

Innovative Medicines Initiative Consultation on Facilitating the translation of advanced therapies to patients in Europe.

This response has been prepared by the UK Medical Research Council (MRC) in conjunction with the Health Research Authority (HRA) and the Medicines and Healthcare products Regulatory Agency (MHRA). In addition, discussions have been had with the Association of British Pharmaceutical Industry (ABPI), Innovate UK (IUK) and the British Society for Cell and Gene Therapy (BSGCT) who will each be submitting their own response.

1. Background and view on the Consultation Document

The concept paper provides a very accurate and thorough review of the advanced therapies field. The report captures the main issues articulately. Much of what is covered in the paper has also been identified by other reviews or projects conducted in the UK in recent years (see section 5).

We agree that after many years in academic development the cell and advanced therapy field has started to yield some very encouraging clinical trial results, indicating that the technology has the potential to revolutionise clinical practice. This has led to significant amounts of money being invested by industry and venture capitalists. The field is at a turning point in focus and now is the time to act to fulfil the potential promised by these recent successes. The basic science and early clinical trials have shown that the technology can work; the challenge now is to work out how best to commercialise and effectively deliver these new medicines to patients as part of the clinical care pathway.

We agree that ATMPs should be a key area of interest in the coming years given the pace of scientific progress and now that more products are reaching patients. We agree that the IMI concept paper highlights the key areas that could benefit from future IMI support. In particular, we are encouraged that IMI have covered regulatory as well as pricing and access issues. It is important that regulatory, health technology assessment and payer organisations are all involved in this work so that evidence generation, marketing authorisation and market access can be streamlined for the benefit of patients. Comparison with what happens in other jurisdictions who are taking the lead in ATMP work such as USA, South Korea and Japan would also be helpful so that global best practice is shared.

Broadly speaking we agree that the issues presented in the concept paper need to be addressed to deliver the full potential of the advanced therapies field. Prioritisation between the areas identified in the preliminary recommendations for discussion, could be challenging. Pre-clinical, clinical (regulatory) and manufacturing are all pieces of the same puzzle and all need to be considered to ensure delivery of the most effective therapies to patients. However, we would like to provide a few reflections below and

consider that the areas of most urgent need can be fleshed out in the autumn workshops.

- A. One key scientific issue that will facilitate the adoption of these therapies (which could benefit from a multi-disciplinary approach) is the development of the tools which enable the community to understand the level, bio-distribution and efficacy of ATMPs and whether they are active/functional and what level of functionality they have. If this could be solved then it would enable much more rapid and evidence based evaluation of new ATMPs.
One example is the issue of immunogenicity (raised in the report) and the lack of tools to enable us to determine if the allogeneic cells have been destroyed or their functionality reduced. Several groups are working on this, but it is a generic issue. It requires the development of a platform. If a robust series of approaches could be developed, then the community would be in a strong position to attract business and trial. In the UK, Academic Health Science Networks are seen as the best way to drive much of this through university/primary care/hospital/funder collaborations.
- B. The regenerative medicine and gene therapy fields are continuing to converge and this could present opportunities to deliver further therapeutic developments for example re. engineered cells.
- C. Delivery and targeting for some ATMP's delivery could be a significant challenge for example targeting solid tumours/tissue can be problematical, both in terms of delivery devices (for example shear forces in needles) and approaches for homing or retention at site.
- D. There needs to be much greater and more meaningful patient engagement in the clinical development phase (section 3.2). Paragraph 7 (final para) mentions communication and education with general public. We agree this is important but feel that it is only a part of the answer; there needs to be more work in directing innovation towards outcomes that matter most to patients as identified in the Accelerated Access Review (see section 5 of this document).
- E. The general policy of gaining greater insight from prior research is supported by the respondents for example by prioritising mapping and the use of registries as suggested in paragraph 6 of section 3.2.

2. Advanced Therapies in the UK

The UK has been at the forefront of supporting development of 'advanced' technologies and translating them for patient benefit. Cell therapy and regenerative medicine are central to UK MRC's Strategic Plan and regenerative medicine is one of the UK Governments "Eight Great Technologies". The Government's recurrent research investment is currently estimated to be of the order of £80M per year, with half of this through MRC.

MRC and Research Council Partners working with Innovate UK have delivered substantial and aligned public investment in the field encompassing:

- £25M MRC/Engineering and Physical Sciences Research Council (EPSRC)/Biotechnology and Biological Sciences research Council (BBSRC) funding for the UK Regenerative Medicine Platform
- £20M MRC capital investment in regen med, aligned with the UKRMP
- £70M Innovate UK funding to establish the Cell and Gene Therapy Catapult
- £55M Innovate UK funding to establish a national cell therapy manufacturing facility, through the CTC
- MRC centre investments in the Edinburgh Centre for Regenerative Medicine (£2.6M, renewal) and Cambridge Stem Cell Institute (£3.1M MRC / £4.3M WT)
- the establishment of the £13M WT/MRC Human Induced Pluripotent Stem Cell

- Initiative
- £11M for 3 Centres for Doctoral Training in Regenerative Medicine (joint EPSRC/MRC funded).
- Since 2009 Innovate UK has supported advanced therapies and regenerative medicine projects with over £54 million in grants. These project grants have been matched with over £25 million additional funding from industry.

3. UK Regenerative Medicine Platform (www.ukrmp.org.uk)

The UK Regenerative Medicine Platform (UKRMP) will be a key initiative to synergise with. It was jointly established by MRC, BBSRC and EPSRC. This £25M initiative promotes translational research in the field and addresses the knowledge gaps and obstacles where more development is needed to underpin the delivery of therapeutic approaches. The UKRMP provides critical linkage between the discovery science base and efforts to promote application, where for example it operates in close cooperation with the Cell and Gene Therapy Catapult (CTC). The Cell and Gene Therapy Catapult are submitting a separate response to the consultation paper.

4. The ecosystem in cell and gene therapy is attractive to industry and investors

- TEL is a global leader in semiconductor technology which has opted to establish its EU life science base in Stevenage, just north of London, to take advantage of the collaborative environment in the UK. MRC has awarded £1.3m to cement academic collaborative opportunity with TEL. This award, led by Manchester and connected to the UKRMP involves a number of UK HEIs, aims to develop novel automation technology and an open-innovation platform for stem cell manufacture. Cell Therapy Catapult although not formally part of the project team, are working with TEL to identify opportunities to use the systems developed in delivering cell therapies within their portfolio (<https://ct.catapult.org.uk/-/cell-therapy-catapult-working-with-tokyo-electron-on-smart-cell-processing-technologies>).
- BioMarin Pharmaceuticals are working in partnership with Amit Nathwani at University College London to develop gene therapies to treat haemophilia. The original development work on the gene therapy for Haemophilia A was funded through the MRC Developmental Pathway Funding Scheme and the current clinical trial is co-funded by MRC through the Biomedical Catalyst. Professor Nathwani has also launched a spin out company to develop his gene therapy technology which has secured £25M in financing (<https://www.ucl.ac.uk/news/news-articles/1215/101215-freeline-therapeutics>).
- Professor Bobby Gaspar at Great Ormond Street Hospital has been funded by MRC to carry out a Phase I/II Trial of a gene therapy for Adenosine Deaminase Deficiency a condition in which affected children lack a functional immune system and without treatment die from infection in the first year of life. This trial, due to read out in early 2018, is already showing really promising results in the children treated. Professor Gaspar has now launched a spin out company, Orchard Therapeutics which has received £21M of investment (<http://www.uclb.com/news-and-events/news-post/uclb-and-f-prime-launch-orchard-therapeutics-to-treat-rare-childhood-diseases>).

5. Reports, Reviews and Resources relevant to the commercialisation of advanced therapies.

There are currently a number of initiatives/ work-streams active in the UK looking at advanced therapies and developing strategies or action plans.

- 1) **KTN workshop on Gene Therapy, Viral Vectors and Therapeutic Vaccine Workshop** – in June 2015 the Knowledge Transfer Network (KTN) held a workshop to consider the issues facing the gene therapy field and specifically addressing the challenges and barriers to commercialisation. A full report of the meeting was published and can be found on the KTN website (<https://connect.innovateuk.org/documents/3112383/28624028/Gene+Therapy+Viral+Vector+Workshop+Outputs/dd71e901-531d-442f-9715-9940cea9bced>).
- 2) **Regenerative Medicines Expert Group (RMEG)** – is a group of assembled to develop a strategy for delivery of regenerative medicine to the UK National Health Service (NHS). The aim of the group is to ensure that the NHS is fully prepared to deliver these innovative new treatments and also to assess the effect of regulation on the development of Regenerative Medicines in the UK. An update from RMEG on progress to support the growth of regenerative medicine in the UK was published in March 2015 (<https://www.gov.uk/government/publications/regenerative-medicine-a-uk-pathway>).
- 3) **Accelerated Access Review (AAR)** – aims to speed up access to innovative drugs, devices and diagnostics for NHS patients. Advanced therapies are a clear example of novel therapy that is included in the review. The AAR published an interim Report in March 2016 (<https://www.gov.uk/government/publications/aar-interim-report-feedback>).
- 4) **Advanced Therapies Manufacturing Task Force** – this is a short-term group Co-Chaired by industry and Government. This group will meet three times over 2016 with the aim of developing an action plan to anchoring advanced therapy manufacturing and its associated supply chain in the UK. More detail can be found [here](#).
- 5) **Viral and other Vectors for Gene Therapy Web Resource** – the UK government funders of research and innovation have a co-ordinated website that provides a resource where both academia and industry can explore options for funding (<https://connect.innovateuk.org/web/viral-and-other-vectors-for-gene-therapy>).
- 6) **White Paper** - The Cell Therapy Catapult, California Institute for Regenerative Medicine, and, the Alliance for Regenerative Medicine held a roundtable in June 2013 to define technological challenges and identify potential solutions in three key areas: manufacturing clinical-grade cell products derived from stem cells, characterizing the cell product, and imaging cells after transplantation. The key recommendations were summarised in a White Paper (https://www.cirm.ca.gov/files/files/funding_page/Key-Tools-Tech-Hurdles-in-Advancing-Stem-Cell-Therapies.pdf).