as a place to do this work and 4) build a £10bn industry.

5.2. Mr Thompson then outlined the industry barriers that need to be addressed which could be grouped in to three main areas: business models, manufacturing and supply chain and clinical and regulatory.

5.3. Mr Thompson defined the assets the Cell Therapy Catapult has, including their facilities and teams, and then outlined the project led approach that the Catapult takes.

5.4. Mr Thompson then went on to summarise findings of survey the Catapult has undertaken which showed that there is a diversity of therapies in the UK but few are company sponsored, with many academic projects being non-commercially focused.

5.5. Furthermore, many of these academic projects will not have regulatory experience. The Cell Therapy Catapult has been working with promising academia generated therapies and UK SME's to accelerate this pathway.

5.6. The Cell Therapy Catapult have also undertaken a cell therapy GMP capability study. This would be published soon.

5.7. A discussion followed Mr Thompson's presentation, in which the following points were raised:

i. A discussion over who the investors in regenerative medicine were to be followed. Dr Mark Bale and Professor Chris Mason highlighted their recent trip to Japan and the adoption model that that Japanese system follows and agreed to circulate a note from this.

ii. It was noted that the proportion of trials in academic environment vs. industry was skewed to academia currently and this was different to most other areas of medicine and was important for RMEG to consider.

6. Regulation of Regenerative Medicines in the UK

6.1. Dr Ian Hudson presented to the group on the subject of regulation of regenerative medicine in UK.

6.2. Dr Hudson outlined the regulatory responsibilities covering the Human Fertilisation and Embryology Act (HFEA), the Human Tissue Authority (HTA), MHRA and the HRA.

6.3. Dr Hudson went on to outline the background to development of the Advanced Therapy Medicinal Products (ATMPs) regulation, the scope of the regulation and the authorisation of ATMPs, which are authorised though Centralised Procedure under which a centralised European marketing authorisation (MA) is granted by the European Commission following assessment by the European Medicines Agency.

6.4. Dr Hudson then went on to discuss 'hospital exemptions' that exist for ATMPs that are prepared on a non-routine basis and used within the same member state with a medical prescription for an individual patient.

6.5. There have been 20 special licences issued for regenerative medicine products in the UK. A special licence is allowed if there are no equivalent licensed products that could be used either within the specification or 'off-label'.

6.6. Dr Hudson outlined the Adaptive Licencing scheme which is used to maximise the use of existing regulatory flexibility's and the Early Access scheme which is designed to enable earlier UK patient access to promising medicines before they are licenced, in areas of unmet medical need.

6.7. A number of discussion points followed Dr Hudson's presentations. To summarise, these were:

i. Whether special licenses could be taken through an early access scheme. However, it was pointed out that it would be difficult for special designated medicines to go through an Early Access scheme as there would be limited opportunity to collect data to the standard produced by clinical trials.

ii. It was questioned whether there could be flexibility in licensing processes to accommodate changes to manufacturing process that only led to small or no obvious changes to the final product. It was noted that it would be important to establish how changes in manufacturing process altered the safety, efficacy and quality of the final product. This might be achieved with small bridging clinical studies or evaluation through testing. It was agreed that further advice would need to be sought on this as there are concerns around how well you can characterise a product at the end.

iii. A discussion took place over the differences between UK and EU hospital exemptions implementation. It was noted that the UK is fairly permissive compared to other member states, and for this reason harmonisation across Europe may not be helpful.

7. Commissioning Through Evaluation

7.1. Mr James Palmer introduced the Commissioning through Evaluation which is a scheme recently developed by NHS England used to provide more evidence of clinical and cost effectiveness when this is limited (although not in the form of a randomised controlled trial).

7.2. 75 Clinical Reference Groups (CRGs) have been set up that include clinicians and patient/public representatives.

7.3. Across the CRGs 14 out of 75 have expressed specific interest in regenerative medicine.

7.4. Mr Palmer outlined that NHS England have a duty to focus on research and innovation and that the commissioning led evaluation is important for the work of regenerative medicine.

7.5. It was noted if will be important for commissioners to know of products that are early in the pipeline so that innovation platform tools can be used and CRGs can offer advice on products.

7.6. Mr Palmer noted a treatment which was funded by the Cancer Drug Fund and has now been brought in to routine commissioning. 6 projects are to follow this.

7.7. The overall goal of Commissioning through Evaluation is to reach a national commissioning policy. However, there is a large financial risk with increases in spend on routine services.

7.8. By pairing with NICE, NHS England will develop criteria for the evaluation and to identify which products can enter the scheme.

7.9. A number of discussion points followed Mr Palmer's presentation. To summarise, these were:

i. A discussion over limited funding available to support innovation in NHS England and the QALY threshold applied by NICE when making recommendations for use in the NHS. Mr Palmer advised that products are already being commissioned by NHS England that are valued beyond the NICE threshold e.g. Ivacaftor to treat Cystic Fibrosis. It was noted that it was difficult to ascribe value to regenerative medicines and whilst at the outset may be expensive, they address unmet needs and innovation may lead to future cost savings. In these respects, it was noted that Value Based Pricing might capture these other benefits better than the current system and could be more favourable to regenerative medicines.

ii. Two other issues raised were 1) the generally small patient groups for many regenerative medicines and thus small markets and 2) whether the UK is ready to deal with the likely high upfront costs of regenerative medicine. It was discussed that it is important to look at the longer term costs and benefits but that the funding and reimbursement model needs to be addressed. It was noted there is an opportunity and it may be more productive to look at costs and benefits from regenerative medicine as a whole sector, rather than focusing on individual patients or diseases as this approach was more likely to stimulate innovation that could bring costs down.

8. Next steps and close

8.1. It was agreed that the Secretariat would circulate the presentations from the meeting.

8.2. The next meeting of the Group will be on 30 April.

8.3. The Chair thanked all for attending and those that made presentations and closed the meeting.