



European Society
for Blood and Marrow
Transplantation

How can we facilitate the delivery of advanced therapies to patients?

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No conflict of interest

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- Focus on Advanced Therapy Medicinal Products (ATMPs) as defined by Regulation (EC) n°1394/2007
 - Gene therapy
 - Tissue engineering and Cell therapy from human and xenogeneic cells
 - Cells and tissues associated with medical devices (Combined)



Use of human body elements (genes, cells, tissues) for therapeutic purposes
Transformation into medicinal products, often ATMPs



Strict and specific legal frameworks for ATMPs within regenerative medicine

- Cases of market failures and consequences
- Clinical delivery Issues
- Solution 1: The UK Advanced Therapies Treatment Centres
- Solution 2: Complementary activities
- Solution 3: New approach from Social and Human Sciences

Withdrawal

Withdrawal

Chondrocele	Glybera	MACI	Provenge	Holoclax	Imlygic	Strimvelis	Zalmoxis	Spherox	Alofisel
TEP	GTMP	Comb. TIP	CTMP	TEP	GTMP	GTMP	CTMP	TEP	TEP
Orthop.	Gastro.	Orthop.	Onco.	Ophtal.	Onco.	Immun.	Graft vs. host	Orthop.	Gastro.
2009	2012	2013	2013	2015	2015	2016	2016	2017	Pending
Norm. MA	Norm. MA	Excep. MA	Norm. MA	Cond. MA	Norm. MA	Norm. MA	Cond. MA	Normal	
-	Orphan	-	-	Orphan	-	Orphan	Orphan	-	Orphan
Tigenix (BE)	UniQure (NL)	Vericel (USA)	Dendreon/Valeant (USA)	Chiesi (IT)	Amgen Europe (NL)	GSK (UK)	MolMed (IT)	CO.DON (DE)	Tigenix (BE)

SUSPENDED

TEP: Tissue Engineered Product; GTMP: Gene Therapy Medicinal Product; CTMP: Cell Therapy Medicinal Product; Comb.: Combined; MA: Marketing Authorisation

- Clinical adoption has been recognized as a main challenge in the field of advanced therapies
 - From bench to bedside approach, Translational medicine
 - Product’s “life cycle”
 - “One of the greatest changes to the delivery of medicine in recent times” (Medicine Manufacturing Industry Partnership, Advanced Therapies Manufacturing Action Plan: Retaining and Attracting Advanced Therapies Manufacture in the UK, 2017)
 - Different aspects between existing healthcare delivery mechanisms for drug and devices and those required for tissue, cell or gene-based products



Clinical delivery issues

- Clinical complexity: Highly sensitive (living) tissues and cells, complexity of the processes
- Need for specific skills and training
- Need for new logistical arrangements
 - Manufacturing: on site, expensive bioprocessing equipment...
 - Transport: often short shelf life
 - Storage: specific equipment
- Funding of products: high cost, risk-sharing agreements and data gathering
- Limits of healthcare systems: limited health budget and resources, already busy
- Managing patients' hopes and hypes

Regulatory requirements



The UK Advanced Therapies Treatment Centres

- 2015 and 2017: Thank tanks' proposals of establishment of specialist cell and gene therapy delivery centres in the UK
- 2017: UK Government devoted £30 millions for a network of Advanced therapies treatment centres in the UK
- February 2018: project started under the coordination of the Cell and Gene Therapy Catapult.

It involves 3 Consortia that received funding

- Midlands and Wales Advanced Therapy Treatment Centre
- Northern Alliance Advanced Therapies Treatment Centre
- A Coordinated strategy to scale-up advanced therapies for patients in Manchester

Midlands and Wales Centre	Northern Alliance Centre	Manchester Coordinated strategy
<p>National Institute for Health Research Birmingham Biomedical Research Centre Nottingham Uni Hosp. NHS Trust Velindre NHS Trust</p> <p>NHS Blood and Transplant</p> <p>Asymptote Ltd World Courier Logistics Ltd Thermo Electron Ltd Cell Medica Ltd Miltenyi Biotec Ltd Trakcel Ltd</p> <p>Cellular Therapeutics Ltd</p> <p>Rexgenero Ltd Orbsen Therapeutics UK Ltd</p>	<p>The Newcastle upon Tyne Hospitals NHS Foundation Trust NHS Lothian NHS Greater Glasgow and Clyde Leeds Teaching Hospital NHS Trust Academic Health Science Network for the North East and North Cumbria</p> <p>NHS Blood and Transplant Scottish National Blood Transfusion Service Edinburgh University Newcastle University</p> <p>Asymptote Ltd (part of GE Healthcare) World Courier Logistics Ltd Thermo Electron Ltd Cell Medica Limited Miltenyi Biotec Limited TrakCel Limited Datatrial Ltd</p> <p>Chiesi Ltd Autolus Limited Roslin Cell Therapies Limited Alcyomics Limited</p>	<p>The Christie NHS Foundation Trust Manchester University NHS Trust</p> <p>Christie Pathology Partnership</p> <p>University of Manchester</p> <p>Asymptote Ltd</p> <p>Datatrial Ltd Celluar Therapeutics Limited Chaucer Group Limited AstraZeneca plc Agenus UK Ltd Aptus Clinical Limited Formedix Limited</p>



The UK Advanced Therapies Treatment Centres

- How?
 - Partnerships between NHS (patient access, clinical and tissue and blood expertise) and industry (investment and manufacturing expertise)
 - Consolidation of resources around these centres and coordination
- Where?
 - Sites already pioneering the development and clinical trials of ATMPs, with will to improve expertise in manufacturing and delivery
- Why?
 - To develop coordinated systems with the necessary skills for at-scale clinical delivery
 - To facilitate the establishments of validated standards of quality and safety of ATMPs.

- A specific role for haematological services
 - Similarities shared between many ATMPs and existing conventional haematological treatments
 - Haematologists departments well placed for ATMPs development but needs to accommodate with new issues and requirements (see Lowdell & Thomas 2017)
- New manufacturing centres, examples:
 - Cell and *Gene* Therapy Catapult large GMP manufacturing centre in Stevenage in the UK: £55 millions investment, 100m² of clean room space
 - YpoSkesi in France: 121 millions euros, 6000m² to be expanded
- Enhanced coordination between gatekeeping institutions (regulatory agencies and reimbursement bodies) in the UK
- Early contact with regulators favoured at EU and UK levels



The support of social and human sciences

- The REGenableMED project (PI: A. Webster, University of York)
“Regenerative medicine and its development and implementation: an analysis of emergent value systems and health service readiness”

Universities of York (SATSU); Sussex (Centre for Global Health Policy); Edinburgh (INNOGEN); Birmingham (national Horizon Scanning Centre).

May 2014- July 2017

Sociology/Science & Technology Studies; business modelling; law & regulation; horizon scanning & scenario methods

REGenableMED



- In parallel with Technology Level Readiness (TRL), **Institutional readiness (IR)** (See Webster 2017)
 - TRL focus on innovation as “working”, current approach of acceleration for the market
 - IR: “the capacity and willingness of key pre-existing organisations and inter-organisational structures to adopt, respond to and utilise novel technologies”
 - Need for innovation to be “workable”, i.e. to make sense in their context of application: clinical delivery, administration to the patient within the clinic.
 - “Responsible acceleration”

The support of social and human sciences

- But also Workability through
 - Practices (See Isasi et al 2017)
 - Public private partnerships and re-negotiation of science in context (See Addison 2017)
 - More coordination between various actors, and particular roles of intermediary agencies (such as UK Gene and Cell Therapy Catapult; See Gardner and Webster 2017)
- To address clinical delivery issues, especially
 - Diversity of ATMPs: to take into account the context
 - Unclear requirements due to early stages therapies

Reports

- Regenerative Medicine Expert Group: Building on our own Potential: A UK Pathway for Regenerative Medicine (2015). Available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/415919/build-on-potential.pdf
- Medicine Manufacturing Industry Partnership, Advanced Therapies Manufacturing Action Plan: Retaining and Attracting Advanced Therapies Manufacture in the UK, 2017: <http://www.abpi.org.uk/our-work/mmip/Documents/Advanced-Therapies-Manufacturing-Taskforce-report.pdf>
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- REGenableMED project, Policy Briefing, Clinical Delivery, February 2017: https://www.york.ac.uk/media/satsu/members-area-internal/regenablemedmembersarea/RM%20Policy%20Briefing%20Clinical%20delivery%20_final.pdf

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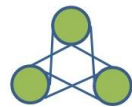
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Thank you for your attention!

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<http://www.york.ac.uk/satsu/regenablemed>

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