Online consultation on advanced therapies | summary of feedback received

On 25 April 2016, the Innovative Medicines Initiative (IMI) launched an online consultation on advanced therapy medicinal products (ATMP) with the goal of identifying the potential of IMI as a platform for enhancing ATMP research and development. The consultation was open to all citizens and organisations, and contributors were encouraged to consider in particular the following questions:

- Have the key challenges that can be addressed through collaborative, public-private initiatives been properly identified?
- Which of the proposed potential initiatives should be prioritised?
- Are any areas missing?
- What are the key European or national initiatives that IMI shall synergise with?

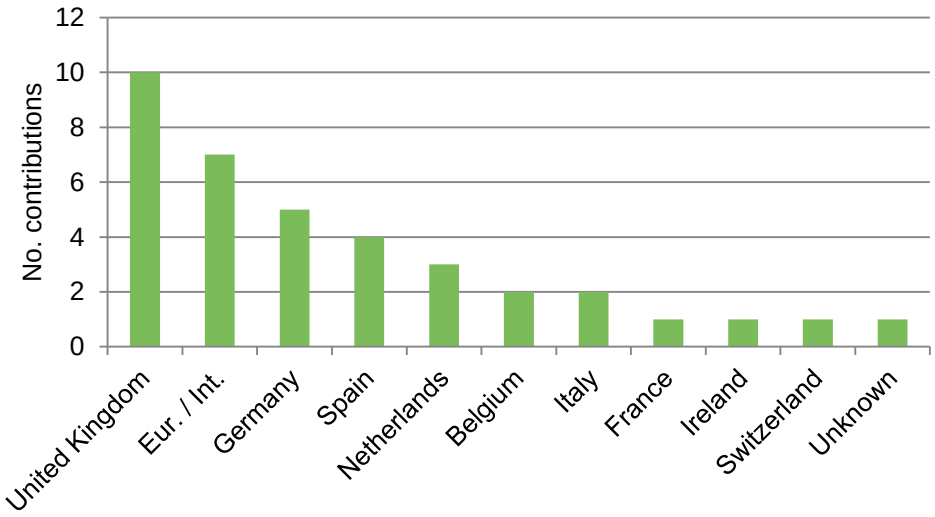
The deadline for submitting contributions was 26 July 2016.

This document summarises the feedback received. In addition, all contributions are published online on the IMI website, with the exception of those clearly marked as confidential. A list of contributors is also provided at the end of this document. The subject will be discussed further at the IMI Stakeholder Forum on 28-29 September 2016 in Brussels, Belgium.

Overview of the contributors

- Total number of contributions received**: 34**
- Volume of comments: **over 120 pages**

Breakdown: contributions by country



Notes:
- Contributions with multiple authors are attributed to multiple countries.
- Eur. / Int. = contributions sent by European / international organisations.
- One comment sent in personal capacity gave no information on the country of the sender.

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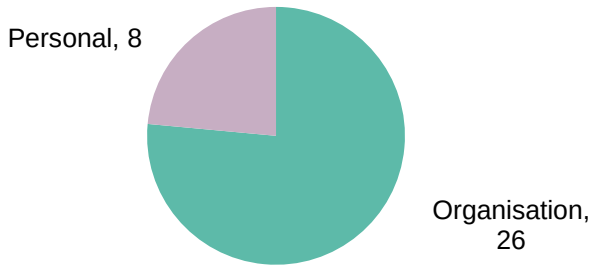
Breakdown: organisation vs personal contributions



Overview of comments received

- The paper did not make reference to existing documents of relevance.
- The document did not refer to potential links with ongoing projects and initiatives.
- In general it was felt that the main key areas of unmet need were covered.
- The questions were relevant.
- It was clear that an IMI initiative(s) in this space could not solve all of the issues.
- A public / private initiative would indeed be hugely beneficial in tackling some of the major hurdles.

Specific comments – preclinical development

- Molecular imaging needs more prominence as a set of tools that can really help in both preclinical and clinical research.
- Choosing the right models for a specific disease was crucial and there was lots of discussion around the maturity of organoids versus small or larger animal models (who determines what a robust preclinical assessment means?).
- Immunogenicity was a major hurdle for some of the approaches taken and several submissions appealed for more research in this area.
- Defining the product for use in preclinical assessments was seen to be a challenge (quality standards / research batches vs good manufacturing practice (GMP) batches etc.).
- Use the framework of risk-based approach (already part of the EU regulatory system).

Specific comments – clinical development

- Small number of patients involved in these types of trials (by definition).
  - Clinical trial designs are highly case and disease dependent.
  - Need long-term monitoring of patient and socio-economic impact.
  - Potential treatment areas will expand.
- Need to assess benefit risk profiles early on.
  - The role and use of the Hospital Exemption (HE).
  - 85% of clinical trials involving ATMPs are academically led.

- ‘HE should be considered as complementing rather than competing with CMA [conditional marketing authorisation].’
- Suggestion of a mapping exercise to understand the national interpretations of the HE clause.
- Reminder that HE can only be obtained for one member state.
- HE harmonisation across the EU is crucial.
- HE can sometimes dilute regulatory oversight and disincentivise private investment.

- The lack of funding for clinical trial design and implementation.

Specific comments – manufacturing

- Lack of GMP facilities in hospitals – who should manufacture these products?
- Should we invest in improving academia-based product development?
- Lack of quality standards for these products.
- Lack of robust potency assays for ATMPs.
- Supply of new materials (cells, vectors etc.).
- Heterogeneity of product types (viral / non-viral; cells; nucleic acids; other biologics etc.).
- Pharmaceutical grade raw materials – lack of pharmacopoeial monographs for these.
- Requirement for networks for qualification of suppliers?
- Scaling up once clinical proof of concept is achieved.

Specific comments – pricing, reimbursement and access

- Do not assume that the current health technology assessment (HTA) methodologies and frameworks cannot work for ATMPs.
- Requirement for constant dialogue among the actors (clinician researchers, patients, regulators, HTA bodies, payers).
- Mapping of existing resources (registries, HE and compassionate use records) and use of real world evidence of clinical utility is needed.

Summaries of answers to the key questions

1. Have the key challenges that can be addressed through collaborative, public private initiatives been properly identified?

- In general – yes… but…
  - More discussion is required to determine a focused approach.
  - Determine which areas would deliver the most value to stakeholders.
  - Clinical proof of concept is a key milestone for many of these interventions.

2. Which of the proposed potential initiatives should be prioritised?

- Lots of support for preclinical testing and manufacturing.
- Significant interest in the education and training needs for all involved in the ATMP space.

- Develop shared validated vector systems.
- Develop shared validated analytical tools.
- Develop regulatory pathways for ATMPs.
- Set up specific manufacturing hubs (in public or private space?)
- Build economic models.
- Build registries, mapping and inventories of what is available.
- Addressing the current lack of funding for clinical assessments:
  - first in man clinical proof of concept.

3. Are any areas missing?

- Education and training for health professionals and patients, regulators, HTA experts and payers in the ATMP space.
- Full breadth of product types not articulated in enough detail:
  - Define these e.g. genes, and other nucleic acids (RNA, antisense), delivered using both viral and non-viral vectors; cells derived from autologous, heterologous or stem cell sources; other bioproducts requiring sophisticated delivery systems.
- Need for economic models.
- Appropriate hospital-based infrastructures to address specific clinical needs for assessments of ATMPs.

4. What are the key European or national initiatives that IMI should synergise with?

- European Medicines Agency (EMA)
- European Clinical Research Infrastructure Network (ECRIN)
- Catapult (UK)
- European infrastructure for translational medicine (EATRIS)
- Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)
- European Society for Blood and Marrow Transplantation (EBMT), International Society for Cellular Therapy (ISCT), Joint Accreditation Committee ISCT EBMT (JACIE)
- European Statements of Hospital Pharmacy
- National societies for gene and / or cell therapies
- European network for Health Technology Assessment (EUnetHTA)

Existing IMI projects

- ADAPT-SMART (Accelerated development of appropriate patient therapies: a sustainable, multi-stakeholder approach from research to treatment-outcomes)
- EBiSC (European bank for induced pluripotent stem cells)
- GETREAL (Incorporating real-life clinical data into drug development)
- STEMBANCC (Stem cells for biological assays of novel drugs and predictive toxicology)

List of contributors

Organisations

Organisation	Country
Academic AMTP Working Party The Netherlands and Belgium (Flanders)	Netherlands / Belgium
Agence de la Biomédecine	France
Alliance for Regenerative Medicine (ARM)	International
Andalusian Agency for Health Technology Assessment (AETSA)	Spain
Association of the British Pharmaceutical Industry (ABPI)	United Kingdom
British Society of Gene & Cell Therapy (BSGCT)	United Kingdom
Cell and Gene Therapy Catapult (CGT)	United Kingdom
Centro de Investigación Biomédica en Red - Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN)	Spain
European Association of Hospital Pharmacists (EAHP)	European
European Eye Bank Association (EEBA)	European
European infrastructure for translational medicine (EATRIS)	European
European Society for Blood & Marrow Transplantation (EBMT)	European
European Society for Molecular Imaging (ESMI)	European
EuroTech Universities Alliance	European
Genetic Alliance UK	United Kingdom
Guild of Healthcare Pharmacists (GHP)	United Kingdom
Innovate UK	United Kingdom
Medical Research Council (MRC) in conjunction with Health Research Authority (HRA) & Medicines and Healthcare products Regulatory Agency (MHRA)	United Kingdom
Miltenyi Biotec GmbH	Germany
National expert group on ATMPs in the Netherlands	Netherlands
National Institute for Health and Care Excellence (NICE)	United Kingdom
Newcastle Cellular Therapies Facility	United Kingdom
NHS ATMP Working Party – a subgroup of the National Pharmaceutical NHS QA Committee	United Kingdom
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VDI/VDE Innovation + Technik GmbH	Germany

Contributions sent in a personal capacity

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