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EuroGCT D4-1: Landscape mapping, report on mapping of European cell and gene therapy landscape at multiple levels

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Deliverable Report

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Project acronym: EuroGCT

***Project title: European Consortium for Communicating
Gene and Cell Therapy Information***

Deliverable: D4.1. Landscape Mapping

***Report on mapping of European cell and gene therapy landscape at
multiple levels***

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List of acronyms

ATMP: Advanced Therapy Medicinal Products

EuroGCT: The European Consortium for Communicating Gene and Cell Therapy Information

IMHT: The EuroGCT Information Management Hub Team, comprised of project staff employed directly by the project, based at the University of Edinburgh (UEDIN) and Aix-Marseille University (AMU)

ELSI: Ethical, Legal and Societal Issues

EMA: European Medicines Agency

EU: European Union

GA: Grant Agreement

ICH: The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

NoE: Gene and Cell Therapy Network of Expertise

WP: Work Package

D4.1 Landscape mapping, report on mapping of European cell and gene therapy landscape at multiple levels

1 Introduction

WP4, entitled “An Information and Engagement Hub for the Research and Regulatory Communities”, is focussed on development of an information hub for the research and regulatory communities, that facilitates access of these communities to information on the practical steps needed for cell and gene-based therapy development and promotes information exchange within and between these communities. Once developed, this tailored section will create a ‘one-stop shop’ on where to seek further information and guidance relating to manufacturing guidelines, regulatory requirements, intellectual property rights, market acceptability and ethical matters related to advanced therapies development. WP4 will also promote liaison between cell and gene-based therapy stakeholders and the regulatory agencies.

As part of this development, a key objective of WP4 is to map the European cell and gene-based therapies landscapes at multiple levels, *encompassing*:

- (i) Practical steps required for advanced therapies development including: manufacturing guidelines (including analytics/characterisation), legal, regulatory (including preclinical testing strategies) and ethical and socio-economic aspects (including patient attitudes, health economics and market acceptability)
- (ii) Activity related to cell and gene therapy development including: the academic, clinical and industrial (contract research organisations, biotech, pharma) landscapes, health economists and government agencies.

and to use this information to provide:

- (iii) a set of practical guidelines and concise format fact sheets for researchers approaching or engaged with development of new therapies,
- (iv) an inventory of information and links on where to seek further information and guidance
- (v) a multi-layered searchable map of the cell and gene-based therapy landscape in Europe, mounted on www.eurogct.org and openly accessible.

Tasks (i) and (ii) above were reported in **D4.8**, submitted in the first reporting period. **D4.1** therefore reports on (iii) and (iv); (v) will be reported in month 48.

2 Summary

Deliverable 4.1 is a report on the mapping of the European gene-based and cell therapies landscape. This deliverable provides an update to the earlier deliverable, **D.4.8 Initial Landscape Mapping**, which was submitted in the first reporting period. **D4.8** reported the mapping, performed by EuroGCT, of the European landscapes associated with gene and cell therapy related product development pathways including ethical, legal, regulatory and societal issues (ELSI). Related, **D4.7 Information collation**, also submitted in the first reporting period, detailed our methodology for information collection and curation. The work reported in **D4.7** and **D4.8** resulted in creation of a development framework for a practical tool entitled “Development pathways for bringing gene and cell therapies from the lab to patients” with the

short website name of “Research Pathways” (see **D4.8**). This tool was organised as a Web tree, into which general information on the development pathways for bringing gene and cell therapies from the lab to patients (hereafter the “Research Pathways Tree”) was organised. The Research Pathways Tree also included the organised information (mapping/inventory of information) of the practical steps required for cell and gene therapy development in Europe as well as links on relevant and existing information and guidance.

The present report, **D4.1**, therefore moves beyond the initial mapping to focus on implementation of these processes. This has required a combination of actions: Identification of the detailed information required to populate the Research Pathways Tree was described in **D4.8**; in this reporting period, we have: 1) created original EuroGCT resources around development pathways for bringing gene and cell therapies from the lab to patients, the Research Pathways Tree (see **D4.8 Annex 1** for details), 2) co-developed resources through collaboration, 3) selected and signposted to existing high quality resources (based on the methodology detailed in **D4.7**), and 4) launched an updated ‘Research Pathways’ database featuring improved navigability and information organisation. In the following sections, we provide the details of each action we have taken, our thought processes and some challenges we have come across.

The outputs are published on the EuroGCT website in the Research Pathways section (www.eurogct.org/research-pathways) as a searchable and filterable database and will continually be updated throughout the course of the project. (See also: **D4.2**).

3 Development of an inventory of information and links on information and guidance

This deliverable is built on the initial work reported in **D4.8** and further updated and populated with new information collated based on methodology listed in **D4.7**. In this section, we report the development and expansion processes of our information inventory, as well as the updates on website functions to facilitate user access.

3.1 Development of EuroGCT original resources

3.1.1 Ongoing content development for all entries within the ‘Research Pathways’ tree

The Research Pathways Tree is set out using a structure of entries and sub-entries (see **D4.8 Annexe 1**). In months 18-30, the writing of the full content of entries and sub-entries of the Research Pathways Tree has been implemented, agreed by the core ELSI team, using the sub-entry template shown in **D.4.8 Annexe 3**. The General Overviews drafts previously written for Research Pathways sub-entries (see **D.4.8 Annexes 4.a to 4.i**) have been further developed, completed and internally reviewed by the relevant ELSI groups.

3.1.2 Network of Expertise (NoE) resources

The scope of our ‘Research Pathways’ is vast, as it aims to cover information regarding gene and cell-based therapies broadly: mainly ATMPs, but also other gene and cell therapies that are not ATMPs such as ‘Human body elements and medical devices’, in accordance with our entry on ‘Therapy Classification’. It also aims to cover information on product development,

especially on ATMPs, all the way from fundamental research to patient access (lab to patient), their technical and ELSI aspects.

To benefit from additional expertise and research interest on the ELSI aspects of gene and cell therapy, EuroGCT has involved the ELSI Network of Expertise (NoE) members drafting content. The entries drafted by NoE members have been internally reviewed and submitted for comments to the relevant ELSI Working Groups. Once finalised, these written entries will be published on the EuroGCT website.

Work is ongoing both to complete the Research Pathways section, and to inform researchers and regulators on the ongoing evolution of the European Union legislation in the field (e.g. proposal for a regulation on substances of human origin, proposal for a regulation and a directive reforming the pharmaceutical legislation).

3.1.3 Multiple levels

For this deliverable, we have adopted a multiple levels approach in the mapping of the gene and cell therapy landscape. For instance, in terms of legislative and regulatory aspects we focused on the EU law first, but we also link to national laws when it is possible and relevant. Indeed, national competent authorities, mainly in charge of implementing and overseeing the implementation of the EU legislation, can sometimes adopt more stringent measures on a national basis than those required by EU legislation, either in response to local epidemiological risks or considering that a higher level of safety can be ensured with more stringent provisions. This is the case in tissues and cells donor' testing requirements and blood donor' testing requirements.

In terms of legal classification, it is also necessary to encompass national and European levels of regulation to determine the applicable legal framework to gene and cell therapies. The consideration and the articulation of the different levels of regulations is illustrated in the "Human body elements for therapeutics applications" entry (<https://www.eurogct.org/research-pathways/therapy-classification/human-body-elements-therapeutic-applications>) in the legal classification: for instance, the EU legislation on tissues and cells (directives) applies to the entire development chain of cells or tissues transplants, while it applies to the donation, collection/procurement and testing only regarding the development of advanced therapy medicinal products. Further steps of ATMPs' development depend on the EU pharmaceutical legislation (in particular, the ATMP regulation). As the directives need to be transposed into national laws while regulations have direct effect, the first steps of development of ATMPs are more dependent on national laws (national transpositions of directives and possible more stringent national rules) than further steps of their development that solely depend on European Union law (e.g., centralised marketing authorisation).

Finally, we are covering both binding EU legislation, and non-binding EU guidance and other resources. We are linking to these various levels of resources in terms of being binding or not.

3.2 Co-developing resource through collaborations

EuroGCT is part of a collaborative project named 'The Advanced Therapy Medicinal Products Patient and Public Involvement and Engagement Working Group (ATMP Engage)'. This collaboration brings together UK-based stakeholders with an interest in ATMPs to discuss and collaborate on Patient and Public Involvement and Engagement (PPIE) activity. The output of

this collaboration is the ATMP Engage PPI Directory (<https://www.eurogct.org/ppi-directory>). It contains patient and public involvement (PPI) resources for developers of cell and gene therapies, including toolkits, guidelines, advice, templates, and case studies. The resources collated within this directory spans EU and UK and are applicable to users independent of their geographical locations. The ATMP Engage PPI Directory constitutes the Patient and Public Involvement section of our Research Pathways database, and its content will be continuously updated and expanded during the project span.

3.3 Signposting to existing resources

3.3.1 EuroGCT Partner's resources

An important part of the work of WP4 is to signpost to additional existing resources on gene and cell therapy development relevant to the research and regulatory communities. To achieve this, we ask for consortium partners' input on resources produced by their organisations, or suggestions on information that were useful in their own research and development activities. Resources suggested by this route are then assessed, and promoted through links in the Research Pathways section as appropriate. A few examples of resources collected through this route include:

- Resources by ATMP Sweden (<https://www.eurogct.org/atmp-sweden-resources>)
- Resources by CGT Catapult (<https://www.eurogct.org/cell-and-gene-therapy-catapult-cgt-catapult-resources>)
- Resources by ATTC, managed by CGT Catapult (<https://www.eurogct.org/advanced-therapies-treatment-centre-attc-resources>)
- Resources by ECRIN (<https://www.eurogct.org/european-clinical-research-infrastructure-network-ecrin-resource>)

3.3.2 External resources

We similarly seek to link to resources produced externally to our partnership. Through our dissemination and networking activities reported in **D2.2**, we have connected with a number of organisations and projects external to EuroGCT. We have asked these organisations for their expert insight on helping us identify relevant resources produced by them or others. A non-exhaustive list of such resources include:

- European Advanced Translational Research Infrastructure in Medicine (EATRIS) resources (<https://www.eurogct.org/european-advanced-translational-research-infrastructure-medicine-eatris-resources>)
- European Joint Programme on Rare Diseases (EJP RD) resources (<https://www.eurogct.org/european-joint-programme-rare-diseases-ejp-rd-resources>)
- The Association of the British Pharmaceutical Industry (ABPI) Resources (<https://www.eurogct.org/association-british-pharmaceutical-industry-abpi-resources>)

3.3.3 External resources through searches

Additional resources are identified and collated by the Information Officer - product development pathway and the Information Officers - Ethics, Legal and Regulatory issues, according to the methodologies reported in **D4.7**.

3.4 Research Pathways Database--updated structure and information organisation

The EuroGCT online research and regulatory community hub, Research Pathways (**Figure 1**), is built on the initial information published (see deliverable **D4.9**). New information collated within the current reporting period is vast and mapping it onto the website requires careful planning on the content presentation, both structurally and functionally. Moreover, the nature of the information on product development is structurally complex—it requires cross-linking between sections and also represents interactions and/or parallel development effort between various stakeholders at every stage of development. Simultaneously, this organised information needs to make sense and remain findable by users. This presents a great challenge and a need in web development on features to support this complex information organisation and presentation. Below we report on each of these new features and functions and explains how they support the landscape mapping activity.

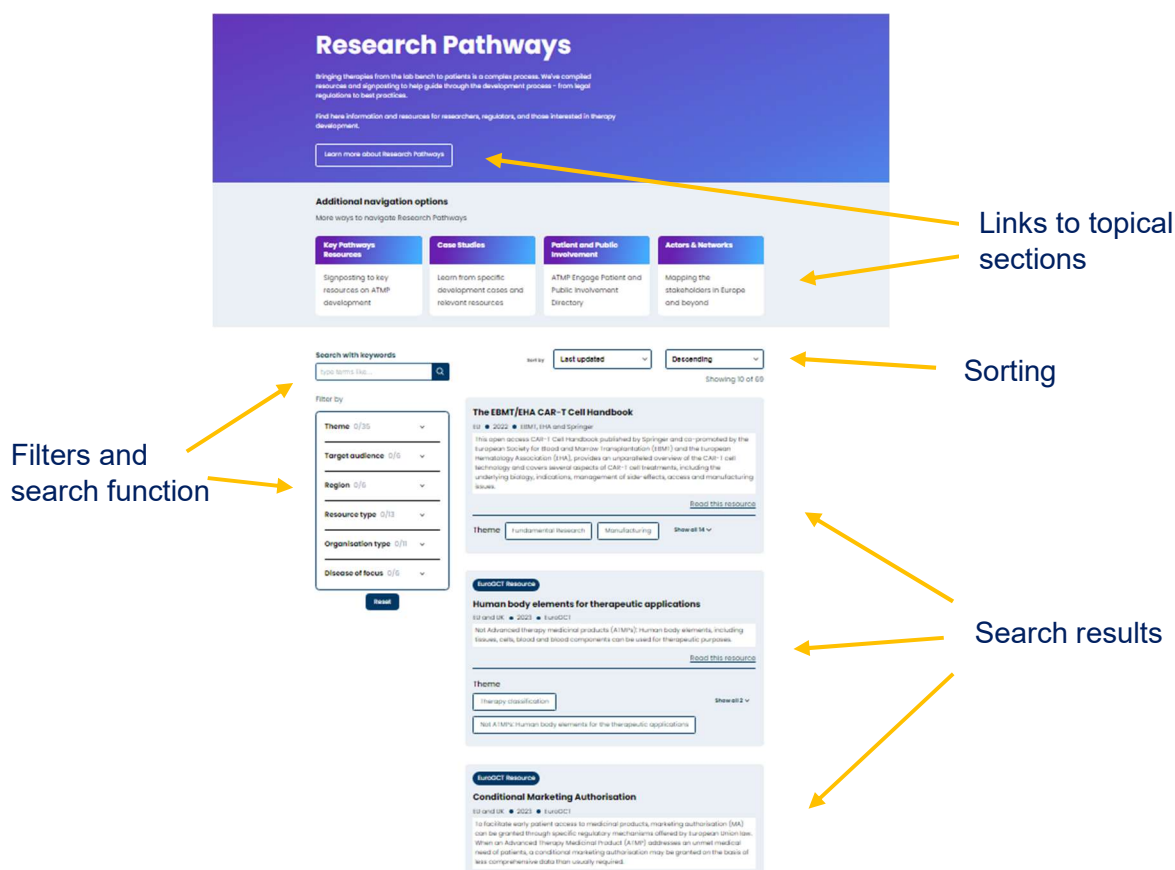


Figure 1. Screenshot of the Research Pathways search page (cropped).

3.4.1 Website structure

The IMHT undertook a review of the user experience for the Research Pathways section and have updated the section’s original design from a hierarchical structure to a database model. This essentially translates to a flattened website structure for improved searchability and usability—resources that are originally buried at the bottom layer based on the hierarchical structure can now be exposed and becomes findable.

3.4.2 Tagging with taxonomy terms

The key to improved searchability is the thoughtfully designed taxonomies used for tagging. The taxonomies terms are used for pulling the tagged resource pages when a specific filter is applied. The IMHT has designed the set of taxonomy terms in **Table 1**:

Main filter category	Subcategory (1st layer)	Subcategory (2nd layer)
Theme	Research and Innovation	Fundamental Research Clinical research Translational Science Funding Incentives Early interaction with regulators
	Therapy classification	Legal classification ATMPs Not ATMPs: Human body elements for the therapeutic applications Not ATMPs: medical devices containing tissues and cells
	Manufacturing	Manufacturing Authorisation Good Manufacturing Practice Investigational medicinal products dossier Capability Scalability Packaging and labelling
	Commercialisation	Market access for ATMPs Distribution Advertising Pharmacovigilance Pricing & reimbursement
	Data	Data protection Data storage Data collection, processing, controlling Data sharing / Open Data Mission creep / data misuse
	Patient & Public Involvement	
	Ethics	
Target audience	Researchers / developers Healthcare providers Public / patients Regulators Industry Other	
Region	EU/EEA EU (National level) UK North America Global Other	

Resource Type	Legal text Guides / Guidelines Maps / Flowcharts Forms / Checklists Reports / Booklets Presentation slides / Posters Journal Briefing / Blog posts Case studies Training / e-Learning / Webinar Tools Database / Repositories Other	
Organisation type	Regulatory Authorities Academic Bodies Healthcare Providers Industry Patient Advocacy Organisations / Charity Journal Associations / Societies / Networks Research Infrastructure / Research Centres Translational Centres Funding Bodies Other	
Disease of focus	Blood Immune Conditions Eye Muscle and Skeletal Neurological Other	

Table 1. Taxonomy terms used in Research Pathways database

Theme filter is mainly based on the Research Pathways Tree structure reported in **D4.8**. Patient & Public Involvement and Ethics are added, as they are key topics running alongside the entire product development pathway. Resources specific to a type of therapy are tagged and can be searched for according to its legal classification (ATMPs, Not ATMPs: Human body elements for therapeutic applications, or Not ATMPs: medical devices containing tissues and cells).

Target audience filter refers to whom the resource is written for. Some resources are strictly targeting experts while some may be written in lay language.

Region filter concerns the geo- and political regions the information is effective in. For example, resources on regulations effective only within individual EU Member States will be tagged with the 'EU (National level)' tag, and not the 'EU/EEA tag'. Information on scientific development regardless of geo- or political region, or those indicated within the resource scope will be tagged with the 'Global' tag, examples include: ISSCR Guidelines for Stem Cell Research and Clinical Translation (<https://www.eurogct.org/isscr-guidelines-stem-cell-research-and-clinical-translation>), WHO Human Genome Editing (HGE) Registry (<https://www.eurogct.org/who-human-genome-editing-hge-registry>) and more.

Resource type filter allows users to use the nature of the resource, whether it is a guideline, a database, a webinar, a journal article...etc to help narrow down search results.

Organisation type filter breaks down the type of organisations who produced the resources. For example, EuroGCT's original resources will be tagged as 'Associations / Societies / Networks'.

The **Disease of focus filters**, although not a primary focus for the Research Pathways section as the main attention is placed on the development process, can still be utilised in several ways. Users can use it to search for information related to the development of medicinal products related to specific types of condition if this information is available. It also provides a future handle to crosslink relevant information with the content that are hosted within the 'Discover' section of our site for the interested non-specialists to follow through.

3.4.3 New search and filter functions

To improve user experience in their searches, we introduced search functions including search by keywords, and checkboxes to apply filters to the taxonomy terms, and implemented the sorting by field and order.

3.4.4 Direct access to topical sections

Key Research Pathways section contains the collection of resources developed by EuroGCT WP4. The same set of resources can either be accessed directly through this hierarchical-structured page, or by filtering/searching within the main database.

Key Pathway Resources section contains collated key resources on ATMP development by medicines agencies, and existing complementary work produced by other projects and organisations.

Case Studies section contains case studies on ATMP development. We will describe this new section in detail in the next section '4. A set of practical guidelines and concise format fact sheets for researchers approaching or engaged with development of new therapies.'

Patient and Public Involvement links to the ATMP Engage Patient and Public Involvement (PPI) Directory, a searchable and filterable directory with PPI resources for developers of cell and gene therapies.

Actors and Network section contains our initial mapping of stakeholders in ATMP development in Europe and beyond. This will be further developed and reported in **D4.3** which is due in month 48.

3.4.5 Multiple entry points

We have built in multiple entry points to access the same piece of information to facilitate user access, especially for key resources. This feature answers the expectations of various types of users, taking into account their different knowledge and experience, and consequently potential different approaches in looking for relevant information. For example, the ATMP Engage PPI database can be accessed through the links in the topical sections; it can also be accessed through the top menu as well as be searched for directly in the database. EuroGCT's original resources can be accessed through the 'Key Research Pathways' section as well as be searched for in the database. Key resources produced by other organisations can be found in the 'Key Pathway resources' topical section, and also be found directly in the database. We use multiple entry points to highlight the importance of these resources, and for drawing user's attention. It also considers the different knowledge and experience, and thus their possible different approaches in looking for relevant information.

3.4.6 Visual elements and user experience

We have implemented web design to improve visual presentations. We have also developed webpage features to enhance the crosslinking functions on the site, for example, the textboxes used in the Case Study content type (**Figure 2**) is clickable and links back to relevant search results in the main Research Pathways database.

The information regarding ATMP development is vast, complex and interconnected, and requires custom-designed website features and functions to support its presentation. We have developed features on our website to support this information mapping.

We anticipate the improved searchability and usability will greatly enhance users' experience in searching and navigating within the section, and in turn improve engagement and learning.

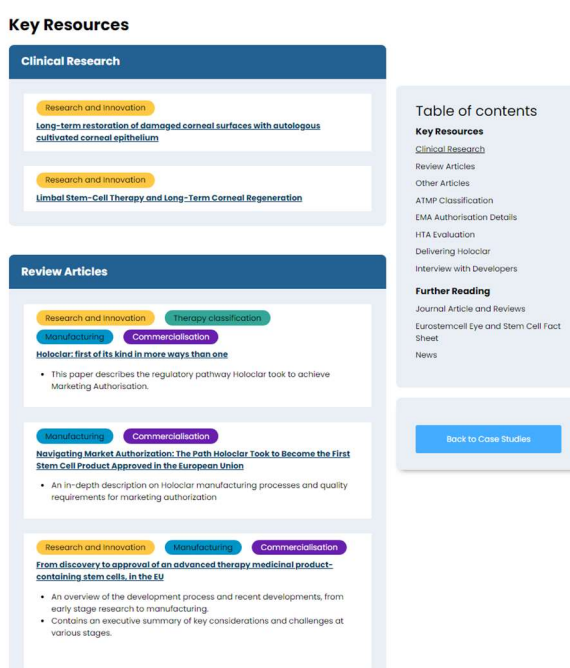


Figure 2. Textboxes and features within case study content type enhances the linkage with relevant information in Research Pathways. This screenshot (cropped) is taken from: <https://www.eurogct.org/case-study-holoclar>.

3.5 Research Pathways Coverage

In this section, we report on the current coverage of the Research Pathways entries published on the Research Pathways database using 'Themes', as 'Theme' is built based on the draft tree reported in **D4.8**. **Table 2** below lists all Theme entries: marked in **green** are the entries that has the General Overviews published; marked in **blue** are those with full entries published; marked in **pink** are those only covered with signposting to external resources; marked in **grey** is covered by co-developed resources. See **Annexe 1** for a complete list and screenshots of published EuroGCT General Overviews and full entries.

Main filter category	Subcategory (1st layer)	Subcategories (2nd layer and beyond)
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Theme	Research and Innovation	<ul style="list-style-type: none"> • Fundamental Research • Clinical research <ul style="list-style-type: none"> • Clinical trials • Translational Science • Funding • Incentives <ul style="list-style-type: none"> • Intellectual Property rights <ul style="list-style-type: none"> ◦ Patentability • Early interaction with regulators <ul style="list-style-type: none"> • Support for (innovative) medicines' development <ul style="list-style-type: none"> ◦ Support for innovative medicines' development at the EMA level • Support for ATMPs' development
	Therapy classification	<ul style="list-style-type: none"> • Legal classification • ATMPs <ul style="list-style-type: none"> • ATMPs and Orphan medicinal products • Not ATMPs: Human body elements for the therapeutic applications • Not ATMPs: medical devices containing tissues and cells
	Manufacturing	<ul style="list-style-type: none"> • Manufacturing Authorisation • Good Manufacturing Practice • Investigational medicinal products dossier • Capability • Scalability • Packaging and labelling
	Commercialisation	<ul style="list-style-type: none"> • Market access for ATMPs <ul style="list-style-type: none"> • Standard Marketing authorization pathway: centralized procedure <ul style="list-style-type: none"> ◦ Marketing Authorisation Application file • Expediting marketing authorisation pathways <ul style="list-style-type: none"> ◦ Conditional MA ◦ MA under exceptional circumstances ◦ Accelerated Assessment ◦ Specificities of the marketing authorisation dossier for biosimilars • Distribution • Advertising • Pharmacovigilance • Pricing & reimbursement
	Data	<ul style="list-style-type: none"> • Data protection <ul style="list-style-type: none"> • Data Classification • Main Principles • Data Protection Authorities • Data storage • Data collection, processing, controlling • Data sharing / Open Data • Mission creep / data misuse
	Patient & Public Involvement	
	Ethics	

Table 2. Theme table to show current coverage of the published Research Pathways content.

Sub-entries within 'Market access for ATMPs' have all been completed and published on the Research Pathways information hub. Marketing authorisation constitutes the main mandatory step for ATMPs manufactured at the industrial scale to be commercialised in the European Union. These entries collectively provide summarised information in accessible language,

signpost to various relevant webpages on the EMA website, and links to external resources, notably EU binding legislation, guidance, and relevant literature. They provide users with easier access to the most relevant and high-quality information, and help them make sense of these various and complementary external resources. The sub-entries in 'Data' is also close to complete. These suites of information fulfil a 'one-stop-shop' for developers as required by the GA and will play a significant role in improving products development.

The curated information currently presents an almost full breadth of coverage for the Research Pathways. Besides the breadth of coverage, we are also working on increasing the depth of Research Pathways contents by publishing more resources written by the EuroGCT consortium. Several entries have been written in full and are under internal review or in the final drafting phase, including:

- *Clinical trials;*
- *Patentability;*
- *Early interactions with regulators;*
- *Manufacturing Authorisation*

As the project progresses, we will continue and reinforce our approach to collect information, write, review, and publish the content for each entry of the Research Pathways tree. The involvement of the Network of Expertise members will be continued and strengthened to achieve this objective.

We have started to see uptake by our online audience in several pieces of EuroGCT's original resources. The entries on 'Manufacturing Authorisation', and 'Packaging and labelling' are among the top-accessed pages within WP4. These pages appear in top 20 search results in Google using relevant query terms, and more often, are ranked within top 5 using exact search terms. We have also recorded a significantly longer user retention time for these EuroGCT original resource pages. More details on webpage traffic and online uptake can be found in **D2.2** and **D2.4**.

4 A set of practical guidelines and concise format fact sheets for researchers approaching or engaged with development of new therapies

4.1 Complexity in therapy classification

The practical guidelines for gene and cell therapies in development are dependent on their legal classification.

Therapy classification determines the legal mechanisms that govern the regulation of gene and cell therapies and subsequent guidelines to follow, but the classification is a non-trivial task for a therapy in development.

For Research Pathways, we focus on a subset of gene and cell therapies, ATMPs, although other gene and cell therapies that are not ATMPs but are transplants/transfusions or medical devices are also considered in the sub-entry on "therapy classification". The definitions of each type of ATMPs are listed according to EU law:

- For Gene Therapy Medicinal Product (GTMP) and Somatic Cell Therapy Medicinal Product (sCTMP): Directive 2001/83/EC, Annex I, Part IV, as modified by Commission Directive 2009/120/EC;

- Tissue Engineered Product (TEP): Article 2(1)(b) of Regulation (EC) No. 1394/2007
- Combined advanced therapy medicinal product (cATMP): Article 2(1)(d) of Regulation (EC) No. 1394/2007

Despite the legal definitions and criteria, it remains difficult to know exactly what kind of gene and cell therapy is being developed:

First, colloquial terms for therapies in development are often different from their legal classification. For example, authorised CAR-T cell therapies are considered gene therapy medicinal products (GTMPs) under current European Union legislations as opposed to its wordings 'cell therapies'. Another example is the therapy based on autologous chondrocytes for orthopaedic purposes (first ATMPs authorised in the EU, Chondrocelect, now withdrawn from the market by the marketing authorisation holder for commercial reasons) was generally called "cell therapy" although it was classified as a Tissue Engineered Product and not as a Cell Therapy Medicinal Product by the EMA/CAT.

Second, the classification for a therapy in development is also greatly dependent on the preparation steps. In the case of developing skin equivalents for healing skin wounds, different choices of the preparation steps results in different therapy classification:

- If cells are mechanically separated and sprayed on wound bed to help heal the wound:
 - ⇒ this is not an ATMP.
- If growing epithelial cells (keratinocytes) from patient or donor's skin to stimulate healing:
 - ⇒ if enzymes are used to separate between epithelium and epidermis:
 - this therapy is an ATMP;
 - ⇒ if individual cells are isolated, and cultured in medium:
 - this therapy is a sCTMP;
 - ⇒ if combined with sheets, mesh, support scaffold:
 - this therapy is a cATMP.
- Alternatively, if the donor's dermis structure is used as a scaffold to graft on patient's wound bed, and then spray patient's keratinocyte cells on to this scaffold:
 - ⇒ this therapy is a TEP.

As therapy classification is a non-trivial task, EMA has advised that the final classification should be considered on case-by-case basis, and taking into account the scientific recommendation on ATMP classification provided by the EMA's Committee for Advanced Therapies (CAT).

Therefore, it is recommended for developers to contact regulators at the national and/or European levels (including mainly the EMA, national medicines agencies and national reimbursement bodies) as early as possible in order to clarify the regulatory pathway applicable the gene and cell therapy in development and their associated regulatory requirements and incentives.

In response to this need, we have built and presented key information in the Research Pathways entries. EuroGCT's original resources 'Therapy Classification' and its sub-entries within will help increase developers' understanding of therapy classification. Entries within 'Early interactions with regulators' will also help tackle the complexity of classification, as they encourage developers to get in touch with regulators early, and explain what services and procedures are established for supporting their development activities.

4.2 New content type—Case Study

In addition to presenting key information in Research Pathways, another step we took towards tackling the complexity of classification is to develop a new content type—Case Studies. It also aims to achieve Task 3 listed in GA (see page 5, task (iii) of this deliverable). The case studies pages collate existing resources including research articles, review articles, interviews, news articles, EMA authorisation details, HTA appraisals and more related to the development of specific products.

A dedicated case studies topical section (<https://www.eurogct.org/case-studies>, **Figure 3**) is set up to host the new content type, and can be accessed through the Research Pathways information hub. It currently contains two case studies for two approved ATMPs: 1) Holoclar, a Tissue Engineered Product (TEP), and 2) Strimvelis, a Gene Therapy Medicinal Product (GTMP). In these two case studies, we collated existing publicly available information about each stage of their development, from early-stage research to approval and beyond, to serve as a guide for the research community to learn about the development process, the keys to success, the challenges and how the developers overcame them.

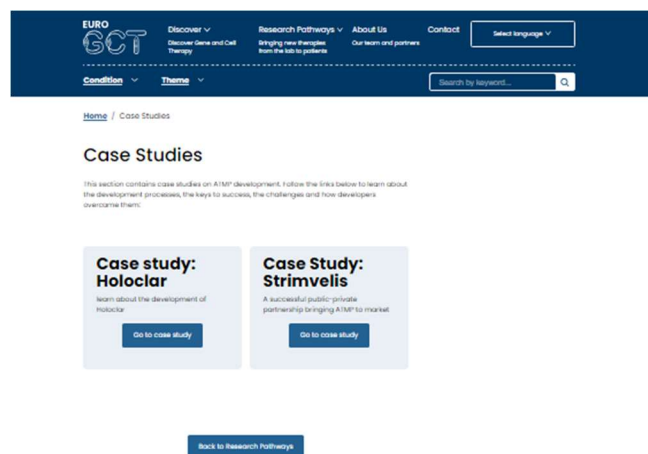


Figure 3. Screenshot of the new Case Studies topical page (<https://www.eurogct.org/case-studies>).

As previously mentioned, the case study content type has specially designed features to implement the necessary complex crosslinking function to connect its various parts to the main Research Pathways database. Therefore, these case studies also serve a second purpose—they provide storylines for readers to walk through the resources collated in the Research Pathways database.

We are conscious that ATMPs have unique considerations and complexities at every stage in the development process, from pre-clinical and trial development to licencing and patient access. These considerations and complexities often are product specific. We will try to provide as many product development stories as possible, to help researchers find anchor points and use them as references to facilitate their own development activities.

There are more case studies for additional types of therapies in the pipeline. We are currently in the process of forming a collaboration with a team developing CAR-T therapy in Spain. Through this collaboration, we hope to co-develop a case study on their CAR-T therapy development to report on the key development processes, guidelines to follow, and serves as

a learning resource for the researcher and developer community. We are also in the process of co-developing a case study with the developers of Libmeldy, an EMA-approved GTMP.

Besides case studies that span the entire or a large part of the development pathway, we also hope to develop shorter case studies to capture researchers'/developers' practical considerations at specific time points during development. An example is about early classification considerations in developing skin equivalent for healing wounds--different choices of the preparation steps can result in different therapy classification (ATMP or not ATMP; if ATMP, which sub-type) and this in turn determines the requirements that the product must meet, and the relevant procedures leading to commercialisation. These short-format case studies are designed for experience-sharing among the researchers'/developers' community. These small lightbulb moments and thoughts happening behind the scenes often are not revealed in research articles but will benefit many if shared with the community.

During the second half of the project, developing more case studies will be one of the main focuses. Contents will be published upon completion and iteratively updated throughout the project span.

5 Conclusion and future steps

EuroGCT has developed an indexed catalogue of resources and links through the following:

- 1) created a collection of EuroGCT's original resources for Research Pathways (**Annexe 1**);
- 2) collaborated and co-developed the ATMP-Engage Patient and Public Involvement (PPI) Directory;
- 3) selected and signposted to existing high quality resource;
- 4) launched an updated 'Research Pathways' database featuring improved navigability, information organisation and presentation. The custom-designed website features and functions supports the mapping of information developed and collated.

This catalogue of resources is mounted on the Research Pathways Information Hub and ensures the researcher and developer community can easily find the high-quality information they need throughout the product development process. It provides a 'one-stop-shop' for these communities and is anticipated to play a significant role in improving product development.

The new case studies topical section (<https://www.eurogct.org/case-studies>) contributes to tackling the complex issue of therapy classification that determines the legal mechanisms and subsequent guidelines a therapy in development has to follow. Considering each gene and cell therapy have unique considerations and complexities at every stage in the development process, we aim to increase the number and variety of therapy types in our case studies. We have rolled out two case studies on approved ATMPs, and are in the process of developing more content for this section. We are also developing shorter case studies for capturing practical considerations during a specific time point in development.

All of the above outputs are published on [EuroGCT's website](https://www.eurogct.org) in the Research Pathways section (www.eurogct.org/research-pathways) as a searchable and filterable database with direct links to topical sections including the newly launched 'Case Studies' section. All contents within will continually be updated to increase the breadth and depth of our information mapping throughout the course of the project.

6 List of Annexes

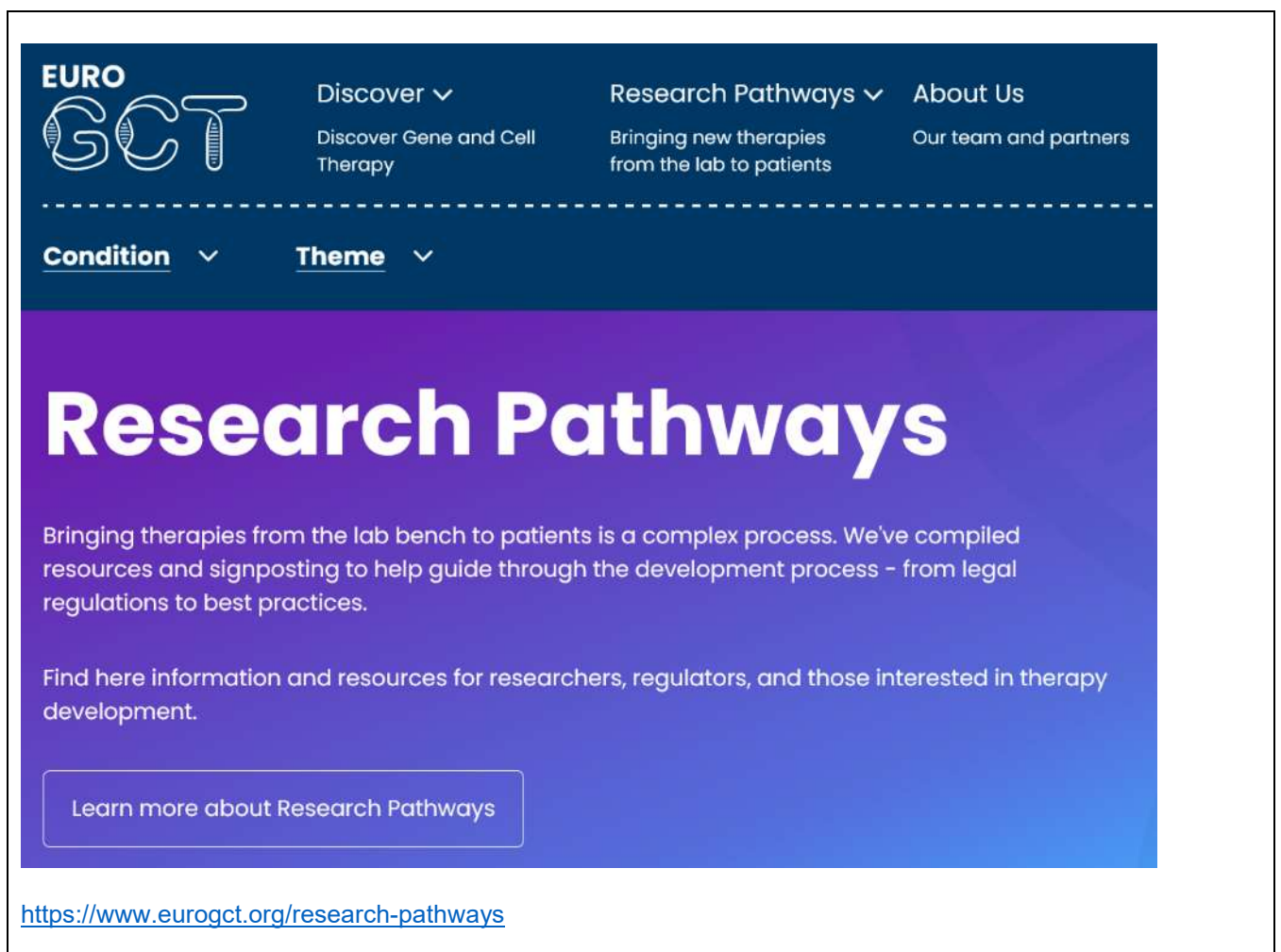
Annexe 1. Summary of activities and outputs: all published EuroGCT original resources in Research Pathways

EuroGCT

Annex 1 to Deliverable D 4.1

Summary of activities and outputs

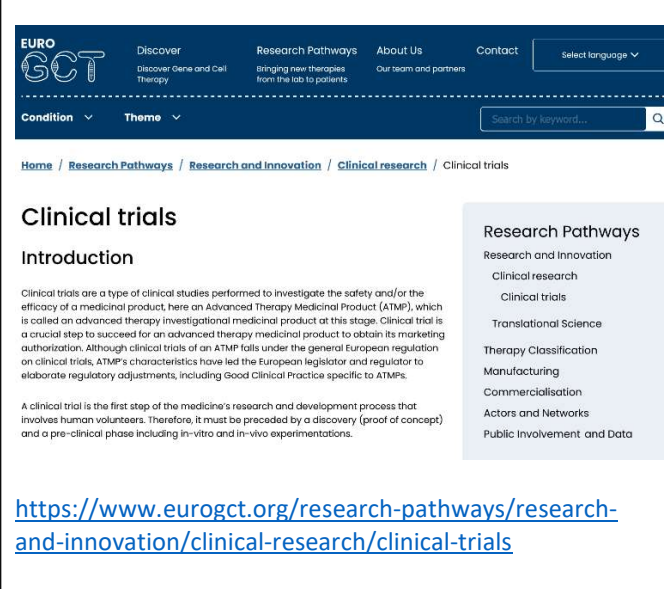
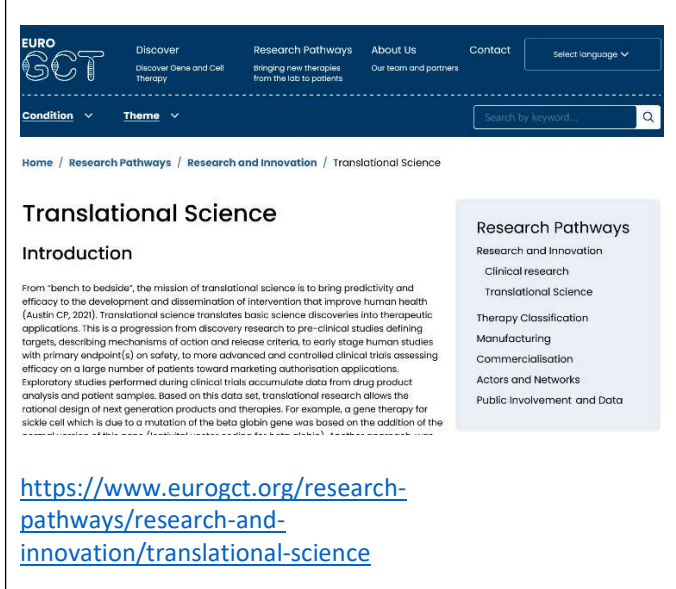
The General Overviews and the full entries contents of the 'research pathways' tree published within the Research Pathways section of the [EuroGCT website](#) are based on the following templates previously developed by the ELSI working group members:



The screenshot shows the top section of the EuroGCT website. It features a dark blue header with the EuroGCT logo on the left. To the right of the logo are three navigation items: 'Discover' with a dropdown arrow, 'Research Pathways' with a dropdown arrow, and 'About Us'. Below these are three sub-headers: 'Discover Gene and Cell Therapy', 'Bringing new therapies from the lab to patients', and 'Our team and partners'. A dashed line separates this header from a second dark blue bar containing two filter options: 'Condition' and 'Theme', both with dropdown arrows. Below this is a large purple-to-blue gradient section with the title 'Research Pathways' in large white font. Underneath the title is a paragraph: 'Bringing therapies from the lab bench to patients is a complex process. We've compiled resources and signposting to help guide through the development process - from legal regulations to best practices.' This is followed by another paragraph: 'Find here information and resources for researchers, regulators, and those interested in therapy development.' At the bottom of this section is a white button with the text 'Learn more about Research Pathways'. Below the entire screenshot is a blue hyperlink: <https://www.eurogct.org/research-pathways>

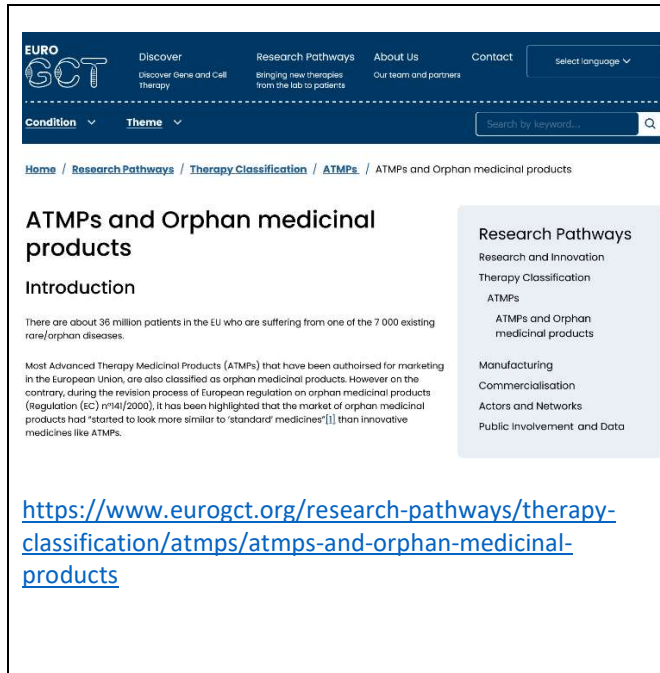
Full entry content	General Overview
<p>Table of contents</p> <ul style="list-style-type: none"> Introduction Stakeholders Definitions Challenges Opportunities and incentives Interactions with regulators Practical steps European Union Legislation European Union Guidelines Relevant literature More Acknowledgements 	<p>Table of contents</p> <ul style="list-style-type: none"> Introduction Stakeholders Definitions Challenges Opportunities and incentives Acknowledgements

The General overviews and the full entries contents regarding “Research & Innovation” that have been published on the [EuroGCT website](https://www.eurogct.org) are the following:

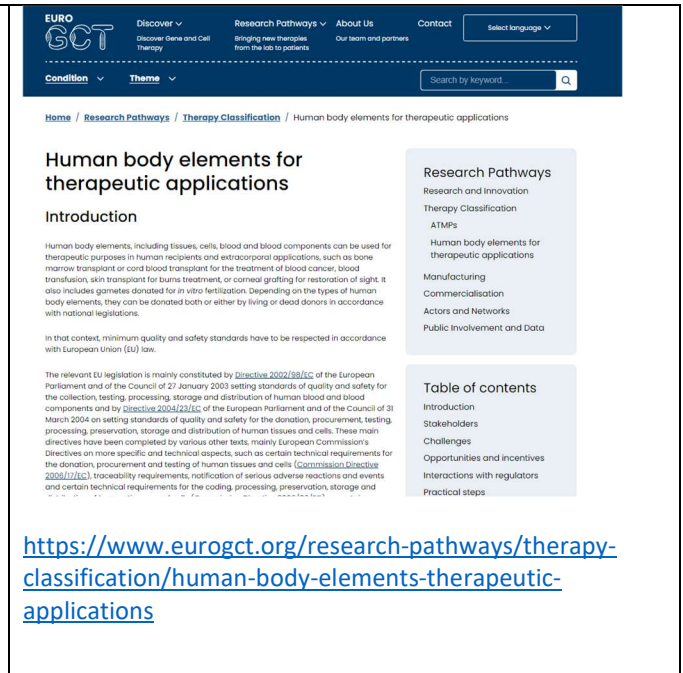
 <p>The screenshot shows the EuroGCT website interface for the 'Clinical trials' page. The navigation bar includes 'Discover', 'Research Pathways', 'About Us', and 'Contact'. The main content area features a breadcrumb trail: Home / Research Pathways / Research and Innovation / Clinical research / Clinical trials. The page title is 'Clinical trials' with a sub-section 'Introduction'. The text describes clinical trials as a type of clinical study performed to investigate the safety and efficacy of a medicinal product. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Clinical research, Clinical trials, Translational Science, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, and Public Involvement and Data. A URL is provided at the bottom: https://www.eurogct.org/research-pathways/research-and-innovation/clinical-research/clinical-trials</p>	 <p>The screenshot shows the EuroGCT website interface for the 'Translational Science' page. The navigation bar is identical to the previous page. The breadcrumb trail is: Home / Research Pathways / Research and Innovation / Translational Science. The page title is 'Translational Science' with a sub-section 'Introduction'. The text explains that translational science aims to bring predictivity and efficacy to the development and dissemination of interventions that improve human health. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Clinical research, Translational Science, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, and Public Involvement and Data. A URL is provided at the bottom: https://www.eurogct.org/research-pathways/research-and-innovation/translational-science</p>
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 <p>The screenshot shows the EuroGCT website interface for the 'Support for innovative medicines' development at the EMA level' page. The breadcrumb trail is: Home / Research Pathways / Research and Innovation / Early interactions regulators / Support innovative-0. The page title is 'Support for innovative medicines' development at the EMA level' with a sub-section 'Introduction'. The text discusses the European Medicines Agency's role in regulating medicines and supporting innovative products. A sidebar on the right lists 'Research Pathways' including Research and Innovation, test book page, Fundamental research, Clinical research, Translational Science, Funding, Incentives, Early Interactions with regulators, Support for innovative medicines' development, Support for innovative medicines' development at the EMA level, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, and Public Involvement and Data. A URL is provided at the bottom: https://www.eurogct.org/research-pathways/research-and-innovation/early-interactions-regulators/support-innovative-0</p>	 <p>The screenshot shows a sidebar from the EuroGCT website titled 'Research Pathways'. It lists various categories: Research and Innovation, test book page, Fundamental research, Clinical research, Translational Science, Funding, Incentives, Early Interactions with regulators, Support for innovative medicines' development, Support for innovative medicines' development at the EMA level, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, and Public Involvement and Data.</p>
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The General overviews and the full entries contents regarding “Therapy Classification” that have been published on the [EuroGCT website](https://www.eurogct.org) are the following:



The screenshot shows the top navigation bar with 'EURO GCT' logo, 'Discover', 'Research Pathways', 'About Us', and 'Contact' menus. Below the navigation is a breadcrumb trail: Home / Research Pathways / Therapy Classification / ATMPs / ATMPs and Orphan medicinal products. The main heading is 'ATMPs and Orphan medicinal products' with a sub-heading 'Introduction'. The text states: 'There are about 36 million patients in the EU who are suffering from one of the 7 000 existing rare/orphan diseases.' It also mentions that 'Most Advanced Therapy Medicinal Products (ATMPs) that have been authorised for marketing in the European Union, are also classified as orphan medicinal products.' A right-hand sidebar contains a 'Research Pathways' menu with options: Research and Innovation, Therapy Classification, ATMPs, ATMPs and Orphan medicinal products, Manufacturing, Commercialisation, Actors and Networks, and Public Involvement and Data. At the bottom, a URL is provided: <https://www.eurogct.org/research-pathways/therapy-classification/atmps/atmps-and-orphan-medical-products>



The screenshot shows the top navigation bar with 'EURO GCT' logo, 'Discover', 'Research Pathways', 'About Us', and 'Contact' menus. Below the navigation is a breadcrumb trail: Home / Research Pathways / Therapy Classification / Human body elements for therapeutic applications. The main heading is 'Human body elements for therapeutic applications' with a sub-heading 'Introduction'. The text states: 'Human body elements, including tissues, cells, blood and blood components can be used for therapeutic purposes in human recipients and extracorporeal applications, such as bone marrow transplant or cord blood transplant for the treatment of blood cancer, blood transfusion, skin transplant for burns treatment, or cornea grafting for restoration of sight, it also includes gametes donated for in vitro fertilization. Depending on the types of human body elements, they can be donated both or either by living or dead donors in accordance with national legislations.' It also mentions: 'In that context, minimum quality and safety standards have to be respected in accordance with European Union (EU) law.' The relevant EU legislation is mentioned as 'Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and by Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. These main directives have been completed by various other texts, mainly European Commission's Directives on more specific and technical aspects, such as certain technical requirements for the donation, procurement and testing of human tissues and cells (Commission Directive 2005/17/EC), traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells (Commission Directive 2005/18/EC)'. A right-hand sidebar contains a 'Research Pathways' menu with options: Research and Innovation, Therapy Classification, ATMPs, Human body elements for therapeutic applications, Manufacturing, Commercialisation, Actors and Networks, and Public Involvement and Data. Below it is a 'Table of contents' menu with options: Introduction, Stakeholders, Challenges, Opportunities and incentives, Interactions with regulators, and Practical steps. At the bottom, a URL is provided: <https://www.eurogct.org/research-pathways/therapy-classification/human-body-elements-therapeutic-applications>

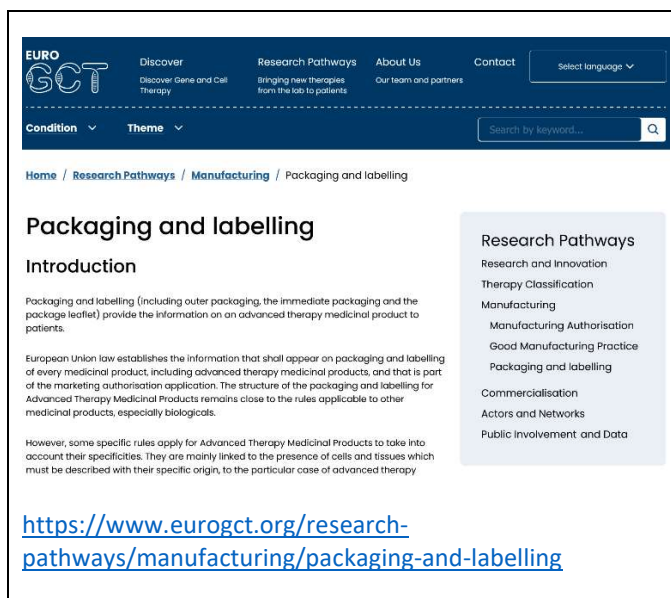
The General overviews and the full entries contents regarding “Manufacturing” that have been published on the [EuroGCT website](https://www.eurogct.org) are the following:



The screenshot shows the EuroGCT website interface for the 'Manufacturing Authorisation' page. The top navigation bar includes 'Discover', 'Research Pathways', 'About Us', and 'Contact', along with a language selection dropdown. Below the navigation is a search bar and breadcrumb trail: 'Home / Research Pathways / Manufacturing / Manufacturing Authorisation'. The main heading is 'Manufacturing Authorisation' with a sub-heading 'Introduction'. The introductory text states that manufacturing in the EU is subject to authorisation. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Therapy Classification, Manufacturing, Manufacturing Authorisation, Good Manufacturing Practice, Packaging and labelling, Commercialisation, Actors and Networks, and Public Involvement and Data. At the bottom, a URL is provided: <https://www.eurogct.org/research-pathways/manufacturing/manufacturing-authorisation>

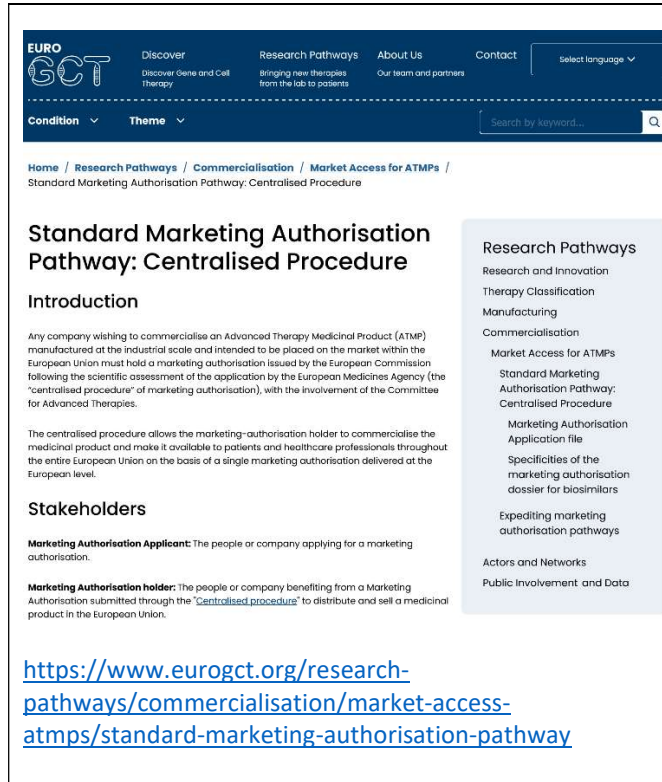


The screenshot shows the EuroGCT website interface for the 'Good Manufacturing Practice' page. The top navigation bar is identical to the previous page. The breadcrumb trail is: 'Home / Research Pathways / Manufacturing / Good Manufacturing Practice'. The main heading is 'Good Manufacturing Practice' with a sub-heading 'Introduction'. The introductory text explains that under EU law, manufacturing or importation requires authorisation. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Therapy Classification, Manufacturing, Manufacturing Authorisation, Good Manufacturing Practice, Packaging and labelling, Commercialisation, Actors and Networks, and Public Involvement and Data. At the bottom, a URL is provided: <https://www.eurogct.org/research-pathways/manufacturing/good-manufacturing-practice>



The screenshot shows the EuroGCT website interface for the 'Packaging and labelling' page. The top navigation bar is identical to the previous pages. The breadcrumb trail is: 'Home / Research Pathways / Manufacturing / Packaging and labelling'. The main heading is 'Packaging and labelling' with a sub-heading 'Introduction'. The introductory text explains that packaging and labelling provide information on advanced therapy medicinal products. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Therapy Classification, Manufacturing, Manufacturing Authorisation, Good Manufacturing Practice, Packaging and labelling, Commercialisation, Actors and Networks, and Public Involvement and Data. At the bottom, a URL is provided: <https://www.eurogct.org/research-pathways/manufacturing/package-and-labelling>

The General overviews and the full entries contents regarding “Commercialisation” that have been published on the [EuroGCT website](https://www.eurogct.org) are the following:



EURO GCT Discover Research Pathways About Us Contact Select language

Discover Gene and Cell Therapy Bringing new therapies from the lab to patients Our team and partners

Condition Theme Search by keyword

Home / Research Pathways / Commercialisation / Market Access for ATMPs / Standard Marketing Authorisation Pathway: Centralised Procedure

Standard Marketing Authorisation Pathway: Centralised Procedure

Introduction

Any company wishing to commercialise an Advanced Therapy Medicinal Product (ATMP) manufactured at the industrial scale and intended to be placed on the market within the European Union must hold a marketing authorisation issued by the European Commission following the scientific assessment of the application by the European Medicines Agency (the “centralised procedure” of marketing authorisation), with the involvement of the Committee for Advanced Therapies.

The centralised procedure allows the marketing-authorisation holder to commercialise the medicinal product and make it available to patients and healthcare professionals throughout the entire European Union on the basis of a single marketing authorisation delivered at the European level.

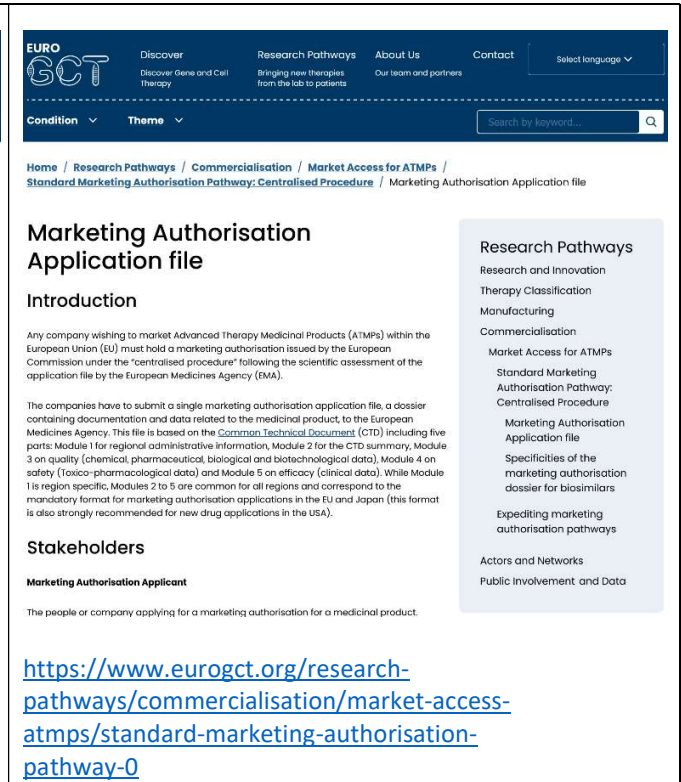
Stakeholders

Marketing Authorisation Applicant: The people or company applying for a marketing authorisation.

Marketing Authorisation holder: The people or company benefiting from a Marketing Authorisation submitted through the “Centralised procedure” to distribute and sell a medicinal product in the European Union.

<https://www.eurogct.org/research-pathways/commercialisation/market-access-atmps/standard-marketing-authorisation-pathway>

Research Pathways
Research and Innovation
Therapy Classification
Manufacturing
Commercialisation
Market Access for ATMPs
Standard Marketing Authorisation Pathway: Centralised Procedure
Marketing Authorisation Application file
Specificities of the marketing authorisation dossier for biosimilars
Expediting marketing authorisation pathways
Actors and Networks
Public Involvement and Data



EURO GCT Discover Research Pathways About Us Contact Select language

Discover Gene and Cell Therapy Bringing new therapies from the lab to patients Our team and partners

Condition Theme Search by keyword

Home / Research Pathways / Commercialisation / Market Access for ATMPs / Standard Marketing Authorisation Pathway: Centralised Procedure / Marketing Authorisation Application file

Marketing Authorisation Application file

Introduction

Any company wishing to market Advanced Therapy Medicinal Products (ATMPs) within the European Union (EU) must hold a marketing authorisation issued by the European Commission under the “centralised procedure” following the scientific assessment of the application file by the European Medicines Agency (EMA).

The companies have to submit a single marketing authorisation application file, a dossier containing documentation and data related to the medicinal product, to the European Medicines Agency. This file is based on the **Common Technical Document (CTD)** including five parts: Module 1 for regional administrative information, Module 2 for the CTD summary, Module 3 on quality (chemical, pharmaceutical, biological and biotechnological data), Module 4 on safety (toxicological data) and Module 5 on efficacy (clinical data). While Module 1 is region specific, Modules 2 to 5 are common for all regions and correspond to the mandatory format for marketing authorisation applications in the EU and Japan (this format is also strongly recommended for new drug applications in the USA).

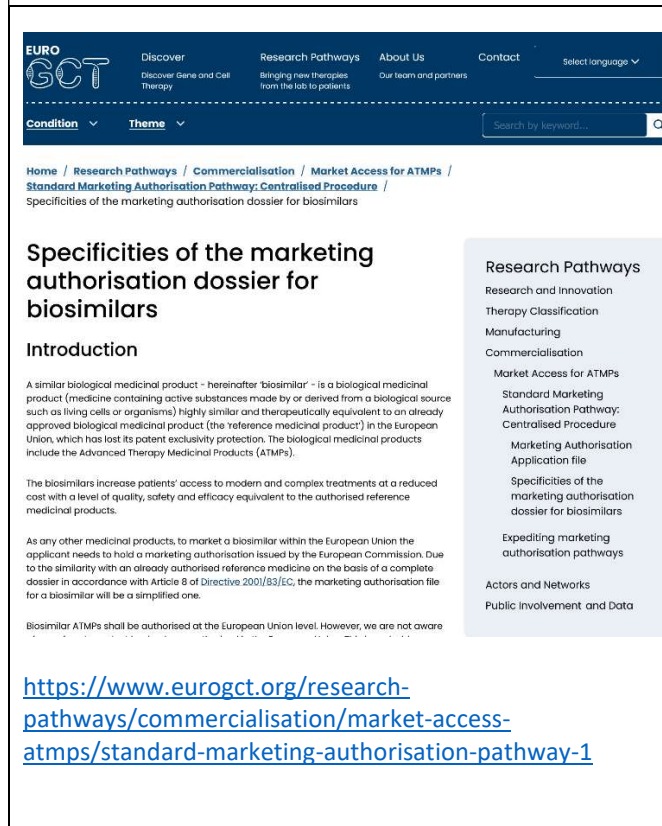
Stakeholders

Marketing Authorisation Applicant

The people or company applying for a marketing authorisation for a medicinal product.

<https://www.eurogct.org/research-pathways/commercialisation/market-access-atmps/standard-marketing-authorisation-pathway-0>

Research Pathways
Research and Innovation
Therapy Classification
Manufacturing
Commercialisation
Market Access for ATMPs
Standard Marketing Authorisation Pathway: Centralised Procedure
Marketing Authorisation Application file
Specificities of the marketing authorisation dossier for biosimilars
Expediting marketing authorisation pathways
Actors and Networks
Public Involvement and Data



EURO GCT Discover Research Pathways About Us Contact Select language

Discover Gene and Cell Therapy Bringing new therapies from the lab to patients Our team and partners

Condition Theme Search by keyword

Home / Research Pathways / Commercialisation / Market Access for ATMPs / Standard Marketing Authorisation Pathway: Centralised Procedure / Specificities of the marketing authorisation dossier for biosimilars

Specificities of the marketing authorisation dossier for biosimilars

Introduction

A similar biological medicinal product - hereinafter ‘biosimilar’ - is a biological medicinal product (medicine containing active substances made by or derived from a biological source such as living cells or organisms) highly similar and therapeutically equivalent to an already approved biological medicinal product (the ‘reference medicinal product’) in the European Union, which has lost its patent exclusivity protection. The biological medicinal products include the Advanced Therapy Medicinal Products (ATMPs).

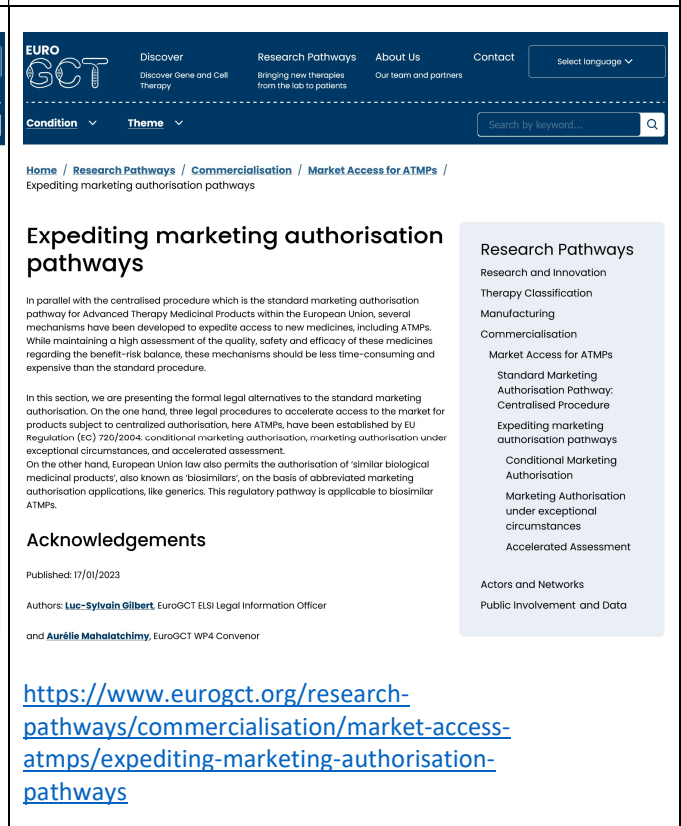
The biosimilars increase patients’ access to modern and complex treatments at a reduced cost with a level of quality, safety and efficacy equivalent to the authorised reference medicinal products.

As any other medicinal products, to market a biosimilar within the European Union the applicant needs to hold a marketing authorisation issued by the European Commission. Due to the similarity with an already authorised reference medicine on the basis of a complete dossier in accordance with Article 8 of Directive 2001/83/EC, the marketing authorisation file for a biosimilar will be a simplified one.

Biosimilar ATMPs shall be authorised at the European Union level. However, we are not aware

<https://www.eurogct.org/research-pathways/commercialisation/market-access-atmps/standard-marketing-authorisation-pathway-1>

Research Pathways
Research and Innovation
Therapy Classification
Manufacturing
Commercialisation
Market Access for ATMPs
Standard Marketing Authorisation Pathway: Centralised Procedure
Marketing Authorisation Application file
Specificities of the marketing authorisation dossier for biosimilars
Expediting marketing authorisation pathways
Actors and Networks
Public Involvement and Data



EURO GCT Discover Research Pathways About Us Contact Select language

Discover Gene and Cell Therapy Bringing new therapies from the lab to patients Our team and partners

Condition Theme Search by keyword

Home / Research Pathways / Commercialisation / Market Access for ATMPs / Expediting marketing authorisation pathways

Expediting marketing authorisation pathways

In parallel with the centralised procedure which is the standard marketing authorisation pathway for Advanced Therapy Medicinal Products within the European Union, several mechanisms have been developed to expedite access to new medicines, including ATMPs. While maintaining a high assessment of the quality, safety and efficacy of these medicines regarding the benefit-risk balance, these mechanisms should be less time-consuming and expensive than the standard procedure.

In this section, we are presenting the formal legal alternatives to the standard marketing authorisation. On the one hand, three legal procedures to accelerate access to the market for products subject to centralized authorisation, here ATMPs, have been established by EU Regulation (EC) 726/2004: conditional marketing authorisation, marketing authorisation under exceptional circumstances, and accelerated assessment.

On the other hand, European Union law also permits the authorisation of ‘similar biological medicinal products’, also known as ‘biosimilars’, on the basis of abbreviated marketing authorisation applications, like generics. This regulatory pathway is applicable to biosimilar ATMPs.


Acknowledgements

Published: 17/01/2023

Authors: **Luc-Sylvain Gilbert**, EuroGCT ELSI Legal Information Officer
and **Aurélié Mahalatchimy**, EuroGCT WP4 Convenor

<https://www.eurogct.org/research-pathways/commercialisation/market-access-atmps/expediting-marketing-authorisation-pathways>

Research Pathways
Research and Innovation
Therapy Classification
Manufacturing
Commercialisation
Market Access for ATMPs
Standard Marketing Authorisation Pathway: Centralised Procedure
Expediting marketing authorisation pathways
Conditional Marketing Authorisation
Marketing Authorisation under exceptional circumstances
Accelerated Assessment
Actors and Networks
Public Involvement and Data


Discover
Discover Gene and Cell
Therapy
Research Pathways
Bringing new therapies
from the lab to patients
About Us
Our team and partners
Contact
Select language ▾

Condition ▾ Theme ▾
Search by keyword...

Home / Research Pathways / Commercialisation / Market Access for ATMPs / Expediting marketing authorisation pathways / Conditional Marketing Authorisation

Conditional Marketing Authorisation

Introduction

Any company wishing to market Advanced Therapy Medicinal Products (ATMPs) within the European Union must hold a marketing authorisation issued by the European Commission under the "centralised procedure" following the scientific assessment of the application by the European Medicines Agency, (Article 3(1) and Annex Ia. of the Regulation (EC) No 726/2004)

Different options are offered by European Union law for being granted a marketing authorisation through specific regulatory mechanisms to facilitate early patient access to medicinal products, including Advanced Therapy Medicinal Products, while maintaining a high assessment of the quality of these medicines, and of their safety and efficacy regarding the benefit/risk balance.

When an Advanced Therapy Medicinal Product addresses an unmet medical need of patients, a conditional marketing authorisation may be granted on the basis of less comprehensive data than usually required. In this case, the benefit of immediate availability of the medicine to patients shall outweigh the risk inherent in the fact that additional data are still required. The comprehensive data will be further provided by the applicant within a precise timeframe post authorisation. (Article 14-a of the Regulation (EC) No 726/2004).

Stakeholders


Conditional Marketing Authorisation Applicant: The people or company applying to the

Research Pathways

- Research and Innovation
- Therapy Classification
- Manufacturing
- Commercialisation
- Market Access for ATMPs
- Standard Marketing Authorisation Pathway;
- Centralised Procedure
- Expediting marketing authorisation pathways
- Conditional Marketing Authorisation
- Marketing Authorisation under exceptional circumstances
- Accelerated Assessment

- Actors and Networks
- Public Involvement and Data

<https://www.eurogct.org/research-pathways/commercialisation/market-access-atmps/expediting-marketing-authorisation-0>


Discover
Discover Gene and Cell
Therapy
Research Pathways
Bringing new therapies
from the lab to patients
About Us
Our team and partners
Contact
Select language ▾

Condition ▾ Theme ▾
Search by keyword...

Home / Research Pathways / Commercialisation / Market Access for ATMPs / Expediting marketing authorisation pathways / Marketing Authorisation under exceptional circumstances

Marketing Authorisation under exceptional circumstances

Introduction

Any company wishing to market Advanced Therapy Medicinal Products (ATMPs) within the European Union must hold a marketing authorisation issued by the European Commission.

Different options are offered by the European Union for being granted a marketing authorisation through specific regulatory mechanisms to facilitate early patient access to medicinal products, including ATMPs, while maintaining a high assessment of the quality of these medicines, and of their safety and efficacy regarding the benefit-risk balance.

A marketing authorisation under exceptional circumstances for medicinal products may be granted when the applicant is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indication to be treated is too rare, the present state of scientific knowledge is insufficient to provide comprehensive information, or it would be unethical to collect this information. (Article 14(b) of Regulation (EC) No 726/2004, current version with amendments) and (Annex I Part II 6 of Directive 2001/83/EC, current version with amendments)

This procedure is particularly relevant for orphan medicinal products and rare diseases if the criteria considered for the approval under exceptional circumstances are fulfilled.


By January 2023, 3 ATMPs were granted a marketing authorisation under exceptional circumstances in the European Union: *Glybera**, *Upstazor**, and *Eboxyl**.

Research Pathways

- Research and Innovation
- Therapy Classification
- Manufacturing
- Commercialisation
- Market Access for ATMPs
- Standard Marketing Authorisation Pathway;
- Centralised Procedure
- Expediting marketing authorisation pathways
- Conditional Marketing Authorisation
- Marketing Authorisation under exceptional circumstances
- Accelerated Assessment

- Actors and Networks
- Public Involvement and Data

<https://www.eurogct.org/research-pathways/commercialisation/market-access-atmps/expediting-marketing-authorisation-1>


Discover
Discover Gene and Cell
Therapy
Research Pathways
Bringing new therapies
from the lab to patients
About Us
Our team and partners
Contact
Select language ▾

Condition ▾ Theme ▾
Search by keyword...

Home / Research Pathways / Commercialisation / Market Access for ATMPs / Expediting marketing authorisation pathways / Accelerated Assessment

Accelerated Assessment

Introduction

Any company wishing to market Advanced Therapy Medicinal Products (ATMPs) within the European Union must hold a marketing authorisation issued by the European Commission. Different options are offered by the European Union for being granted a marketing authorisation through specific regulatory mechanisms to facilitate early patient access to medicinal products, including Advanced Therapy Medicinal Products.

The accelerated assessment is a procedural tool to reduce the centralised procedure review period of a marketing authorisation applicant from 210 to a maximum of 150 days, excluding clock stops. An applicant may request an accelerated assessment for medicinal products if they are of major public health interest, in particular from the viewpoint of therapeutic innovation. The request shall be duly substantiated and its acceptance will be decided by the Committee for Medicinal Products for Human Use (CHMP), (Article 14 § 9 of Regulation (EC) No 726/2004). Nevertheless, the decision on accelerated assessment has no impact on the future CHMP opinion on whether a marketing authorisation should be granted.

The accelerated assessment is particularly adapted to Advanced Therapy Medicinal Products, one of whose characteristics is to be innovative.

Stakeholders


Accelerated Assessment Applicant: The people or pharmaceutical company applying to reduce the EMA's CHMP timeframe to review a marketing authorisation application for a medicinal product expected to be of major public health interest. If the CHMP accepts the

Research Pathways

- Research and Innovation
- Therapy Classification
- Manufacturing
- Commercialisation
- Market Access for ATMPs
- Standard Marketing Authorisation Pathway;
- Centralised Procedure
- Expediting marketing authorisation pathways
- Conditional Marketing Authorisation
- Marketing Authorisation under exceptional circumstances
- Accelerated Assessment

- Actors and Networks
- Public Involvement and Data

<https://www.eurogct.org/research-pathways/commercialisation/market-access-atmps/expediting-marketing-authorisation-2>


Discover
Discover Gene and Cell
Therapy
Research Pathways
Bringing new therapies
from the lab to patients
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Home / Research Pathways / Commercialisation / Advertising

Advertising

Introduction

Advertising of medicinal products, including ATMPs, is mainly regulated by National laws apart from minimums binding requirements established by EU law.

Nevertheless, those minimum requirements provided for the main rules in the field of advertising of ATMPs:

- The advertising of ATMPs to the general public is prohibited.
- The advertising of ATMPs without marketing authorisation is prohibited.
- The advertising of ATMPs to persons qualified to prescribe or supply medicinal products is allowed under strict conditions. These conditions mainly include minimum information to be included in advertising, obligations for medical sales representatives, obligations for marketing authorisation holders, limitations of in-documents to persons qualified to prescribe or supply medicinal products.

In addition, EU law imposes several obligations on Member States, especially to establish adequate and effective methods to monitor the advertising of medicinal products, to enable the courts or administrative authorities to act in the public interest in case of misleading advertising, and to determine and impose penalties in case of infringements of EU law on advertising of medicinal products.

Thus, Member States are free on the choices of means to respect their obligations, and apart from the common EU requirements, the regulation of advertising of ATMPs may differ according to each national Member States, e.g. prior vetting or not to monitor the advertising of medicinal products.

Stakeholders

Advertiser: the person or organization who is organising the advertising of a medicinal product it is commercialising.

Research Pathways

- Research and Innovation
- Therapy Classification
- Manufacturing
- Commercialisation
- Market Access for ATMPs
- Advertising

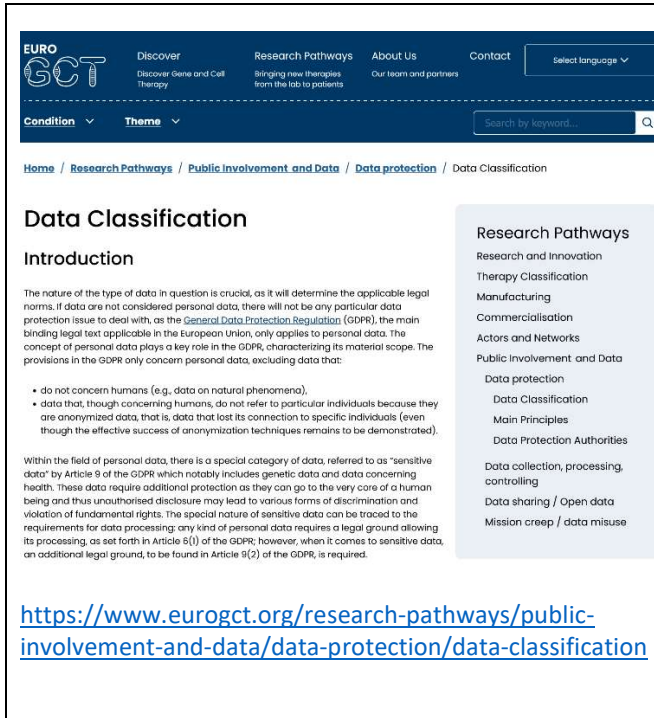
- Actors and Networks
- Public Involvement and Data

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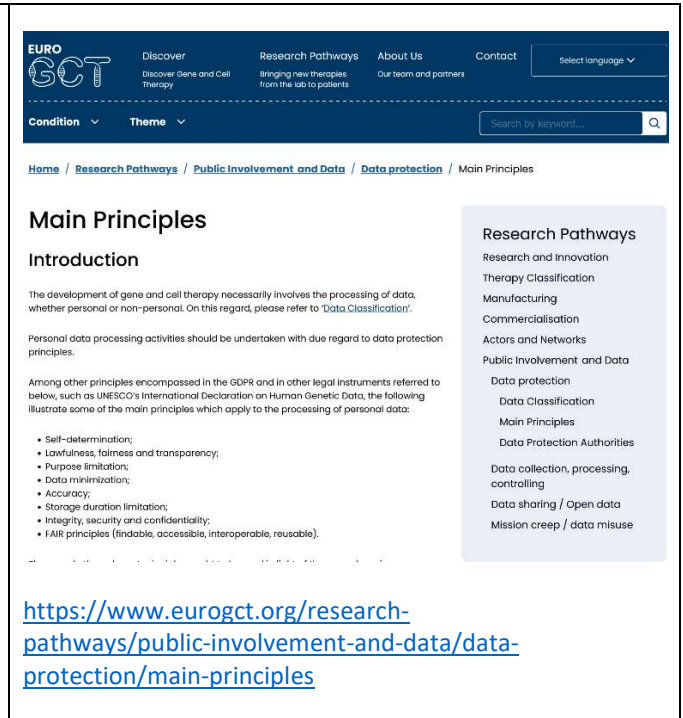
- Introduction
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- Definitions
- Challenges
- Opportunities and incentives
- Interactions with regulators
- Practical steps
- European Union Legislation
- European Union Guidance
- Acknowledgements

<https://www.eurogct.org/research-pathways/commercialisation/advertising>

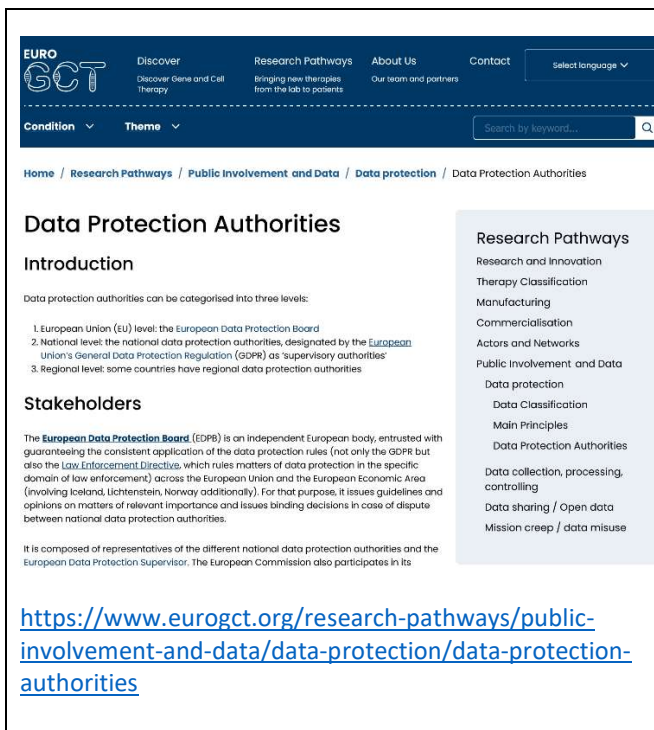
The General overviews and the full entries contents regarding “Patient Involvement & Data” that have been published on the [EuroGCT website](https://www.eurogct.org) are the following:



The screenshot shows the 'Data Classification' page on the EuroGCT website. The navigation bar includes 'Discover', 'Research Pathways', 'About Us', and 'Contact'. The breadcrumb trail is: Home / Research Pathways / Public Involvement and Data / Data protection / Data Classification. The main heading is 'Data Classification' with an 'Introduction' sub-heading. The text explains that the nature of data is crucial for legal norms and that the General Data Protection Regulation (GDPR) applies to personal data. It lists key points: data not concerning humans, data concerning humans but anonymized, and sensitive data. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, Public Involvement and Data, Data protection, Data Classification, Main Principles, Data Protection Authorities, Data collection, processing, controlling, Data sharing / Open data, and Mission creep / data misuse. A URL is provided at the bottom: <https://www.eurogct.org/research-pathways/public-involvement-and-data/data-protection/data-classification>



The screenshot shows the 'Main Principles' page on the EuroGCT website. The navigation bar is the same as the previous page. The breadcrumb trail is: Home / Research Pathways / Public Involvement and Data / Data protection / Main Principles. The main heading is 'Main Principles' with an 'Introduction' sub-heading. The text states that the development of gene and cell therapy involves processing of data and that personal data processing should be undertaken with due regard to data protection principles. It lists principles such as self-determination, lawfulness, fairness and transparency, purpose limitation, data minimization, accuracy, storage duration limitation, integrity, security and confidentiality, and FAIR principles. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, Public Involvement and Data, Data protection, Data Classification, Main Principles, Data Protection Authorities, Data collection, processing, controlling, Data sharing / Open data, and Mission creep / data misuse. A URL is provided at the bottom: <https://www.eurogct.org/research-pathways/public-involvement-and-data/data-protection/main-principles>



The screenshot shows the 'Data Protection Authorities' page on the EuroGCT website. The navigation bar is the same. The breadcrumb trail is: Home / Research Pathways / Public Involvement and Data / Data protection / Data Protection Authorities. The main heading is 'Data Protection Authorities' with an 'Introduction' sub-heading. The text states that data protection authorities can be categorized into three levels: European Union (EU) level, National level, and Regional level. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, Public Involvement and Data, Data protection, Data Classification, Main Principles, Data Protection Authorities, Data collection, processing, controlling, Data sharing / Open data, and Mission creep / data misuse. A URL is provided at the bottom: <https://www.eurogct.org/research-pathways/public-involvement-and-data/data-protection/data-protection-authorities>



The screenshot shows the 'Data collection, processing, controlling' page on the EuroGCT website. The navigation bar is the same. The breadcrumb trail is: Home / Research Pathways / Public Involvement and Data / Data collection, processing, controlling. The main heading is 'Data collection, processing, controlling' with an 'Introduction' sub-heading. The text explains that the development of medical research and healthcare is guided by the exploitation of health data, which is sensitive and requires strict regulation to protect individual rights. A sidebar on the right lists 'Research Pathways' including Research and Innovation, Therapy Classification, Manufacturing, Commercialisation, Actors and Networks, Public Involvement and Data, Data protection, Data collection, processing, controlling, Data sharing / Open data, and Mission creep / data misuse. A URL is provided at the bottom: <https://www.eurogct.org/research-pathways/public-involvement-and-data/data-collection-processing-controlling>

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Condition Theme

Home / Research Pathways / Public Involvement and Data / Data sharing / Open data

Data sharing / Open data

Introduction

Data sharing is an important activity in scientific research for allowing various analyses and maximising the potential of the data for serving advances in health knowledge and innovation. Data sharing allows initial research purposes to be achieved and data reused for other research purposes, including replication studies.

Collaborative research and scientific publication requires sharing data as part of research integrity duty.

Data sharing can intervene at different time of the research, either during a research project (research data sharing) or after a research project (research results sharing). While both aspects have similarities in terms of rules to respect, open data practices are specific data sharing concerning research results that will be dealt in the dedicated section "Open data". Nevertheless, both sections are complementary and shall be read as a whole.

Of note, the sharing of (human) biological samples for research analyses shall be considered

Research Pathways

- Research and Innovation
- Therapy Classification
- Manufacturing
- Commercialisation
- Actors and Networks
- Public Involvement and Data
- Data protection
- Data collection, processing, controlling
- Data sharing / Open data
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<https://www.eurogct.org/research-pathways/public-involvement-and-data/data-sharing-open-data>

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Condition Theme

Home / Research Pathways / Public Involvement and Data / Mission creep / data misuse

Mission creep / data misuse

Introduction

Data misuse, also known as mission creep, in the context of this research pathway entry - goes to the core of (mis)using a patient's personal health data, beyond the purpose(s) for which it was collected. Whilst it may sometimes be closely related to function creep, a very well-known phenomenon in the field of science and technology studies (describing an instance where systems or technologies expand beyond their initial scope of deployment) - mission creep or data misuse is more focused on the legitimacy and purposes for which patient data is collected, used, stored, and processed.

The findings of a [Special EuroBarometer on Data Protection](#) demonstrated that citizens were often worried about how they could control their own data. Hence, European Union (EU) law establishes the relevant legislation to ensure the proper use and protection of patients' rights to privacy when their relevant health data is collected and processed. This is in addition to the Charter of Fundamental Rights of the European Union, addressing patients' concerns regarding privacy, data sharing and accessing their own health data, is necessary in a healthcare context (including care given through eHealth or mHealth), or in a cross-border

Research Pathways

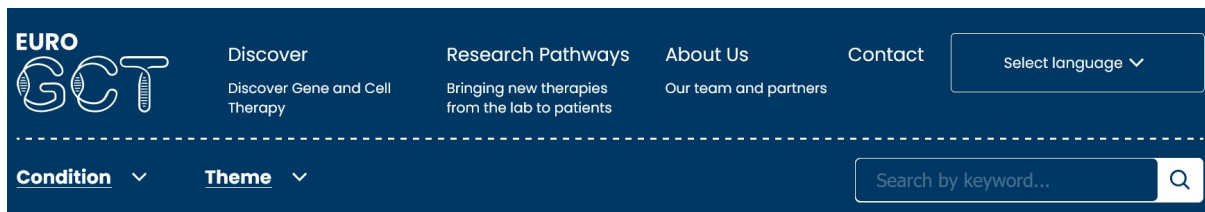
- Research and Innovation
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<https://www.eurogct.org/research-pathways/public-involvement-and-data/mission-creep-data-misuse>

Actors and Networks

The 'Actors and Networks' contribution to the mapping of the European landscape related to gene and cell therapy is currently ongoing. This mapping encompasses multiple levels of actors and networks: international, national and regional ones. Some actors and networks have already been identified in the 'research pathways' entries and sub-entries in the 'Stakeholders' and 'Definition' sections and published on the [EuroGCT website](#). The regulatory actors and networks landscape mapping will be regularly completed and updated and published alongside the completion of the entries and sub-entries contents.

The 'Actors and Networks' contents published on the [EuroGCT website](#) are the following:



The screenshot shows the top navigation bar of the EuroGCT website. It features the EURO GCT logo on the left, followed by navigation links: 'Discover' (Discover Gene and Cell Therapy), 'Research Pathways' (Bringing new therapies from the lab to patients), 'About Us' (Our team and partners), and 'Contact'. There is a 'Select language' dropdown menu. Below the navigation bar, there are filters for 'Condition' and 'Theme', and a search bar with the placeholder text 'Search by keyword...'.

[Home](#) / [Research Pathways](#) / Actors and Networks

Actors and Networks

The thriving field of gene and cell therapy is supported by a large community of academic, clinical, translational, industrial and patient organisations. This section maps the stakeholders and their activities in Europe and beyond.

Actors Activity Map

The EuroGCT project will develop a searchable map of the Advanced Therapy Medicinal Products (ATMP) landscape in Europe, including activity by stakeholders including academic, clinical, translational, industrial (contract research organisations, manufacturing facilities, biotech, pharma) and patient organisations.

In the meantime, please see:

ESGCT's Gene and Cell Therapy community heatmap and GMP facilities

[ESGCT heatmap](#)



ATMP Sweden's ATMP map

[ATMP Sweden map](#)



Research Pathways

- Research and Innovation
- Therapy Classification
- Manufacturing
- Commercialisation
- Actors and Networks
- Public Involvement and Data

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- Actors Activity Map
- Networks
- National Medicines Agencies
- National Health Technology Assessment (HTA) Bodies
- Research Ethics Committees
- Training Providers

Networks

Find here a list of societies, associations, regional, national and international networks for gene and cell therapy.

Explore links to EuroGCT's 47 partner organisations, networks, and societies representing gene and cell therapy researchers across Europe.

EuroGCT Partners



National and International Societies

- International Society for Cell & Gene Therapy (ISCT)
- The International Society for Stem Cell Research (ISSCR)
- European Society of Gene & Cell Therapy (ESGCT)
- European Society of Human Genetics (ESHG)
- American Society of Gene & Cell Therapy (ASGCT)
- American Society of Human Genetics (ASHG)
- Australasian Gene and Cell Therapy Society (AGCTS)
- British Society for Gene and Cell Therapy (BSGCT)
- French Society of Cellular and Gene Therapy (SFTCG)
- German Gene Therapy Society (DGGT)
- Netherlands Society of Gene and Cell Therapy (NVGCT)
- Swedish Society of Gene and Cell Therapy (SSGCT)
- Society for Inherited Metabolic Disorders (SIMD)

<https://www.eurogct.org/research-pathways/actors-and-networks>

Regional Networks

- Alliance for Regenerative Medicine (ARM)
- ATMP Sweden
- ATMP manufacture community (amc)
- ATMP Manufacturing Ireland
- Advanced Therapy Network (ATN)
- BioPhorum Cell and Gene Therapy (CGT)
- Deutsche Gesellschaft für Gentherapie e.V. (DG-GT)
- European Federation of Pharmaceutical Industries and Associations (EFPIA)
- European Patients' Forum (EPF)
- European Joint Programme on Rare Diseases (EJP RD)
- European Society for Blood and Marrow Transplantation (EBMT)
- EURORDIS-Rare Diseases Europe
- EuroStemCell
- Forum for Innovative Regenerative Medicine (FIRM)
- The Global Alliance for iPSC Therapies (GAIT)
- Genetic Alliance UK
- HESI Cell Therapy—TRACKing, Circulation, and Safety (CT-TRACS) committee
- International Consortium for Personalised Medicine (ICPerMed)
- International Rare Diseases Research Consortium (IRDiRC)
- Stem Cells Australia
- The Advanced Therapy Treatment Centres (ATTC) Network
- The Association of the British Pharmaceutical Industry (ABPI)
- The International Alliance for Biological Standardization (IABS)
- UK BioIndustry Association (BIA)

<https://www.eurogct.org/research-pathways/actors-and-networks>

EU Projects

- Human Pluripotent Stem Cell Registry (hPSCreg)
- COST Action HAPLO-IPS
- AUTOSTEM
- AIDPATH
- RESTORE
- EJP RD – European Joint Programme on Rare Diseases
- COST Action CorEuStem – The European Network for Stem Cell Core Facilities
- GAPP JOINT ACTION – Co-Funded by the Health Programme of the EU
- i-BioLex – Fragmentation and defragmentation of the law on biomedical innovations
- SIENNA Project
- Strengthening Training of Academia in Regulatory Science (CSA STARS)
- T2Evolve – a consortium working to accelerate the process of developing CAR T-cell therapy in the European Union (EU)
- A list of EU-Funded actions on substances of human origin can be found [here](#)

<https://www.eurogct.org/research-pathways/actors-and-networks>

National Medicines Agencies

- Austria Austrian Agency for Health and Food Safety
- Belgium Federal Agency for Medicines and Health Products (FAMHP)
- Bulgaria Bulgarian Drug Agency
- Croatia Agency for medicinal products and medical devices of Croatia
- Cyprus Ministry of Health – Pharmaceutical Services
- Czechia State Institute for Drug Control
- Denmark Danish Medicines Agency
- Estonia State Agency of Medicines
- Finland Finnish Medicines Agency
- France National Agency for the Safety of Medicine and Health Products
- Germany Federal Institute for Drugs and Medical Devices
- Germany Paul Ehrlich Institute
- Greece National Organization for Medicines
- Hungary National Institute of Pharmacy and Nutrition
- Iceland Icelandic Medicines Agency
- Ireland Health Products Regulatory Authority (HPRA)
- Italy Italian Medicines Agency (AIFA)
- Latvia State Agency of Medicines
- Liechtenstein Office of Health / Department of Pharmaceuticals
- Lithuania State Medicines Control Agency
- Luxembourg Ministry of Health
- Malta Malta Medicines Authority (MMA)
- Netherlands Medicines Evaluation Board
- Netherlands Healthcare and Youth Care Inspectorate, Ministry of Health, Welfare and Sport
- Norway Norwegian Medicines Agency (NoMA)
- Poland Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
- Poland Chief Pharmaceutical Inspectorate
- Portugal National Authority of Medicines and Health Products (INFARMED)
- Romania National Authority of Medicines and Medical Devices of Romania
- Slovakia State Institute for Drug Control
- Slovenia Agency for Medicinal Products and Medical Devices of the Republic of Slovenia
- Spain Spanish Agency for Medicines and Health Products
- Sweden Swedish Medical Products Agency

<https://www.eurogct.org/research-pathways/actors-and-networks>

Other National Competent Authorities in EU

- List of Competent Authorities for Tissues and Cells can be found [here](#)
- List Competent Authorities for Blood and Blood Components can be found [here](#)

National Health Technology Assessment (HTA) Bodies

- Austria [Austrian Institute for Health Technology Assessment \(AIHTA\)](#)
- Belgium [Belgian Health Care Knowledge Centre \(KCE\)](#)
- England [The National Institute for Health and Care Excellence \(NICE\)](#)
- France [Haute Autorité de Santé \(HAS\)](#)
- Hungary [National Institute of Pharmacy and Nutrition \(OGYÉI\)](#)
- Germany [Gemeinsamer Bundesausschuss \(GBA\)](#)
- Germany [The independent Institute for Quality and Efficiency in Health Care \(IQWiG\)](#)
- Ireland [The National Centre for Pharmacoeconomics \(NCPe\)](#)
- Italy [Italian Medicines Agency \(AIFA\)](#)
- Netherlands [The National Health Care Institute \(ZIN\)](#)
- Norway [Norwegian Medicines Agency \(NoMA\)](#)
- Portugal [National Authority of Medicines and Health Products \(INFARMED\)](#)
- Scotland [Scottish Medicines Consortium \(SMC\)](#)
- Spain [Spanish Agency for Medicines and Health Products \(AEMPS\)](#)
- Sweden [Tandvårds- och läkemedelsförmånsverket \(TLV\)](#)

<https://www.eurogct.org/research-pathways/actors-and-networks>

Research Ethics Committees

- [European Network of Research Ethics Committees \(EUREC\)](#)
- National associations or national bodies of RECs can be found at: [EUREC - National information](#)

Training Providers

Catalogued educational resources and webinars on gene and cell therapies can be found by following the links below:



ATMP Research & Development

[Read More](#)



Patient Education and Engagement

[Read More](#)



Other Training Resources

[Read More](#)

<https://www.eurogct.org/research-pathways/actors-and-networks>