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of Research, Technology
and Space

GCT
National Strategy
Gene- and Cell-based Therapies

National Strategy for Gene- and Cell-based Therapies

A multi-stakeholder strategy
Coordinated by the Berlin Institute of Health at Charité
Commissioned by the former Federal Ministry of Education and Research
(BMBF, now BMFTR)

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Executive Summary

Starting situation

Gene- and cell-based therapies (GCTs) are a central field of innovation in biomedical research and clinical care. They offer highly promising approaches for the treatment of diseases that have remained incurable to date and can also support regenerative processes. At the same time, there is a pressing need for research to improve efficiency, safety and availability. Although Germany is a leader in basic research and in relation to certain technological developments, it faces specific challenges when it comes to implementation in medical care. This could lead to a situation in which Germany loses pace with its international counterparts and patient care is compromised. Other countries such as the USA, China, the United Kingdom, France, Italy and Spain have already established effective ecosystems for the development of GCTs. While Germany has an opportunity to play a leading role, achieving this will require more effective interaction and linking of various stakeholders in the fields of science, business, politics and society.

Objectives and approach

The National Strategy for GCTs strives to provide a holistic concept for Germany, integrating and networking all elements of the value chain – from basic research through to healthcare provision. Its foremost objective is to promote patient welfare through GCTs, offering new prospects for seriously ill patients who otherwise may not have effective treatment options. The National Strategy for GCTs has been developed in a process characterized by extensive stakeholder engagement, integrating different perspectives from the spheres of science, business, politics and society as well as from patients. Over 150 experts contributed to the development of the eight topics identified in the National Strategy. Detailed targets have been formulated and specific measures recommended for each of these fields. Commissioned by the former Federal Ministry of Education and Research (BMBF, now Federal Ministry of Research, Technology and Space, Bundesministerium für Forschung, Technologie und Raumfahrt - BMFTR) and coordinated by the Berlin Institute of Health at Charité (BIH), the National Strategy emphasizes the enormous potential of GCTs for patient care, the healthcare industry and Germany as a key location for the pharmaceutical industry, for example with the potential to create new jobs in a highly innovative, pioneering field.

Overview of the topics

The National Strategy for GCTs has been developed through collaboration between multiple stakeholders. It comprises the following eight topics:

Topic I: Stakeholder networking and support

This topic aims to promote the development and application of GCTs through national networking, collaboration between science, healthcare, industry and politics, and international links. Measures include establishing a governance structure to oversee implementation of the National Strategy, setting up a national GCT map and expanding communications with regulators, patients' organizations, investors and other stakeholders. Establishing and stabilizing this governance structure, e. g., via formation of an expert council to advise policymakers and by preparing an annual report, should facilitate the strategic long-term implementation of measures.

Topic II: Training and development of skills

Well-trained specialists are essential for the successful development and use of GCTs. Measures include creating training programs for academic and non-academic occupational groups, implementing interdisciplinary Master's and doctoral programs and establishing national training centers. These measures are intended to help tackle the shortage of qualified staff and accelerate the urgently needed translation of GCTs into medical care in Germany.

Topic III: Technology transfer

The technology transfer should ensure that the results of biomedical research are applied for the benefit of patients, the economy and society. This requires a coherent translation chain, from patenting through to clinical proof of concept. Measures include improving the framework conditions for identifying and realizing innovative potential, providing holistic consultancy and assessment for transfer projects, recognizing transfer services as part of scientific reputation-building and making it easier to exploit the potential of scientific output.

Topic IV: Standards, norms and regulatory framework

Regulatory conditions have to be urgently improved to enhance Germany's innovative strength. Measures include defragmenting the regulatory environment for GCTs, boosting resources at the central federal higher authority, improving EU legislation and protecting, preserving and expanding opportunities for academic research and innovation, above all by introducing a "sandbox" system.

Topic V: Quality and capacity of GMP production

Ensuring the quality and performance of production capacities in line with good manufacturing practice (GMP) in Germany will be crucial to the country's efforts to remain internationally competitive. This includes establishing and expanding GMP infrastructure in line with demand, especially for starting materials and complex GCT products, ensuring the availability of qualified professionals, increasing GMP production efficiency and accelerating GMP production. Furthermore, translational processes must be optimized through development and risk-based streamlining of structures and framework conditions. A central GCT-GMP and regulatory affairs committee should be responsible for driving forward attainment of these targets.

Topic VI: Research and development

It is essential that the research and translation infrastructure is improved. Decentralized hubs should be made available to the scientific community and production capacities should be expanded. Incubators for start-ups should foster innovations, while testing facilities should ensure the efficacy and safety of innovations. New funding formats and collaborations between industry and academia should accelerate the transfer of research results to clinical studies, while the introduction of GMP-light procedures and generally swifter approval procedures should strengthen Germany as a location for research and innovation. Integrating patients at an early stage will ensure that due consideration is given to their needs.

Topic VII: Marketing authorization and transition to patient care

Prompt access to high-quality GCTs can significantly improve the chances of survival and quality of life for the most seriously ill patients. Optimizing the authorization and use of GCTs will require amendments and new structures. Establishing interdisciplinary GCT treatment facilities and close collaboration between research and healthcare will be vital. In addition, treatment quality must be ensured by providing training, standardizing diagnostic processes and introducing therapy decision boards. Remuneration for the activities involved must be ensured through adjusted remuneration models. More flexible reimbursement and healthcare models should create greater latitude in the AMNOG procedure (Act on the Reform of the Market for Medicinal Products in Germany) to ensure access to new, high-quality and innovative therapeutics. Finally, the data landscape must be optimized through standardized data recording, networking of existing registers and maintenance of a national GCT register.

Topic VIII: Interaction with society

The field of GCTs requires intensive dialog with various stakeholders. The public should be given comprehensive information about GCTs, while decision-makers should be supported by strengthening interaction with political stakeholders. Measures in this topic include establishing a central communication platform, offering target group-specific information resources, providing targeted reports to committees at state and federal level, and involving funding organizations, as well as identifying and encouraging donations from foundations, private individuals and civil society.

Priority measures in each topic:

Topic I: Stakeholder networking and support

1. Establish a governance structure which involves relevant stakeholders (in a bottom-up approach)
2. Create a national GCT network map
3. Prepare an annual progress report on the National Strategy for GCTs

Topic II: Training and development of skills

4. Establish and expand training and development programs for specialists in all occupational groups
5. Create incentive systems, bonus systems and career concepts – especially but not exclusively – for academic careers

Topic III: Technology transfer

6. Establish a GCT-focused product development unit capable of training, advising and supporting technology transfer facilities and stakeholders in translational projects
7. Enable start-ups through clear, standardized investment and licensing conditions, and facilitate access to the necessary infrastructure
8. Establish transfer services as an equal criterion for the evaluation of academic institutions

Topic IV: Standards, norms and regulatory framework

9. Defragment the regulatory environment for GCTs by concentrating procedures and responsibilities, including for manufacturing authorizations, at the Paul-Ehrlich-Institut (PEI)
10. Strengthen the PEI with additional resources
11. Introduce the sandbox approach as a space for innovation

Topic V: Quality and capacity of GMP production

12. Create a central GCT-GMP and regulatory affairs committee made up of all relevant stakeholders (incl. the Federal Ministry of Health (BMG), the PEI, academia and industry) to analyze and continuously drive forward progress towards the objectives in this topic in a timely, demand-based manner
13. Provide targeted and sufficient financial resources from the federal government, state governments and other funding providers to establish, expand and operate GMP infrastructure in line with demand, including a production facility for critical starting materials for GCTs

Topic VI: Research and development

14. Establish a national GCT network with hubs
15. Establish new, flexible funding formats with short lead times to meet needs not sufficiently addressed to date
16. Define patient integration standards for project budgets and remuneration for patient representatives in recognition of their work in projects and selection procedures

Topic VII: Marketing authorization and transition to patient care

17. Ensure quality assurance, including anchoring therapy decision boards in diagnostics and treatment for patients by adjusting remuneration models
18. Maintain the necessary flexibility in benefit assessments and price-setting in the AMNOG process to uphold access to, and availability of, GCTs for patients
19. Standardize the recording and documentation of post-marketing data by networking existing registers and maintaining a method-specific national GCT register

Topic VIII: Interaction with society

20. Establish a central, web-based point of contact for provision of quality-controlled information
21. Collate and create target group-specific information resources for different stakeholder groups

Summary

Gene- and cell-based therapies (GCTs) represent one of the most significant topics for the future of biomedical research and clinical patient care. Under current conditions, however, Germany is barely able to remain internationally competitive as a location for researchers, industry and clinicians in terms of product developments and clinical applications in this field. To enhance Germany's competitive ability as a location for research and innovation with long-term effect, and above all ensure that patients have access to these novel therapies, the measures proposed in this document must be discussed with political decision-makers and implemented without delay. This will only be possible via a collective effort and with shared responsibilities of all relevant stakeholders, which is why the multi-stakeholder approach initiated here should be progressed in a focused, decisive and quick manner. In addition to the willingness to develop framework conditions and processes within the GCT community, this will also require proactive and constructive engagement from political stakeholders. The overarching objective is to develop innovative products and applications that target the causes of disease, promote health and are safe, efficient, financially viable and widely available.

Introduction

Starting situation

GCTs are core elements of future medicine, as they offer a curative approach for the treatment of patients with severe or life-threatening diseases. There are numerous variants of GCTs: some are based on established procedures, while others rely on novel materials, mechanisms of action and manufacturing processes. Gene-based therapies use nucleic acids, such as DNA or RNA, to regulate or supplement biological functions. Cell-based therapies produce and/or transfer cells in an organism for therapeutic purposes, often using genetically modified cells as a combination of both approaches.

Definition:
The following non-exhaustive list is provided by way of definition for gene- and cell-based therapies (GCTs):

- Therapy approaches with advanced therapy medicinal products (ATMPs):
  - Somatic cell therapeutics (including in the form of stem cells, immune system cells or mesenchymal stromal cells)
  - Gene therapeutics in the form of substitution, addition or suppression therapies with the help of viral or non-viral vectors or genome editing
  - Tissue engineering products, e. g., the production of tissues for surgical use, including the use of novel biomaterials
- Therapy approaches with novel biological products, e. g., mRNA-based and other nucleic acid-based procedures, extracellular vesicles or exosomes, which are used in the context of a GCT approach
- Other approaches of this type in the context of gene- and cell-based therapies

However, the following procedures are not included in our definition of GCTs:

- Approaches that are developed as gene and cell-based therapies for other objectives (e. g., mRNA vaccinations against infectious diseases)
- Approaches that are **exclusively** based on low molecular-weight substances and/or recombinant proteins (including antibodies)

Not only do GCTs modify diseases and relieve symptoms, they also directly address the genetic or epigenetic cause of the disease process – which makes it possible to cure the disease. In some cases, GCTs can reverse severe symptoms and prevent the pathogenesis, progression and complications of disease. GCTs can have a groundbreaking impact through their potential to offer treatment prospects for previously incurable diseases, replace established therapies and regenerate tissue. At the same time, fundamental issues regarding the efficacy and safety of GCTs are the subject of intensive scientific investigations. GCTs have the potential to serve wide-ranging applications. In addition to rare, genetic disorders, these potential applications include more common, often complex acquired and/or degenerative diseases. In Germany alone, millions of patients stand to benefit if safe, novel GCTs are made available.

While basic research and application-focused technology development for GCTs is already being pursued successfully in Germany, the translation of promising approaches from research and development to patient care remains a particular challenge. Although local technology clusters have already been established, the GCT research landscape has not been sufficiently networked at the supraregional or national level to date, due in part to a lack of potential synergy effects and regional differences in authorization procedures. Despite positive examples of successful GCT applications being developed in Germany at present and in the past, there is a risk that Germany will lose pace in the international race to create value with these key medical technologies. Talented individuals and companies are increasingly moving abroad to further their innovative research and development activities. Consequently, Germany's appeal in the eyes of national and international investors is suffering. In relation to patient care, there is also a risk that access to novel therapies will be insufficient or highly cost-intensive.

Other countries such as the USA, China, the United Kingdom, France, Italy and Spain have established effective ecosystems – and, in some cases, national strategies – in the systematic pursuit of value generation during the development of novel therapies, including GCTs. Given the vast development potential that the field of GCTs still holds, and the critical mass of stakeholders evident in the country's academic and industrial sectors, Germany has an opportunity to take on a leading role in this area of innovative pharmacy and healthcare. Achieving this, however, will require a definition of the necessary measures followed by swift and decisive implementation. This will depend upon close collaboration between the public and private sectors along with optimized networking and the formation of development centers

with international appeal. Regional initiatives to develop technology transfer programs can play an important role in this: in the context of international competition and the widely distributed responsibilities in our federal system, it is essential that all relevant stakeholders are involved in developing and maintaining a National Strategy for GCTs.

Objectives of the National Strategy

The objective of the National Strategy for GCTs is to create an **integrative and solution-oriented concept for Germany**. In this context, all parts of the translation value chain should be strengthened and networked independent of specific indications – from basic research through to patient care. It will be necessary to bolster collectively identified topics, reduce the friction at interfaces between different parts of the value chain, optimize and expedite existing processes and regulatory procedures, and ensure greater permeability and continuous interaction between the various stakeholders. While the European and international framework conditions must be included in all considerations, measures must be implemented in a user-friendly, patient-friendly manner in Germany's federal system, with as little bureaucracy as possible. It is important that existing synergy potential in the examined areas is fully exploited to strengthen Germany's position in Europe, and Europe's position globally, with lasting effect.

The National Strategy's overarching objective is to improve patient welfare. Ultimately, GCTs provide new hope and prospects for many patients, especially those who suffer from severe and/or life-threatening diseases, some of which are very rare, and for which no effective treatment options currently exist. The central duty of science is to ensure careful and responsible development of new procedures while anticipating and avoiding potential risks. In the interests of equitable healthcare provision, it must be ensured that GCTs are made accessible to all patients in the German healthcare system in the form of clinical studies and authorized therapies, including the necessary transparency through generally comprehensible and evidence-based information.

Approach and process

The National Strategy for GCTs, including its objectives and measures, has been developed in a comprehensive and open participative process based on a multi-stakeholder approach.

This integrative process has facilitated the inclusion of many relevant perspectives and innovation-promoting ideas from stakeholders in the fields of science, business, politics and society, along with associations, public bodies, foundations, ethics committees and patients' organizations. In an iterative process, eight topics were identified together with the GCT community and, subsequently, corresponding working groups (WGs) were assembled. Each working group engaged with its topic in further detail, defined objectives and recommended specific measures for implementation. The Berlin Institute of Health at Charité (BIH) coordinated the development of the National Strategy set out in this document on behalf of the former Federal Ministry of Education and Research (BMBF, now BMFTR). The working groups engaged with their respective topics independently and coordinated their contributions. In total, more than 150 renowned experts from across Germany actively contributed to the production of this document.

The National Strategy for GCTs, in line with the mandate issued by the former Federal Ministry of Education and Research (BMBF, now BMFTR), is an **initiative developed with input from multiple perspectives and features political objectives and long-term proposals** for education and research, healthcare and business. It has been developed in the context of existing federal strategies and legislative initiatives, particularly the Pharmaceutical Strategy, the High-Tech Strategy, the Start-up Strategy and the Future Research and Innovation Strategy, along with the Health Data Use Act (GDNG), the Research Data Act (FDNG) and the Medical Research Act (MFG). Nevertheless, this document does not strive to provide a systematic scientific review, offer an ethical and legal opinion or achieve objectivity free of interests. Instead, it aims to **depict the conditions and necessities for the successful development and application of GCTs** based on the knowledge, experiences and opinions of stakeholders involved in practice. All central ethical, legal and societal aspects should be understood in this context. This paper has been written from the perspective of Germany as a country that has a federal structure in the hope that it will act in a more federated manner in the future – with regard to and in close collaboration with patients and their representatives, as well as science, business, society and institutions in the global healthcare system.

A unique aspect of the resulting strategy is the consensus achieved across interest groups, which underpins the objectives and specific measures. The diverse array of proposed measures serves as both an incentive and an aspiration: an incentive to take well considered, concerted action and set intelligent focuses, and an aspiration to integrate all relevant stakeholders to ensure the project's success. All contributors to

the National Strategy for GCTs share the ambition of collectively developing a high-tech field that has significant potential, is becoming increasingly important for healthcare provision and will bring significant scientific and technical developments. The overarching objective is to create innovative products and applications that focus on the causes of disease, promote health and are safe, efficient, financially viable and widely available.

In addition to its high significance for the welfare of patients and society as a whole, this National Strategy also holds considerable potential for the healthcare industry and for Germany as a location for pharma – in terms of innovation, research and business, and through its potential to create jobs in Germany.

Development of the document

Acting on behalf of the former BMBF (now BMFTR), the BIH served as a moderator and catalyst in the development process of the National Strategy for GCTs. In the first stage of development, a draft of the strategy's objectives was devised and specific topics drawn up, forming the basic framework for the National Strategy. The challenges in each topic were sketched out to enable development of appropriate objectives and specific measures. The topics were compiled and substantiating descriptions developed together with stakeholders from relevant fields during discussions at public events and based on written feedback.

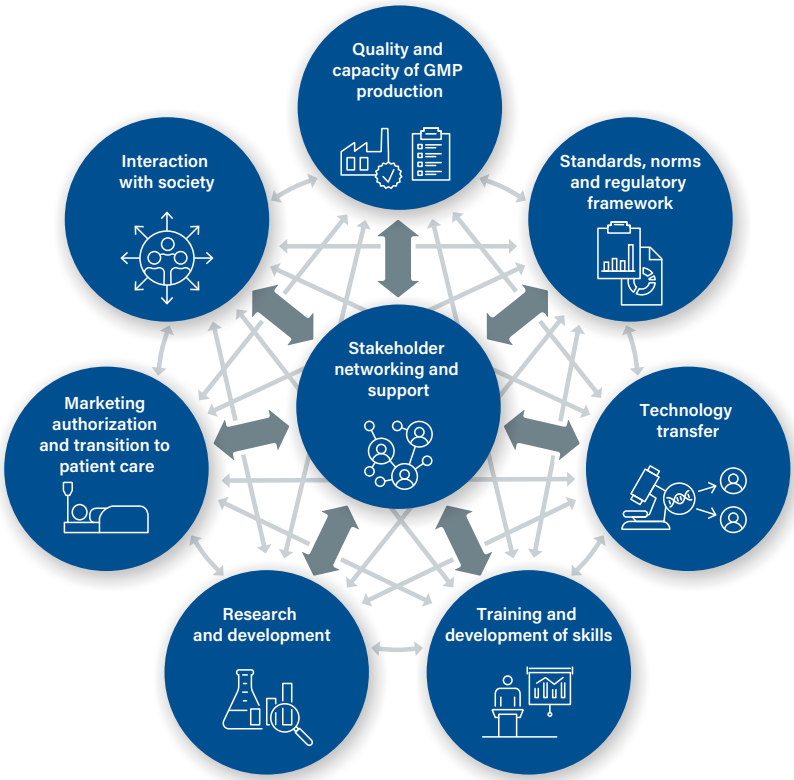
A further coordination meeting was held in mid-June 2023: this roundtable meeting involved organized associations and advocacy groups (the complete list is available at the end of the document) to ensure that a wide range of people from the GCT community were involved in establishing consent regarding the basic framework of the National Strategy, thereby making it possible to consider the different concerns of all involved stakeholders. The final version of the draft was agreed on at this roundtable meeting and presented to the former BMBF (now BMFTR) following final amendments on 30 June 2023.

In the next phase, which started in July 2023, stakeholders were given the opportunity to nominate individuals to participate in working groups, which were tasked with developing objectives and measures with specific proposals for solutions in the described topics. In the period from October 2023 to June 2024, the working groups developed the strategy document in a transparent process, with the BIH providing support in the form of coordination and moderation.

A second roundtable meeting was held in May 2024: the results of their respective topics were discussed and the document was finalized, incorporating final comments. The National Strategy was published and handed over to the former BMBF (now BMFTR) on 12 June 2024, with the aim of enabling the relevant stakeholders to implement the proposed measures.

In each topic, the respective working group has:

- defined the starting situation and challenges
- drawn up specific proposals for solutions to the identified aspects
- identified the stakeholders required to implement the proposed measures
- estimated the resource requirements
- defined the timeline for implementation, and
- specified measurable indicators that can be used to evaluate the success of measures' implementation.



Overview of the identified topics

The National Strategy for GCTs has been developed through collaboration between multiple stakeholders and comprises the following topics:

Topic I: Stakeholder networking and support

Expanding, improving and defragmenting national networking structures in the GCT research and development landscape with all relevant partners

Topic II: Training and development of skills

Establishing training and development programs for early career professionals and specialists, and developing career concepts, bonus concepts and interaction concepts

Topic III: Technology transfer

Optimizing the requirements and processes for high-performance technology transfer and the conditions for spin-offs and start-ups

Topic IV: Standards, norms and regulatory framework

Optimizing standards for responsible pre-clinical and clinical research and development, improving the regulatory framework and guaranteeing quality assurance for product manufacturing and development

Topic V: Quality and capacity of GMP production

Promoting the establishment and networking of academic GMP capacities, strengthening interaction with private sector production facilities, attracting and training specialist staff and securing supply chains

Topic VI: Research and development

Optimizing framework conditions for pre-clinical and clinical studies, improving the involvement of patients and patients' organizations, establishing novel funding formats, and identifying and providing targeted support for fields relevant for the future

Topic VII: Marketing authorization and translation to patient care

Establishing structures for patients' diagnosis, treatment and follow-up care, improvement of the clinical application of GCTs and transition of GCTs to standard healthcare

Topic VIII: Interaction with society

Generating interest in and providing reliable information on GCTs for society, fostering a humanistic discourse and ensuring targeted promotion of potential benefits of GCTs through increased involvement and participation of research funding organizations, foundations and parts of civil society willing to donate

Topic I: Stakeholder networking and support

Summary

The proposed concepts and measures in Topic I are intended to defragment GCT research and establish a national value chain. These measures aim to promote the development and application of these therapies across all phases of life and all specialist fields. They include expanding national networking structures, interacting with political decision-makers, fostering collaboration between science, clinical practice, industry and other stakeholders, and strengthening international links.

It aims to increase the visibility of stakeholders and the network, promote interdisciplinary collaboration, provide comprehensive information on GCT activities and initiate discussions to strengthen the value chain. The objective is to position GCTs as a strategic focus of innovation policy, supported by analysis of their strengths and weaknesses along with intensive communication with different interest groups.

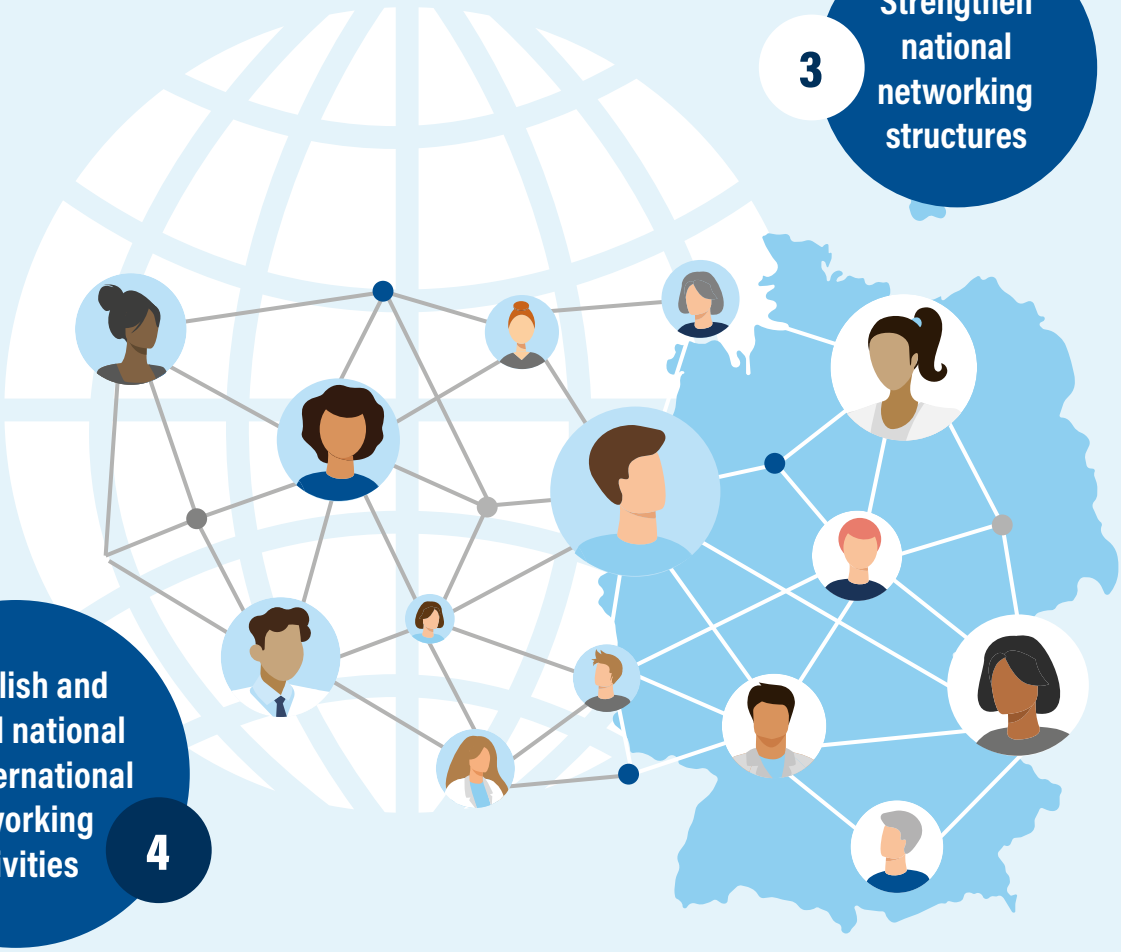
These efforts will be implemented in close coordination with stakeholders, under supervision by the working groups. A proposal is also made for a governance structure to oversee implementation of the National Strategy.

Certain measures will be coordinated by the National Network Office for GCTs. Milestones to measure target attainment include the establishment of a roundtable meeting of stakeholders as an official expert committee, a national GCT map, an informative website, a clinical data register, regular analyses, network meetings, professional development events, progress reports and information events for political stakeholders. In addition, communication with regulators, patients' organizations, funding providers and other stakeholders will be systematically expanded at the national and European levels. The success of the National Strategy for GCTs will require the effective interaction of wide-ranging measures, which must be implemented step by step. There are, initially, three priority measures in Topic I: 1) establish a governance structure involving relevant stakeholders (in a bottom-up approach), 2) create a national GCT network map and 3) prepare an annual progress report on the National Strategy for GCTs.

1 Ensure coordinated implementation of measures in the National Strategy

2 Strengthen political accountability for GCTs - a key topic for the nation's future

3 Strengthen national networking structures



4 Establish and expand national and international networking activities

Background

As an innovative, highly technologically complex field of medicine, GCTs have significant medical and commercial potential. To leverage this potential in Germany and translate these therapies to mainstream clinical care, various national stakeholders with complementary expertise at several levels of this new medical discipline must be brought together in an overarching governance structure, strategically networked and their activities interconnected to utilize the resulting synergies. These stakeholders should cover basic research in the field of genetic cell manipulation, translational research on potential applications of GCTs, clinical studies and clinical use. Systematic interconnection of the key stakeholders and operational levels has been lacking to date.

Identifying the strengths and weaknesses of GCTs and formulating specific needs will be central to establishing and financing a robust value chain for GCT products in Germany. This will require the systematic recording and mapping of stakeholders and activities along with existing bottlenecks. Close coordination processes between academic, non-university and pharmaceutical research, the pharmaceutical industry, venture capital providers, patients' organizations and payers will also be essential. These coordination processes must be developed and maintained over the long term. Finally, a continuous exchange with federal and state-level authorities will be needed to define a favorable regulatory framework for clinical testing and the introduction of innovative GCT products.

The sustainable development of an innovative GCT landscape in Germany, which is robust in both medical and economic terms, will require strategic coordination of accompanying political measures at federal and state levels. These measures include a nationally standardized framework along with targeted measures to strengthen innovative capacity and the value chain in general. A successful innovation policy will require political decision-makers at federal and state level in the fields of science, health and economics to be given comprehensive information and advice.

The success of the National Strategy for GCTs is dependent to a considerable extent on international framework conditions, especially at the European level. These include legal regulations, the availability of starting materials and manufacturing capacities, and access to clinical cohorts and study groups. The National Strategy for GCTs must therefore respond to international developments and systematically exploit the potential offered by international collaborations.

Four overarching objectives have been defined for this topic:

Objectives

1. Ensure coordinated implementation of measures in the National Strategy
2. Strengthen political accountability for GCTs – a key topic for the nation's future
3. Strengthen national networking structures
4. Establish and expand national and international networking activities

Objective 1:
Ensure coordinated implementation of measures in the National Strategy

Explanation:
The field of GCTs is an important building block in modern medicine and is developing very dynamically around the world. At the same time, all areas of translation (from research and clinical testing to application and exploitation) face major new challenges, often specific to the field, which are being addressed in very different ways by national and international competition. Germany is at risk of losing pace and no longer being actively involved in these developments. With this in mind, the National Strategy for GCTs aims to concentrate competencies in Germany and thereby facilitate the flexible adaptation, acceleration and quality enhancement of development and transfer processes. Rectifying the existing structural deficits and necessary adaptations will require the implementation of recommended measures to be centrally coordinated. A permanent expert committee should be appointed, integrating all key stakeholders, to be able to promptly identify new obstacles and determine further areas in need of response and support. A solution-oriented network structure should be established with the ability to bring together stakeholders from science and industry that have to date acted either in parallel or separately in federal and institutional systems.

Measure 1:
Establish a governance structure to implement the National Strategy

Stakeholders required:
Federal Ministry of Research, Technology and Space (BMFTR), roundtable meeting of stakeholders

Description:
The stakeholders involved in the process will develop a governance structure for implementation of the measures outlined in the National Strategy. The roundtable meeting of stakeholders appointed to develop the National Strategy should be maintained as an interim structure. A permanent structure integrating all key stakeholders will be created to define and coordinate further measures to establish a suitable GCT value chain. These measures could be based on a SWOT (strengths, weaknesses, opportunities and threats) analysis and include a new BMFTR High-Tech Strategy for scientific and industrial associations, calls for proposals for translational research associations, access to free manufacturing capacities and infrastructures, and interdisciplinary networking throughout the entire value chain. As part of this structure, the roundtable meeting of stakeholders will be consolidated, e. g., as an officially appointed **permanent council or committee of GCT experts** to ensure that the strategic recommendations in this highly dynamic and innovative field are of necessary breadth and timeliness. The composition of this expert council for GCTs will be reviewed on a regular basis to ensure it is up to date. The appointed members must have a clear mandate from their organization and thus serve as connection points on specific issues between the expert council and the respective organizations. A dedicated office will support the council in its work. The Network Office for GCTs will provide information to members of the roundtable meeting and other interested parties via a regular newsletter.

Timeline and resource requirements
- Short term (within a year): Establishment of a council to manage the implementation process and allocation of resources
- Establishment of an office to issue necessary position papers and provide administrative support for the council and implementation of measures
- Financial resources to organize, implement and appoint the GCT council (including travel and organizational expenses)
- The funding required for the office is estimated at a mid-range six-digit euro amount per year (for personnel and material expenses)

Success indicators

- Effective implementation of measures in the National Strategy for GCTs

Objective 2:
Strengthen political accountability for GCTs – a key topic for the nation's future

Explanation:

To date, the topic of GCTs has been underappreciated in Germany despite its high significance in the fields of health, research and business. Although activities and communication exist at different levels, a holistic perspective of the value chain is lacking, which impairs the strategic coordination of policy measures. The federal government has now identified this necessity and plans to define GCTs as a strategic focus. The objective is to create standardized nationwide framework conditions and improve innovation policy to enhance Germany's competitiveness.

Measure 1:
Prepare an annual progress report on the National Strategy for GCTs

Stakeholders required:
BMFTR, roundtable meeting of stakeholders, Working Group (WG) I, representatives from the GCT community

Description:
Building on the National Strategy for GCTs, the federal government should commission an annual progress report for the field of GCTs. The GCT network, represented for example by the National Network Office for GCTs, will then prepare such a report. This report should give the federal government the opportunity to discuss measures with the different conferences of state ministers as appropriate. It will provide stakeholders working in research, healthcare, business and finance with an overview of current focuses and developments in the highly innovative field of GCTs. The report will document the targets achieved and highlight outstanding measures at federal and state levels. Close inter-ministry coordination between state secretaries will be essential to achieving future-oriented research and innovation policy. Ideally, such discussions would take place on a regular basis in the form of a GCT roundtable meeting of state secretaries.

Timeline and resource requirements

- Medium term (2 years)
- Preparation of the report will require the political will to implement it, the availability of staff at the National Network Office for GCTs, at network partners and in the WGs, plus coordination with government representatives

Success indicators

- Implementation of GCTs as a topic in minister conferences
- Briefings in plenary sessions of the Bundestag and state parliaments

Measure 2:
Implement intra-annual measures to convey successes of the national network for GCTs to political stakeholders at federal and state level

Stakeholders required:
Roundtable meeting of stakeholders, National Network Office, representatives from the GCT community

Description:
Political stakeholders at federal and national level should be regularly informed in writing of the successes achieved by the network (e. g., regarding new treatment approaches, clinical study programs, spin-offs, cluster initiatives, collaborative projects, authorizations issued for GCTs in Germany in comparison with the EU and internationally). The corresponding reports also contain notes on the framework conditions required to further such projects. In

addition, template presentations will be drafted, regularly updated and supplemented with information from Federal Reports on Research and Innovation (BuFI), the German Research Foundation (DFG) Funding Atlas and industry reports to incorporate input from political stakeholders and network partners.

Timeline and resource requirements
- Short term (1 year)
- The intra-year production and dissemination of documents will require ongoing professional editorial input from the National Network Office or the GCT governance office as well as advisory input from suitably experienced network partners

Success indicators
- Analysis of the degree to which recipients are informed on GCT-related issues (analysis commissioned for example by the National Network Office)

Measure 3:
Organize information events for policymakers at innovation locations

Stakeholders required:
Representatives from the GCT community, National Network Office

Description:
Established health initiatives at federal and state level bring together expertise from science, healthcare, regional policy and industry. Examples include the Forum Health Region Baden-Württemberg (Forum Gesundheitsstandort Baden-Württemberg), the Hesse Healthcare Industry Initiative (Initiative Gesundheitsindustrie Hessen), the Bavarian Pharmaceutical Summit (Bayerischer Pharmagipfel), the Healthcare Industry Round Table (Round Table Gesundheitswirtschaft) hosted by the Federal Ministry for Economic Affairs and Climate Action (Bundesministerium für Wirtschaft und Klimaschutz - BMWK, now Federal Ministry for Economic Affairs and Energy, Bundesministerium für Wirtschaft und Energie - BMWE) and the Institute for Biomedical Translation Lower Saxony. These clusters are closely linked with federal and state-level politics. The National Strategy for GCTs will leverage these structures to emphasize the potential of GCTs in health research. There are plans to raise and discuss selected focus topics, including at parliamentary events and at expert summits. The innovation locations in the GCT network present a "shop window" for experts and political audiences, providing an opportunity to showcase potential applications of GCTs that otherwise receive too little attention. One such example is the discussion of gene therapies in pediatric medicine.

Timeline and resource requirements
- Short term (1 year)
- To begin with, individual network partners can put forward proposals for events and organize them independently. At a later stage, corresponding local events should be coordinated and advertised while integrating further network partners

Success indicators
- Participation levels, responses from invited partners

Measure 4:
Establish and maintain contact with German representatives on EU bodies and committees

Stakeholders required:
Roundtable meeting of stakeholders and representatives from the GCT community with existing contacts at EU level, BMFTR

Description:
The EU determines the framework. In light of this, it is important that the National Network Office remains in continuous contact with representatives of the European Commission and the European Parliament. The Commission regulates EU approval and authorization of ATMPs, provides funding for GCT research, and supports healthcare in Europe through programs to improve patient care with innovative health products in Europe (EU calls for tenders, new funding lines such as co-financing of clinical developments between the EU, industry and pharmaceutical companies). A targeted effort should be made to engage German representatives in relevant EU bodies and committees, leveraging existing contacts with network partners.

Timeline and resource requirements
- Short term (1 year)
- Personnel at the National Network Office to coordinate (and implement) lobbying and communication activities with network partners, in particular the EU offices of scientific and pharmaceutical organizations. These EU office could manage some of the communication for the GCT network (with continuous involvement of the WGs)

Success indicators
- Inclusion of GCT-related topics in EU-wide funding lines, calls for tenders, legislation, etc.

Objective 3:
Strengthen national networking structures

Explanation:
Communication and networking between stakeholders take place via individual collaborations, temporary research associations, institutionalized research associations (e. g., the National Center for Tumor Diseases (NCT) and the Bavarian Cancer Research Center (BZKF), medical expert associations and scientific congresses. There are, however, only a few systematic links between stakeholders working on stem cell-based approaches (e. g., ESC Parkinson's therapy, iPSC heart plasters), vector-based gene therapy approaches (e. g., for 5qSMA, sickle cell anemia, PCSK9 or DMD) and (stem) cell-based gene therapy approaches, including more recent approaches in gene-based immunotherapy (e. g., chimeric antigen receptor (CAR) T-cells). To date, no regular, institutionalized dialog with a comprehensive catalog of topics and measures has been established.

Target: Interdisciplinary networking of all stakeholders and relevant clusters should facilitate the provision of comprehensive and rapid information on local, supraregional and national GCT activities, increase the visibility of stakeholders and spark discussions and potential solutions to improve stakeholders' infrastructure, productivity and visibility.

Measure 1:
Establish a central point of contact (GCT website) with structured information about all stakeholders

Stakeholders required:
National Network Office with consultation of the roundtable meeting of stakeholders

Description:
A central GCT website will offer structured information about relevant GCT stakeholders, including their targets, services and position in the GCT landscape (see also Topic VIII, Objective 1, Measure 1). It will also provide a GCT map, media articles and a jobs website. Content will be provided by the working groups, with stakeholders encouraged to provide similar information on their own websites using a standardized GCT design. A network calendar and a newsletter with relevant information will also be available. Key information on international developments in the field of GCTs, especially in the EU, including information on authorized products, ongoing clinical studies and industrial companies from the pharmaceutical and biotech sectors, will have been collated to some degree as part of other initiatives, and should be clearly linked on the GCT website.

Timeline and resource requirements
- Short term (1–2 years)
- Establishment of the website in parallel with the national GCT map
- Achieving this will require additional personnel in the National Network Office, contracts with third parties to set up and design the website, and extensive coordination with network partners, who will also be asked to provide the necessary information
- Long-term website maintenance

Success indicators
- Website go-live (by 2026)
- Website usage profile

Measure 2:
Design and compile a national GCT map depicting relevant stakeholders, structures and other parties, along with their functional interactions

Stakeholders required:
National Network Office with consultation of the roundtable meeting of stakeholders

Description:
The map will provide a structured overview of relevant GCT stakeholders. These include the roundtable meeting of stakeholders, academic groups, research institutes, production facilities, clinical treatment centers, biotech and pharmaceutical companies, regulatory authorities, ethics committees, funding providers and expert associations. The map will include research associations, gene therapy products, cell products and clinical studies. An elected committee, involving WG I and the National Network Office, will structure the map and conduct quality assurance. The National Network Office will set up and maintain the map, which will contain links to stakeholders' websites.

Timeline and resource requirements
- Short term (1 year)
- The National Network Office should be able to make the necessary staff available and award external contracts for graphic design and programming of site navigation and links
- Continuous long-term maintenance of the map must be ensured

Success indicators
- The GCT network map with navigation instruments and links is made publicly available
- Long term: Visitor profile for the map

Measure 3:
Conduct analysis of network components and the links between them, plus subsequent SWOT (strengths, weakness, opportunities, threats) analysis

Stakeholders required:
Roundtable meeting of stakeholders, National Network Office

Description:
The targets, roles and existing networks of GCT stakeholders will be compiled and examined for areas of congruence and potentially conflicting targets. Contact persons will be identified in all GCT working groups to help to minimize strategic incongruities. A SWOT analysis, conducted through direct engagement with relevant sites and possibly supported by external assessments, will review the network to identify areas of potential as well as bottlenecks in the national GCT value chain by international comparison. This analysis will form the foundation for further measures to strengthen the value chain, integrating all relevant fields at federal and state level. The efficacy of these measures will be reviewed via continuous monitoring.

Timeline and resource requirements
- This analysis will commence once network partners and other components have been defined
- An initial (interim) analysis should be compiled in the near term (1 year) and serve as the starting point for further action and the instigation of targeted measures
- The first stage will primarily require personnel (working hours) from the participating networking partners, along with a stakeholder (Network Office) or external contractor to serve as coordinator and moderator

Success indicators
- Interim and final reports are completed and specific topics derived to maximize the network's congruence
- SWOT analysis and derived measures conducted

Measure 4:
Raise profile of GCT network-related issues in the national science community and organize network events

Stakeholders required:
Members of the roundtable meeting of stakeholders, Alliance of Science Organizations, expert associations, National Network Office

Description:
The National Strategy for GCTs, and the topics it raises, should be discussed in detail in the scientific community. The topic should be covered at congresses of relevant expert associations, the Network of University Medicine (NUM), the German Centers for Health Research (DZG), in national scientific organizations such as the German Science and Humanities Council (WR), the Leopoldina, the states' academies of sciences and the German Research Foundation (DFG). In addition, scientific funding programs should be initiated on relevant topics. Furthermore, a regular GCT meeting should be organized with the aim of fostering personal exchanges between network partners and their representatives.

Timeline and resource requirements
- Short term (1 year)
- Suitable information material will be required as the basis of discussions (template presentations, position papers, etc.) and should be created by the network partners (potentially within the WGs) in cooperation with the National Network Office to ensure appropriate design

Success indicators
- Positioning of the topic of GCTs in the proposed events

Objective 4:
Establish and expand national and international networking activities

Explanation:
Interaction between science, clinical practice, industry, investors, authorities, patients' organizations and medical expert organizations can be improved at a national and international level. Although links between stakeholders exist, these links are often irregular in nature and unsystematic. International networking is fragmented: it involves expert associations, research institutes, regulatory authorities, research associations and research collaborations, as well as venture capital providers and pharmaceutical companies involved in national assets and clinical studies. However, these interactions lack methodical integration and development.

Target: The exchange of information between different stakeholders should be improved to drive innovation forward more rapidly and introduce new therapy options safely and effectively. Collaboration between different stakeholders, including patient advocacy groups, research institutes, regulatory authorities, industry and politics will be decisive for the future success of GCTs. In addition to the roundtable meeting initiated as part of the National Strategy process, in-depth dialog formats and partnerships will also be required. The aim is to increase the visibility and relevance of German GCT activities, including attracting third-party research funding and establishing Germany as a leading initiator of clinical research programs. This will require stronger public-private partnerships, the use of international resources and active participation in EU authorization and legislative procedures.

Measure 1:
Provide information for national and international patient advocacy groups

Stakeholders required:
National Network Office, roundtable meeting of stakeholders, representatives from the GCT community

Description:
Although no specific patients' organization for GCTs currently exist, GCTs will become a relevant treatment option for an increasing number of diseases. Higher-level patient advocacy groups should become an integral part of the strategy process moving forward. Further patients' organizations in different areas should be identified and engaged. Training on GCTs for representatives of patients' organizations should be offered and financially supported, (see also Topic II, Objective 1, Measure 1). Easily understandable and accessible information services such as websites, brochures and events should be devised by a dedicated and qualified project manager. At the EU level, European patients' organizations should be actively informed on the issue, e. g., through personal engagement, printed materials and online events (see also Topic VIII, Objective 1, Measure 4).

Timeline and resource requirements
- Short term (1 year)
- Staff to create and disseminate information materials, regular (e. g. annual) cross-checks and updates as needed, financial resources to conduct training
- In the short term, suitable information material must be made available in relevant languages
- Personnel should be dedicated to public relations work (externally contracted if necessary) and additional contributions by network partners (especially clinical facilities and study networks) is required
- Contact could be established by national patients' organizations in the GCT network, by international study groups or by the National Network Office. Staff should be allocated accordingly

Success indicators
- Participation in patient-focused events
- Demand for information materials
- Visits to specific GCT websites
- International patients' associations addressing the identified topics and their continuous engagement and exchange with the respective government or the EU

Measure 2:
Provide information for patients

Stakeholders required:
National Network Office

Description:
Information should be made available in comprehensible terms using established (e. g., a patient magazine) and/or new media formats (e. g., videos) to inform the public – and especially patients – about the opportunities and risks of GCTs along with current developments in this field. The newsletter of dsai.de (an organization for patients with congenital immunodeficiencies) could serve as a positive example (see also Topic VIII, Objective 1, Measure 4).

Timeline and resource requirements
- Short-term implementation (1 year) is feasible
- Medium term (1–3 years): Expand information services to cover the entire breadth of potential applications
- Resources to assist the creation of information materials (via external contracts), involvement of selected network partners, coordination by the National Network Office would be helpful

Success indicators
- Number of times information is accessed on the network's website
- Intensity of contact with patient advocacy groups
- Number of queries directed towards dedicated contact persons

Measure 3:
Provide information for international/ European clinical research groups

Stakeholders required:
National Network Office, representatives from the GCT community

Description:
Study groups and networks (e. g., European Organisation for Research and Treatment of Cancer (EORTC), European Reference Networks (ERNs), etc.) should be made aware of the GCT network's activities to promote German participation in international clinical studies and, conversely, international participation in German GCT studies. Providing disease-specific links to national study groups could assist with this. International cooperation in clinical studies could be supported with specific resources (e. g., Joint Actions, co-financing by German Cancer Aid (DKH), BMFTR, DFG, etc.) if appropriate.

Timeline and resource requirements
- Medium term (2–3 years)
- Information should be shared by network partners actively involved in international networks with administrative support from the National Network Office
- Limited amount of time by personnel at the National Network Office

Success indicators
- Number of participations in international studies by locations in the GCT network

Measure 4:
Establish an exchange of information with national and international regulators

Stakeholders required:
National Network Office, representatives from the GCT community

Description:
An exchange with federal higher authorities (Bundesoberbehörden) such as the PEI will be important to keep the requirements of authorization processes up to date and ensure the supervisory authorities remain closely linked to the innovation process. Representatives of supervisory authorities should be invited to network congresses on a regular basis to discuss regulatory aspects. Regulators should also be persuaded to attend joint events, such as the "PEI Days". A dialog should also be established with ethics committees specialized in the field of GCTs to reflect on national legislation and identify examples of best practice.

Timeline and resource requirements
- Short term (1 year)
- Meetings coordinated by network partners (stakeholders, roundtable meeting, WGs) in coordination with the National Network Office
- Larger meetings will require central resources for organization and implementation
- Short term (1–1.5 years): Coordination and organization potentially performed by WG IV (Regulatory Affairs)
- Resources for events (e. g. invitations for representatives of international regulatory bodies) must be provided

Success indicators
- Adaptation/simplification of approval processes for GCTs
- Achievement of average processing times
- Success rates of approval procedures; positive reports from GCT producers on their experience of the authorization process
- Adaptation and simplification of national implementation practice
- Increase in the number and speed of application procedures

Measure 5:
Appeal to national and international investors and funding providers

Stakeholders required:
National Network Office, representatives from the GCT community

Description:
The network should provide targeted information on technology transfer guidelines, collaborative endeavors suitable for projects and ongoing clinical studies, along with local information services. Regular "Investment Days" and a regular roundtable meeting could bring together stakeholders from science, pharmaceutical companies, venture capital providers and representatives of federal and state governments, offering an opportunity to present pre-clinical therapy concepts and start-up ideas, and discuss financing opportunities for clinical developments and potential support from federal and state governments. At the national level, specific events could be held to attract international capital for development of a GCT start-up scene.

Timeline and resource requirements

- Short term (1 year)
- Coordination by specific WGs in the National Strategy, additional contributions by network partners required
- Central budget for drafting of standardized information material with corporate design (e. g., templates) necessary
- "Investment Days" could be financed by participating investors

Success indicators

- Successful financing rounds for GCT start-ups, drug development and clinical studies

Measure 6:
Exchange and cooperate with public-private partnership (PPP) initiatives, especially the EU's Innovative Medicines Initiative (IMI)

Stakeholders required:
National Network Office

Description:

The European IMI is the world's largest PPP in the field of biosciences. It is an initiative of the European Commission and partners from science, industry and patients' organizations. This initiative aims to improve the development of, and access to, innovative medicines – including GCTs. It promotes interdisciplinary collaboration between all stakeholders involved in research (e. g., universities, research centers, pharmaceutical and other industrial companies, small and medium-sized enterprises, patients' organizations and medicines regulatory authorities). The proposals of the GCT network should be communicated to, and discussed with, the initiative.

Timeline and resource requirements

- Short term (1 year)
- Contact could be established by the Brussels offices of research organizations or the pharmaceutical industry
- Low resource requirements. Include respective links on the GCT map

Success indicators

- Incorporation of GCT issues in IMI funding programs

Measure 7:
Provide targeted information for scientific organizations and associations

Stakeholders required:
National Network Office

Description:

Scientific organizations, associations and foundations act as research supporters, research funding organizations, intermediaries and/or multipliers. If such organizations are not already members of the roundtable meeting of stakeholders, they should be approached directly and regularly via the Alliance of Science Organizations, foundations and associations. Representatives of these organizations' management and senior administrative bodies should be sent information material and invited to specific congresses and network events.

Timeline and resource requirements

- Short term (1 year)
- Budget to create information material
- Input from network partners, coordinated by the proposed governance structure
- Personnel will be required for communication with scientific organizations and associations

Success indicators

- Discussion of the GCT agenda in the targeted organizations and associations and potentially the drafting of a respective statement to specific topics

Measure 8:
Raise the profile of the GCT initiative at international scientific congresses

Stakeholders required:
National Network Office, representatives from the GCT community

Description:
International congresses offer stakeholders the opportunity to present the GCT strategy or disseminate the information along with its interfaces and opportunities for collaboration. To this end the National Network Office provides content for use, e. g., template presentations.

Timeline and resource requirements
- Short term (< 1 year)
- Network parters should create the necessary information material (potentially by the WGs established in the National Strategy) in cooperation with the National Network Office (to ensure adequate corporate design)

Success indicators
- Positioning of the topic of GCTs in the aforementioned events

Measure 9:
Establish an exchange of information with medical service providers and health insurance funds

Stakeholders required:
Roundtable meeting of stakeholders, National Network Office

Description:
A regular exchange of information between healthcare providers and health insurance providers is sought to discuss the challenges involved in the clinical use of GCTs. Joint solutions should be developed, involving the Federal Ministry of Health (BMG) where appropriate. Clinical performance figures for GCTs should be collated and published along with the results of early clinical trials and pivotal studies.

Timeline and resource requirements
- Short term (1 year)
- Contact established and meetings coordinated by WGs or by the National Network Office, low resource requirements

Success indicators
- Catalog of criteria for health insurance providers to cover necessary costs
- Insurance providers agree to meet costs for specific products and indications

Measure 10:
Integrate international entities into the GCT value chain

Stakeholders required:
National Network Office

Description:
At present, bottlenecks in the GCT value chain, especially for academia-led development programs, are often caused by manufacturing capacities that meet the standards of good manufacturing practice (GMP). Using international capacities, particularly elsewhere in the EU, could expedite clinical developments. A central record of these capacities should be compiled and made accessible to stakeholders. Also, the federal and state governments and private partners could establish comprehensive, nationwide structures in Germany (see Topic VI, Objective 1, Measure 1). Collaboration with healthcare providers will be essential for nationwide provision of GCTs. The establishment of reference centers should be considered.

Timeline and resource requirements
- Short to medium term (2 years)
- Staff at network partners (WGs) and at the National Network Office to compile structured information from different countries
- Artificial intelligence (AI)-based information and communication systems could offer support

Success indicators
- Creation of an international map of GCT manufacturing capacities
- Requests from the network to use the map

Topic II: Training and development of skills

Summary

Excellent training and continuous development of skills are essential for the successful development, manufacturing and clinical application of GCTs. For this reason, they are the focus of Topic II. In Germany and elsewhere, there is often a shortage of high-quality staff in different academic and non-academic fields, e. g., in manufacturing, process and methods engineering, analytics, quality control and quality assurance, as well as regarding protection of intellectual property (IP), entrepreneurship, treatment strategies and clinical translatability. As a result, by international comparison, Germany has an insufficient number of investigator-initiated trials (IITs) and start-ups, especially when compared to the USA, China and the United Kingdom.

To change this, the experts in Topic II recommend a substantial strengthening and refining of the national talent pipeline, focusing on the following key points:

- Establish and expand training and development programs for specialists in all occupational groups (i. e., academic and non-academic professionals; scientific, scientific-technical and technical professionals)
- Implement these programs at suitable locations with collaboration from academia and industry (see Topic VI, Objective 1, Measure 1)
- Develop adequate upskilling concepts, career concepts, bonus concepts and interaction concepts

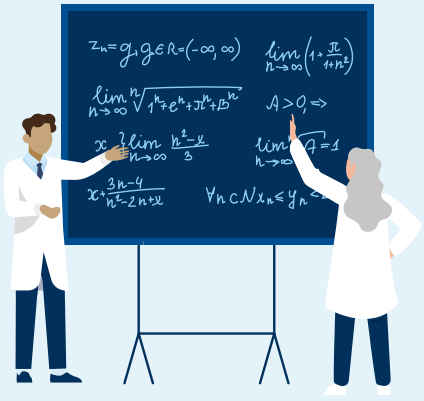
To support implementation of the proposed measures and fully exploit the defined success indicators to accompany the implementation process, dedicated packages of measures have been developed with clearly defined targets, timelines and resource requirements.

The measures described in this section should provide a concept for a multi-track, modular training program for a certificate in "Gene- and Cell-based Therapies", with proposals for implementation regarding extra-occupational, interdisciplinary Master's and doctoral programs as well as targeted training programs. In this regard, we propose establishing national GCT education and training centers to consolidate academic, non-academic and industrial skills. Furthermore, we recommend targeted measures to create incentive and bonus systems, develop career concepts and draft interaction concepts between stakeholders involved in training and career development, e. g., academia and industry.

If these measures and their implementation strategies are enacted promptly, it should be possible to rectify the weaknesses in this area and facilitate the urgently needed translation of GCTs into medical care in Germany with lasting effect.

Establish training and development programs for early career professionals and specialists, and improve the necessary infrastructure for training and development

1



Develop adequate career concepts, bonus concepts and interaction concepts

2

Background

The successful development, manufacturing and clinical application of GCTs is the result of efficient collaboration between interdisciplinary teams. Following this principle, a sufficient number of well-trained specialists in wide-ranging fields with particular expertise in GCTs is a *sine qua non* for the establishment, expansion and maintenance of efficient, internationally competitive structures in the field of GCTs. In Germany, the necessary expertise is lacking in both qualitative and quantitative respects, specifically relating to the implementation of the manufacturing phase (process realization), routine manufacturing, process and methods engineering, analytics, quality control and quality insurance, as well as regarding protection of IP (especially patenting). These are precisely the areas that are essential for effective translation of the results of basic research into clinical practice. However, Germany also lacks the necessary expertise for clinical application of products, above all in gene therapy, and has far fewer IITs than, for example, the United Kingdom or the USA (https://www.liebertpub.com/doi/10.1089/hum.2021.29178.hbu#sec-8).

These countries have already identified the need for interdisciplinary training programs that are specifically targeted at both academic and non-academic staff in the GCT field, and implemented them, e. g., in the Certified Advanced Biotherapies Professional Credential Program offered by the Association for the Advancement of Blood and Biotherapies (AABB) (https://aabb.org/education/certified-advanced-biotherapies-professional-credential) and the Cellular Therapies Certificate Program offered by the AABB and George Washington University (https://www.aabb.org/education/certificate-programs/aabb-cellular-therapies-certificate-program).

Corresponding programs and qualification measures must therefore be swiftly established and/or embedded in existing programs or further expanded where they already exist. In addition, a nationwide, centrally coordinated, Internet-based information platform should be established to facilitate the exchange of relevant expertise between relevant GCT locations (see also Topic I, Objective 3, Measure 1 and Topic VIII, Objective 1, Measure 1).

In terms of skills development and the long-term availability of skilled professionals, upon which economic success inherently relies, it will be essential to dovetail interdisciplinary collaboration, interaction between private-sector companies, academic institutions and training facilities, and cross-sectoral action in a highly-efficient and effective manner. However, generating expertise and connecting GCT locations will not be sufficient. The academic space is financed by taxpayers' money and third-party funding and has a vital purpose in society by fostering innovative activities. However, the critical corresponding incentives are lacking. This is because the time-consuming task of implementing manufacturing processes in line with GMP standards for new therapeutics has not yet been sufficiently acknowledged in the academic space. Nevertheless, this is a fundamental prerequisite for their successful transfer to clinical application (see also Topic VI, Objective 5, Measure 1). Support for this essential step in translation by personnel and infrastructural resources has been scarce to date. The construction, qualification and operation of cleanrooms and the lengthy phase of establishing, implementing and scaling new processes, producing and continuously revising standard operating procedures (SOPs), establishing quality assurance systems and the laborious task of completing regulatory approvals procedures require considerabl personnel, are time-intensive and costly. The manufacturing of cell-based therapeutics in cleanrooms is regarded as an economic (i. e., entrepreneurial) activity and is therefore subject to value-added tax – even when these therapeutics are only manufactured for clinical trials with small numbers of patients in a university context. This considerably increases costs and makes it extremely challenging for universities to manufacture such therapeutics internally for clinical studies. The manufacturing process in cleanrooms must therefore be classified as an integral part of training and development for academic and non-academic professionals, and as part of research and teaching (and thus a sovereign activity), as an essential bridge between pre-clinical research, clinical studies and healthcare provision. Academic careers in this field are significantly more difficult because of the points outlined above, which are so important for the creation of economic value, and many are insufficiently covered, if at all, by standard forms of internal and external performance assessments. "Conventional" academic careers made up of fixed-term contracts are based, first and foremost, on producing publications in a field of research within a specific timeframe. This, in turn, is a requirement for successfully securing third-party funding to finance this research and to obtain postdoctoral teaching qualifications or professorships. In such a system, there is no incentive for scientists to embark on the protracted and costly process of translating their research results into GMP-compliant manufacturing, or to offer existing translational expertise on a regular basis outside of one-off (collaborative) projects. This problem is exacerbated by the Academic Fixed-Term Contract Act (WissZeitVG), which currently limits the duration of post-doctoral

positions to a maximum of four years as a qualification period. In the context of translation (i. e., the development and implementation of processes as a prerequisite for subsequent transfer to clinical practice as a medication), this arrangement is not helpful. Fundamentally, it should be noted that there is a lack of longer-term employment and development opportunities for highly-qualified professionals who have invested significant time and effort in gaining their qualifications.

Treatment of individual patients with proprietary product developments is complicated by the framework of the Medicinal Products Act (AMG) set out in Section 4b (hospital exemption) and in clinical studies (first-in-human, FIH), and particularly by the need to ensure the long-term availability of suitably trained staff and secure corresponding financing. Recruiting and retaining qualified staff outside of professorships requires a longer-term approach to employment, which is significantly constrained by current German legislation.

In summary, it is important to state that scientists' own academic research often ends in the pre-clinical phase, meaning that an insufficient number of technical specialists are being trained for the wide-ranging fields of GMP manufacturing and analytics. Consequently, it is increasingly difficult to develop expertise in the field of translation, which in turn leads to a downward spiral in numbers of both non-academic and academic specialists. Therefore, alternative and innovative measures should be taken to significantly enhance the appeal of working and pursuing a career in translation. This also applies to innovative companies, which are reliant on specialist knowledge and expertise in the GCT field. Finally, ensuring that German authorities possess expert knowledge is essential for effective translation, meaning that decisions can be made fast and on a sound basis. A lack of knowledge creates a bottleneck in translation if it leads to decisions being delayed, being incorrect or not made at all.

We therefore recommend that the following measures be taken to enable Germany to keep pace in this game-changing field of biomedicine and, in the long term, take on a leading position internationally. Given that the expected positive effects regarding training and development of skills will naturally only appear after a lag period, we recommend introducing these measures into the parliamentary decision-making process as quickly as possible and implementing them promptly.

Objectives

1. Establish training and development programs for early career professionals and specialists, and improve the necessary infrastructure for training and development
2. Develop adequate career concepts, bonus concepts and interaction concepts

Objective 1:
Establish training and development programs for early career professionals and specialists, and improve the necessary infrastructure for training and development

Explanation:
In the medium to long term, the deficits outlined above in critical areas of establishing and implementing manufacturing processes for novel GCTs and their subsequent transfer to clinical application can only be solved with lasting effect by implementing the following measures to ensure that Germany remains internationally competitive: targeted training and development, securing specialists who are already suitably qualified, creating incentives to pursue academic and non-academic careers, and long-term, continuous occupation in this field. Here, it is particularly important to involve all relevant occupational groups, as the successful and sustained implementation of GCTs is generally the result of complex interdisciplinary processes.

Measure 1:
Create and implement a concept for multi-track, modular additional training

Stakeholders required:
WG II in collaboration and in a transparent process with other relevant stakeholders/institutions, the BMFTR, the German Medical Association (BÄK) – where medical professionals are concerned, expert associations, Central Authority of the Länder for Health Protection with regard to Medicinal Products and Medical Devices (ZLG), possibly involving the Initiative Studienstandort Deutschland Group C

Description:
A two-track, modular and dynamic training and qualification model should be developed, and offered at existing (or newly established) regional hubs (see Topic VI, Objective 1, Measure 1), where participants can in the medium to long term obtain certificates and additional qualifications (e. g., "Gene- and Cell-based Therapies") that are recognized across Germany. The target groups are all scientific, scientific-technical and technical occupational groups that aim to work in the field of GCTs. These include medical technical assistants (MTAs), biological technical assistants, chemical technical assistants, pharmaceutical technical assistants, industrial professionals, engineers, natural scientists, doctors, pharmacists, attorneys and regulators from regional governments, at both state and federal level, employees at clinical study centers/coordination centers for clinical studies, and members of ethics committees, self-help/patients' organizations and patient advocacy groups. In this context, particular attention should be given to involving regulators and auditors to ensure the standardized development and implementation of statutory provisions nationwide (see also Topic IV, Objective 2, Measures 1 and 2).

The training and qualification concept in the following proposal should not, however, become mandatory for all occupational groups in the field of GCTs. Instead, it should be regarded and offered as an opportunity to obtain evidence of skills that are conducive to further career steps or be used to achieve lasting stability in a highly dynamic professional field. Furthermore, this model should help to resolve the shortage of specialists in the development, GMP-compliant production and clinical use of GCTs, training for auditors and professional development for regulators. The experiences of existing well-established curriculums should be used to continuously adapt and improve this training model. This will require the conception and implementation of a nationwide, centrally coordinated, Internet-based information platform.

This platform should facilitate access to and maintain information about training facilities, GMP manufacturing sites, scientific networks and patient networks, thereby enabling the efficient networking of these entities (see also Topic I, Objective 3, Measure 1 and Topic VIII, Objective 1, Measure 1).

The proposed concept has two phases (see Fig. 1). All participants complete the first phase together, which should be emphasized as a particular strength of this training concept.

Following a core curriculum, members of all participating occupational groups – regardless of their prior experience or educational background – complete different (mandatory) basic modules covering fundamental aspects and core skills in the field of GCTs. This content should serve as a framework for the training schedule, covering the entire process of development, manufacturing, testing and market-placement of GCT products, thus conveying core knowledge and skills in these fields across different occupational groups. This includes technical and scientific content along with medical, engineering (e. g., production technology and automation), business, economic, pharmaceutical and regulatory aspects, ethical, legal and social aspects (ELSAs).

In the second section, elective training, participants are free to select a specialization to set a focus for their training (e. g., GMP management, process realization, translation of ATMPs, regulatory affairs of GMP-production and clinical studies, market access or patient participation in research). This specialization would normally be a logical addition to the participant's existing education and training. All participants must complete a specified number of elective modules to gain the credits required to obtain a corresponding certificate/qualification upon completion of the program.

The modules in both phases – core and elective – should be offered and coordinated jointly by universities, universities of applied sciences, further education institutions and industry. Local coordination offices should be established at institutions seeking to participate in the concept. These offices should also organize interdisciplinary and inter-institutional teaching activities, both at their institution and at other locations, in the interests of promoting networking and shared use of resources in teaching. If specifically commissioned to do so, WG II could produce a detailed teaching program containing the content and modules required to achieve the relevant objectives, which would subsequently have to be discussed with relevant educational institutions and professional associations regarding recognition and awarding procedures for the program. These would include medical associations, pharmacists' associations, chambers of industry and commerce, expert associations, lobbying groups, etc. The qualification could be recognized by the Central Authority of the Länder for Health Protection with regard to Medicinal Products and Medical Devices (ZLG).

Timeline and resource requirements

- Timeline for development of a concept for the core curriculum: Short term (1–2 years)
  Led by WG II in conjunction with other WGs (e. g., WG V) and relevant stakeholders from academia and industry (e. g., relevant industry associations).
  In addition, the relevant professional associations will participate in the development of a collection of modules for the elective phase of training for an additional qualification.
- Timeline for implementation: Medium to long term (3–5 years)
- Resource requirements: Additional staff and (depending on the location and training type) investments in teaching materials will be essential to implementing this measure
- Minimum staffing requirements: One coordinator per training location (suggestion: financed by federal government). In addition, further permanent positions should be created in academic and non-academic roles (depending on each training institution's needs) to support candidates' continuous theoretical and practical training

Dynamic training and qualification model for gene and cell-based therapy

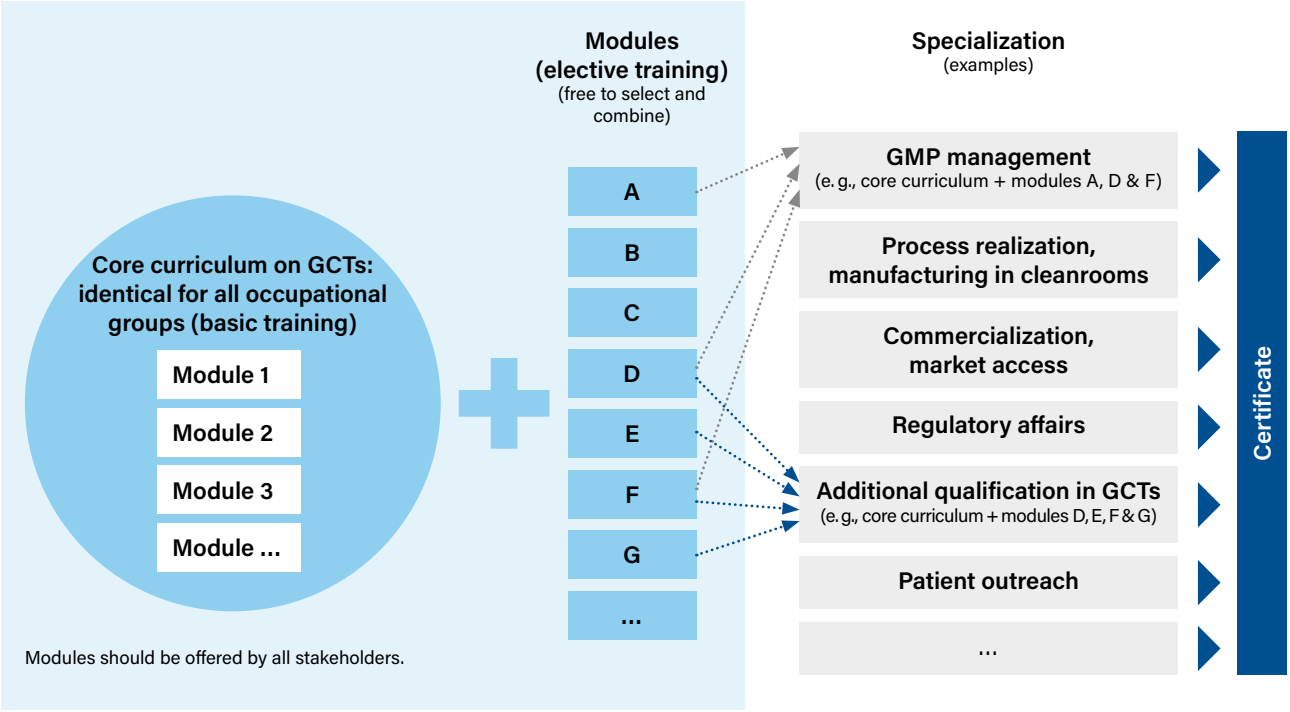


Figure 1: A multi-track structure for additional GCT-training. All participants start by completing the same basic training, which conveys core skills relevant to GCTs in a defined number of modules. In order to obtain a certificate for the respective specialization, participants must successfully complete a defined number of elective modules (based on a credit-point system).

Success indicators

Qualitative:

- Concept developed and implemented nationwide (as an indicator of acceptance)
- Graduates receive job offers
- Evaluation of participant satisfaction and benefits derived from training

Quantitative:

- Number of program applicants and participants
- Number of graduates after five years in comparison with status quo (including monitoring of the success/drop-out rate if appropriate)
- Share of graduates that receive job offers in their field of training and/or shift (the focus of) their professional activities to the field of GCTs
- Number of institutions that offer this form of structured training and development program
- Number of positions in the field of GCTs with appropriately qualified staff

Measure 2:
Establish extra-occupational, interdisciplinary Master's and doctoral programs at universities and universities of applied science (FHs) along with training programs for all occupational groups in the field of GCTs

Stakeholders required:
Universities, FHs and non-academic educational and training institutions

Description:

The establishment of interdisciplinary and cross-faculty Master's and doctoral programs that can also be completed on an extra-curricular basis. This would enable training of early career academic researchers, qualified persons (QPs – cf. EU GMP, Annex 16) and appropriately qualified individuals for manufacturing and testing as well as pharmacovigilance as defined by the Medicinal Products Act (AMG) and the Ordinance on the Manufacture of Medicinal Products and Active Substances (AMWHV) for the highly innovative field

of GCTs. Access to these study programs should also be granted to people with corresponding professional experience in the respective areas to increase the proportion of students with relevant "practical" operational skills in manufacturing. After completing their studies, graduates should be able to work in all areas of GCTs – from basic and pre-clinical research to the development and scaling of manufacturing processes, organization and implementing cleanroom procedures, regulatory affairs to patients' rights and clinical applications. Participants' skills for interdisciplinary communication and cooperation should be fostered from the outset and throughout their studies to solve the multi-faceted tasks and challenges in translating the results of basic and pre-clinical research into clinical practice. The students should develop an understanding of issues including the statutory framework conditions and the regulatory system and be able to apply this knowledge to design manufacturing processes in line with GMP standards. They should also be able to work in clinical production and application in the future. They should consider the development pathways and interdisciplinary requirements for market access that extend beyond demonstrating quality, safety and efficacy. This includes addressing varying assessment procedures for demonstrating (additional) benefits and enabling cost reimbursement, as well as meeting requirements for further evidence generation under standard conditions of use. Examples of such requirements include registry strategies, registry studies, and the collection of routine practice data.

Specialists should also be trained to serve as a link between research and development and the implementation of clinical studies, especially in cooperation with pharmaceutical companies (industry). The overarching aim of these programs is to develop an "open, courageous mindset" in a new generation of researchers who can overcome the challenges of GCTs while complying with regulatory requirements. Given that education and training programs have already been established in this field internationally, e. g., in the English-speaking world at University College Dublin (https://www.nibrt.ie) and the National University of Singapore (https://www.actris.sg/our-service-provision/education-and-training/overview/), suitable study programs could be developed in Germany by following these examples. In view of the interdisciplinary nature of these programs, however, specific regulations could present issues at certain institutions (such as the requirement to establish it in one specific faculty). The universities in question must create cross-faculty regulations that align with this important educational objective. Institutions should also leverage internal operational experience gained through international Marie Skłodowska-Curie programs for Master's students and doctoral candidates. In addition, establishing regular, compact training programs in the form of summer schools for the different occupational groups in the field of GCTs should support and expedite efforts to convey relevant skills for occupational groups involved in operational aspects.

Timeline and resource requirements

- Short to medium term (1–5 years)
- Annual funding in the mid-single-digit million-euro range will be required to develop and implement the specific GCT university-level programs (Master's, PhDs) at universities, universities of applied sciences and research institutes (on the assumption of 200 students per year)
- Annual funding in the mid-single-digit million-euro range will be required for training programs in companies developing and manufacturing GCTs, research institutes and training providers (on the assumption of 800–1,000 participants per year)

Success indicators

Qualitative:

- Graduates from the education and training programs receiving job offers and being integrated in academic, non-academic and industrial careers can serve as a measure of the efficacy of education and training programs at GCT education and training sites
- Reputation and influence: The recognition of GCT education and training sites and certificates/additional qualifications in the national and international scientific community, and their influence on political decisions, funding awards and healthcare policy design, can serve as further success indicators
- Participants' evaluations regarding their willingness to recommend their program, their satisfaction and the program quality

Quantitative:

- Number of applicants for corresponding study programs and summer schools
- Number of graduates after five years in comparison with status quo (including monitoring of the success/drop-out rate if appropriate)
- Number of graduates who receive job offers in relevant areas of industry and/or pursue academic/non-academic careers with a focus on GCTs
- Number of academic institutions that establish/offer such programs in the field of GCTs
- Number of institutions that offer summer schools

for academics and technical laboratory personnel (e. g., MTs)
- Proportion of students who are technical laboratory personnel (e. g., MTs) with relevant professional experience
- Number of partnerships between academia and industry; collaborative research projects and successful technology transfers can reflect the contribution of GCTs hubs in promoting innovation and the commercialization of research results
- Number of clinical studies based on research results produced at GCT hubs or in collaborative research projects between academia and industry

Measure 3:
Establish national GCT education and training centers to strengthen academic, non-academic and industrial skills

Stakeholders required:
WG II, universities, state science ministries, non-academic educational and training institutions, industry

Description:
State-of-the-art education and training services should be offered at different locations in GCT hubs (see Topic VI, Objective 1, Measure 1) to strengthen the national talent pipeline. Based on the excellent research as well as available production and healthcare infrastructure in these hubs, they offer outstanding conditions for talented specialists in all (academic and non-academic) occupational groups to access education and training. Two aspects are relevant in this context:

a. Academic education: Educational programs for doctoral candidates, postdoctoral researchers and other specialists in the field of GCTs. Academia and industry can collaborate closely to develop theoretical and practical training modules to prepare highly skilled specialists as effectively as possible for a career in science or industry
b. Skills training: In addition to academic education, professional development programs and skills training should be offered for industry specialists. This could include theoretical and practical training to meet the needs of specific job profiles, such as process development, GMP manufacturing, quality assurance and regulatory requirements

Timeline and resource requirements
- Long term (5 years)

Success indicators
- Number and quality of specialists who successfully complete the programs and are integrated into academic and industrial careers can serve as a measure of the efficacy of education and training programs

Objective 2:
Develop adequate career concepts, bonus concepts and interaction concepts

Explanation:
To become and remain competitive in the field of GCTs with lasting effect, it will be essential to develop suitable career concepts and create additional options to provide long-term prospects to people employed in the field of GCTs as well as define new occupational groups, where necessary. In this context, it is also important to ensure that provisions are made to protect people already working in this field, not least to foster widespread acceptance of the program. As noted in the introduction, new and straightforward forms/ options of financial support and career advancement must be developed, especially in regard to the translation of research results to manufacturing and clinical practice, as well as commercialization – topics which require improvement in Germany. It will also be necessary to increase the degree of permeability between academic and industrial areas. According to estimates from the U.S. Food and Drug Administration (FDA) – or, to be more precise, from its former commissioner, Scott Gottlieb, and the director of its Center for Biologics Evaluation and Research, Peter Marks, https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics – we can expect to see significantly more than 200 investigational new drugs (INDs) and 10 to 20 new marketing approvals for GCTs/ATMPs per year by 2025. Against this backdrop, the rapid development of strategic and infrastructural educational concepts is increasingly important. A further urgent task will be to develop interaction concepts designed to bring together different occupational groups and stakeholders to foster interaction between industry and academia through a defined development pipeline for GCT products. In this context, it is also important to emphasize interactions with ELSA disciplines and regulatory authorities (the PEI, the Federal Institute for Drugs and Medical Devices (BfArM) and state authorities).

Measure 1:
Create incentive systems, bonus systems and career concepts

Stakeholders required:
Universities, medical associations, relevant lobbying groups, chambers of industry and commerce, industry

Description:
New bonus systems must be established and their reliability increased to make positions in the field of translation (i. e., the translation of research results into marketable products that are ready for use) more attractive. The following list provides a few examples of possible measures:

- Ensure that activities regarding the development of clinical translation are counted towards academic career paths (postdoctoral teaching qualifications, adjunct professorships, tenure track positions) (universities)
- Recognize respective activities and achievements for the training towards specialist qualifications for doctors (Facharztweiterbildung), possibly creating a specific additional qualification; longer-term contracts to secure and consolidate these target positions (universities and medical associations)
- Introduce new forms of indicator-based funding allocation (IMA) at universities for the development of applicable GCT products (universities, federal and state governments)
- Develop return concepts (for professionals returning to Germany from abroad) and transition concepts at the interface between industry and academia (e. g., through “bridging” professorships or joint working groups

comprising members from academia and industry)
- Promote permeability between academia and industry positions (primarily for professionals to move from industry into academia) and create opportunities for temporary secondments to spin-offs
- The translation of research results within universities should not be classified as an entrepreneurial activity. Instead, it should be defined as a sovereign activity and perceived as a vital step that links healthcare with research and development and therefore facilitates the upskilling and professional development of doctors, and the education, training, professional development and upskilling of other staff.

Timeline and resource requirements
- Short to medium term (1–5 years)
- Low additional resource requirements

Success indicators
- A significant increase in activities to implement exploratory research into clinical studies
- Implementation of clinical study results in national and international guidelines
- Increase in the number of licenses awarded for research results to industry partners
- Increase in the number of spin-offs

Measure 2:
Develop an interaction concept to support training and career development for relevant stakeholders

Stakeholders required:
Associations, universities, non-academic training institutions, industry

Description:
Different formats must be established to improve the interaction and permeability between academia, industry and other stakeholders in the field of GCTs, incorporating feedback loops. The formats' structure could draw on the networking proposals in Topic I. Dual education and training concepts would be desirable, covering the time window in the graduate training and postdoc phase in academia and industry. In addition to formats such as programs for clinician scientists, translational scientists, GMP specialists (e. g., new roles of "GCT technicians/analysts") and clinicians, it will be important to consider the ELSA disciplines and the interaction with regulatory authorities. The establishment of shared interaction platforms – designed to foster exchange both within and between occupational groups – can enhance the permeability of information and dialog flows with network-like characteristics. Examples include joint academies for developing education and training platforms tailored to different groups with complementary content, as well as initiatives such as summer schools, congresses, and symposiums.

Over the long term, the interdisciplinary participation of stakeholders from the fields of ethics, law, regulatory affairs and the healthcare system could serve as a form of feedback system, helping to refine and adapt statutory framework conditions and regulatory requirements. "Bridging" professorships between industry and academia should be considered as an urgent requirement in this context, along with the creation of shared structures (e. g., platforms to promote dialog between pharmaceutical and biotech associations, industry and academia).

Timeline and resource requirements
- The BIH could provide financing for interaction programs, including for clinician scientists and translational scientists, along with establishment of a national entrepreneurship program as part of the National Strategy
- Timeline: Pilot phase for the entrepreneurship program to start in January 2024 at three locations; roll-out to further locations from 2025 is conceivable
- Support for clinician scientists and translational scientists from late 2024

Success indicators
- Graduates from the described education and training programs are successful in securing job offers
- Increased mobility for graduates and experienced professionals between academia, industry and research

Topic III: Technology transfer

Summary

Translating knowledge into tangible impact: the technology transfer strives to apply the results of biomedical research to deliver benefits for patients, economy and society. In this context, it is essential to keep the entire translation chain in mind – from patenting new ideas to collecting essential pre-clinical data and establishing effective production processes through to clinical proof-of-concept studies in a suitable patient population. This is the only way we will be able to keep pace internationally with other nations, such as the USA and China, which are leaders in GCTs. From the patients' perspective, a robust transfer of knowledge in Germany and Europe is essential to provide swift access to novel therapies, and influence the pricing. And, of course, a successful translation of GCTs will create jobs and support value creation in Germany and Europe.

To achieve this, it will be necessary to raise awareness of the requirements and opportunities of translation of GCTs. A detailed understanding of the fundamentals of product development will shape technology transfer units in a way that they can support the entire transfer process, from protection of IP to application in clinical practice. In addition to highly qualified specialists, this will require support from a central product development unit (PDU) specializing in GCTs. The targeted deployment of consultants would help to advise on specific aspects of product development, particularly in relation to production and regulatory affairs.

Transfer activities performed by individual scientists, academic institutions and universities should be considered equally in their performance assessments. It also appears necessary to offer employment prospects for researchers who possess specific knowledge essential for the translation of a product to clinical application until they can move to a spin off. To make spin-offs and start-ups attractive for founders and venture capital providers, standardized licensing conditions should be created (drawing on international standards, such as the University Spinout Investment Terms (USIT) Guide). To help spin-offs to get off the ground access to publicly funded infrastructure should be facilitated. Transparent distribution of eventual revenues – taking into account the inventors, but also the institute or hospital where the invention was made – is an important incentive. Revenues should support a fund for future transfer projects at these institutions. We have therefore formulated four specific targets regarding technology transfer, and defined measures designed to achieve them:

1. Improve the framework conditions for early identification and utilization of innovative potential of scientific results
2. Ensure comprehensive consultancy and assessment of transfer projects. This must incorporate the entire development process for an investigational medicinal product (IMP), from production to use in patient care
3. Facilitate efforts to exploit the social and/or economic potential of scientific results
4. Establish recognition of transfer activities and transfer successes as part of individual researchers' and institutions' scientific reputation

1 Improve the framework for early identification and utilization of innovative potential of scientific results

2 Ensure comprehensive consultancy and assessment of transfer projects, incorporating the entire development process from production of an IMP to its use in patient care

3 Facilitate efforts to exploit the social and/or economic potential of scientific results

4 Establish recognition of transfer activities and successes in translation as part of individual researchers' and institutions' scientific reputation

Background

A robust technology transfer system will be necessary for novel therapies, such as GCTs, to enter commercial use and reach the patients in need. This transfer is based on patent protection that is sufficiently broad to justify longer-term product development. It comprises systematic development of research results in line with fundamental requirements and standards of safety, quality, efficacy, producibility and economic viability, with the aim of facilitating the targeted introduction of GCTs into patient care.

Germany is currently unable to keep pace with its international competitors in the field of GCTs, such as the USA and China. Only a limited portion of the research conducted in Germany is successfully translated and further developed either within the country or through German-based initiatives. The technology transfer and resulting value creation for much of Germany's research output in the field of GCTs takes place outside Europe, e. g., in the USA and China. This topic specifically addresses the causes of insufficient technology transfer for GCTs in Germany. Thus, we recommend specific measures that we consider necessary to maintain technology transfer in Germany.

The term **innovation** refers to the **introduction** of new processes, products or services that represent a significant **improvement** – e. g., by creating new markets or optimizing existing solutions.

By contrast, an **invention** is the first creation of a **novel** product or technique.

Technology transfer is the successful development of an invention into an (approved) product – e. g., a drug, treatment method or an accompanying diagnostic procedure with an additional benefit (innovation) for the patient.

In addition to research and development (see Topic VI), technology transfer plays a decisive role in the transition from the laboratory to clinical practice. This transfer is an interdisciplinary process that protects the intellectual property (IP) of research results; systematically minimizes risks; safeguards, qualifies, evaluates and documents product development and, finally, makes an IMP available for clinical use in accordance with regulatory requirements. It requires specific expertise in planning and implementation as well as the appropriate infrastructure. Given the increasing costs during technology transfer, securing IP at an early stage, establishing production processes and commencing initial clinical trials of the new GCT product – with professional support – are crucial to technology transfer in academia. These clinical trials are an important milestone in securing further investment from funding providers, investors and industry partners. Utilizing this investment, additional necessary resources can be provided to facilitate the technology transfer of GCTs to clinical practice in Germany (see also topics IV, V and VII).

Objectives

1. Improve the framework for early identification and utilization of the innovative potential of scientific results
2. Ensure comprehensive consultancy and assessment of transfer projects, incorporating the entire development process of an IMP, from production to use in patient care
3. Facilitate efforts to exploit the social and/or economic potential of scientific results
4. Establish recognition of transfer activities and transfer successes as part of individual researchers' and institutions' scientific reputations

Overall, it is essential that Germany intensifies its efforts to file solid IP from academic research. This requires (i) securing comprehensive international protection for academic institutions' own IP, (ii) ensuring that development activities can proceed as independently as possible from legal restrictions and (iii) do not carry the risk of infringing third-party rights (freedom-to-operate (FTO) analysis). This is the only way to guarantee that the potential of scientific results is fully exploited and can contribute to innovation and economic development. Effective mechanisms to achieve this must be identified and then adapted, tested and made available at national level.

Objective 1:
Improve the framework for early identification and utilization of the innovative potential of scientific results

Explanation:
It is essential to identify the innovative potential of academic research results at an early stage, e. g., by protecting IP in advance of publication, to realize this potential.

Universities and research institutes rely on technology transfer offices (TTOs), which offer training, consultancy and support, to help protect their IP. Scouting programs also help to identify innovative results. In an international comparison, countries such as the USA and China are more advanced than Germany when it comes to raising awareness of patenting processes and promoting an entrepreneurial start-up culture. In these countries, students are introduced to such topics at an early stage and collaborations with industry are actively encouraged. Networking with companies and venture capital providers plays a vital role in accelerating the transfer of research results into market-ready products and supporting the foundation of start-ups out of academia. Therefore, new programs are required to support building such networks, with scientific institutions taking an active role in founding start-ups. Germany needs to identify the innovative potential of scientific results earlier. This requires a mindset change from a purely scientific to an entrepreneurial approach. To achieve this, a multi-layered approach is required.

Measure 1:
Education, training and development

Stakeholders required:
Then boards of management of universities and universities of applied science, teaching staff, patent attorneys, regulatory experts, training providers

Description:
Targeted education, training and development measures on the topics of IP and associated rights, production process development, pre-clinical development, regulatory affairs, product development and entrepreneurship must be implemented and expanded to strengthen innovation and technology transfer at universities and research institutes.

Basic education for students and training for researchers and clinical staff on the topic of IP rights and spin-offs will be necessary for them to develop an awareness of the value of the IP in their research at an early stage. It would also be important to learn to focus on developing potential products, thereby facilitating a better understanding of the commercial significance of their research activities (see Topic II, Objective 1, Measure 1).

Training for researchers: Basic (mandatory) training for researchers and clinical staff on the topic of IP rights and founding a spin-off could be established in a timely manner. In addition, TTOs should collaborate with scientific departments to identify potentially patentable results at an early stage.

In-depth training: In-depth training on specific aspects of translating innovations in the field of GCTs into clinical applications and market-ready products must

be established and expanded for doctoral candidates, clinicians and researchers. This training should also cover specific aspects of GCTs concerning IP rights, pre-clinical and clinical development, regulatory affairs, product development and entrepreneurship.

Training and development for TTO staff: Targeted training and development must be established and made mandatory for researchers moving into the field of technology transfer, and for professionals already working on technology transfer, to train them on the specific topic of IP rights – especially regarding specific aspects of GCT projects. Qualification measures should convey knowledge in areas including regulatory affairs, contract law, network building, project management and data protection. Furthermore, universities and research institutes should establish programs to train patent attorneys with a focus on GCTs.

Universities, research institutes and external education providers should offer corresponding, extra-curricular services in the form of low-threshold and accredited courses, workshops and distant-learning programs. Subsequently, specifically qualified employees must be offered longer-term employment prospects to utilize the established potential.

Timeline and resource requirements

- Short term (1 year): Determine needs and plan the development and implementation of education and training offerings; organize initial workshops/courses
- Medium term (2–3 years): Develop a modular curriculum and translate it into study programs; establish mandatory training; set up courses with/through external education providers
- Long term (4–5 years): Secure accreditation for new education offerings and modules; fully integrate new content into study programs; conduct regular needs analysis and adapt teaching content accordingly

Success indicators

- Number of courses, workshops and (remote) study programs established; number of students, doctoral candidates and researchers; number of IP applications submitted by universities and research institutes
- Feedback from participants in education and training courses

Measure 2:
Strengthen technology transfer offices (TTOs)

Stakeholders required:
TTOs, patent attorneys' offices, political decision-makers, researchers/inventors; boards of management of universities and research institutes

Description:

TTOs at universities and research institutes play a key role in identifying patentable inventions and supporting researchers with patent applications. The TTOs' teams should be strengthened, and the offices themselves should be well funded. In addition, a fixed share of institutional subsidies should be reserved for the field of innovation and technology transfer, with this topic area anchored as an additional independent pillar alongside research and education. Additional resources to advise researchers can help to improve assessment of research results as well as support the drafting and submission of patent applications, thus enabling the necessary IP protection.

A higher number of patent applications will inevitably lead to higher costs to obtain patents. Until sufficient funding is made available for the technology transfer through institutional subsidies, there will be a need for national funding programs that, unlike Germany's discontinued WIPANO (Knowledge and Technology Transfer through Patents and Standards) funding program, offer simple, quick and unbureaucratic access to funding (see Topic VI, Objective 2, Measure 1). Resources for efforts to ensure effective patent utilization lead directly to practical application. This applies to particularly highly innovative fields, such as GCTs.

By employing a dedicated patent attorney, TTOs can offer support with drafting and submission of patent applications and, in partnership with external patent attorneys' offices, help to develop strategies for patent applications. Employees at TTOs should be trained and able to involve the services of consultants with industry experience where necessary to actively pursue patent utilization and support spin-offs in their search for potential investors or licensees (business development).

Timeline and resource requirements

- Short term (1 year): Analyze the status of TTOs and determine the requirements for human and financial resources; organize discussions with political stakeholders to secure the necessary resources, subsidies and funding programs; set up funding programs; establish scouting processes; set up consultancy groups with experience in industry

- Medium term (2–3 years): Recruit staff; create professional development programs for TTOs on patent utilization; implement simple, unbureaucratic processes to secure funding, e. g., for FTO analyses/ calls from funding programs
- Long term (4–5 years): Establish innovation, IP and technology transfer as an independent pillar in academic institutions; regularly review transfer efficiency and adjust TTO strategies if necessary

Success indicators

- Number of inventions identified and reported by TTOs
- Number of patents issued in relation to patent applications submitted
- Number of successful utilization activities and (resulting) level of revenue generated
- Researchers' satisfaction with services offered by TTOs
- Increased efficiency of technology transfer processed (e. g., reduced processing time between an invention being reported and a patent application being submitted)
- Level, suitability and availability of national funding for technology transfer

Measure 3:
Establish structures for the targeted implementation and market preparation of GCT projects

Stakeholders required:
TTOs, researchers, attorneys, economists, clinical trial offices (CTOs), regulators, external consultants, marketing consultants, IT experts, industry partners

Description:
As an early focal point for GCT projects, technology transfer is central to the establishment and coordination of internal and external support structures. TTOs must be structurally and conceptually strengthened to meet this demand. This includes setting up a PDU (see Objective 2, Measure 1). The PDU interlinks interdisciplinary consultancy teams consisting of researchers, clinicians, attorneys, economists, regulators, GMP institutions, CTOs and/or marketing specialists who can provide support throughout the entire development process for GCT therapies. A GCT-specific set of guidelines and an accompanying catalog of measures should be developed to clearly define the steps required and the experts who should be integrated. Ideally, this should be coordinated through a central PDU specializing in GCTs and with activities nationwide. It concentrates the knowledge of the various TTOs and helps inventors to communicate with regulatory authorities and prepare documentation for a clinical trial application. The necessary external consultants and/or companies will be consulted to integrate their specialist knowledge for a specific GCT project and to efficiently overcome regulatory barriers. An online consultancy platform for TTOs could facilitate swift and straightforward communication between TTOs, the PDU and external consultants. This will allow and/ or facilitate a low-threshold consultancy service on regulatory aspects, existing (approved) technologies and third-party rights – taking into account the expertise in the hubs proposed within the GCT initiative (see Topic VI, Objective 1, Measure 1). This would also ensure unbiased assessment, early identification of opportunities and risks, and support for specific concepts (e. g., for decentralized manufacturing (point-of-care production)).

Timeline and resource requirements

- Short term (1 year): Review existing TTO structures and competencies (national perspective); define inter-professional team structures within a TTO, assemble and train interdisciplinary teams; draw up plans for an online consultancy platform for communication between TTOs, the PDU and consultants
- Medium term (2–3 years): Develop a GCT-specific set of guidelines and catalog of measures; establish a low-threshold consultancy service focused on regulatory aspects of GCT projects; establish strategic partnerships with academic institutions (that may also serve as service partners for smaller institutions), external consultants and industry partners
- Long term (5 years): Implement workshops and mentoring programs focusing on the realization of GCTs; set up an online consultancy platform

Success indicators

- GCT-specific guidelines and catalog of measures are introduced and utilized
- An online platform focusing on specific aspects of GCT product development is established
- Workshops are organized; number of participants, participants' satisfaction and demand for this service
- Use of the online consultancy platform and user satisfaction
- Projects successfully overcome regulatory barriers, incl. through targeted and fast implementation in a FIH study
- Initial market launch of new GCT products (also incl. time factor)

Objective 2:
Ensure comprehensive consultancy and assessment of transfer projects, incorporating the entire development process, from production of an IMP to its use in patient care

Explanation:

Innovations in GCTs arise from new technologies (e. g., manufacturing processes, transfection methods, etc.) as well as new therapeutic GCT approaches to treating specific diseases.

Technology transfer "from bench to bedside" can only succeed when a GCT technology meets the necessary requirements for translation to therapeutic application and can be manufactured in a reproducible, scalable and, ultimately, cost-efficient process. With specific regard to GCTs, a mindset change must take place to recognize process development as an unavoidable necessity that requires corresponding planning, funding and implementation. At present, neither academic research nor existing technology transfer units and industrial collaboration partners can meet these requirements on their own. Specialized consultants that are required often charge high fees and are not familiar with the framework conditions of the academic landscape. Therefore, suitable measures must be established to overcome these barriers.

The necessary requirements must be taken into account step-by-step and will involve access to specific infrastructure, qualified staff and sufficient financing. The following will be necessary for a successful technology transfer in relation to GCTs:

a. Economic utilization and societal impact: Classification regarding the current state-of-the-art and/or the therapeutic gold standard, ongoing developments, economic framework conditions and product implementation options.
b. Definition of the technology/the therapeutic GCT: Creation of a technology or product profile (target product profile – TPP) in accordance with ICH Guidelines and/or technical standards, the resulting minimal specifications and requirements for qualification of the technology and/or clinical application of the GCT.
c. Detailed project planning (i. e. timeline, staff requirements, infrastructure requirements, etc.): Creation of a systematic, rational and step-by-step development plan, including risk management, staffing and financing plans.
d. Technical and/or pre-clinical evaluation, qualification, validation and documentation: Planning and implementation of the necessary in vitro, in vivo, pharmacological and experimental trials to qualify and validate the technology/product profile, including corresponding documentation.
e. Development of a manufacturing process in line with GMP standards, plus qualification and validation: Development of cost-efficient production processes and technologies; validation of reproducibility and scalability of the production process; evaluation of the manufacturabilit of the GCT products, including qualified and validated analytical methods to ensure conformity with GMP standards. Continuous development of the process.
f. Clinical study design and regulatory approvals: Planning of an adequate study design, evaluation of feasibility (patient recruitment, end points, statistics), establishment of study monitoring processes, risk management and biostatistics, including approval by an ethics committee and responsible authorities.

Closer links should be established between technology and GCT developers and healthcare experts, experts in regulatory affairs, pre-clinical trials and clinical implementation. Closer networking of science, regulatory affairs and industry through a PDU can more effectively leverage the potential of process and technology standardizations. Achieving this will require the following specific measures:

Measure 1:
Establish a product development unit (PDU) to support project planning and implementation

Stakeholders required:
Political decision-makers, the PEI as the responsible regulatory authority, appropriate academic institution

Description:
The establishment of an independent, central PDU, which should be based at an appropriate academic institution, will offer scientists and research institutions considerable support in terms of technology transfer by providing professional guidance regarding the creation and implementation of a risk-minimized, product-specific project plan. This type of PDU concept has, for example, significantly advanced transfer activities at the German Center for Infection Research (DZIF) and should therefore be adopted to the field of GCTs. The PDU will accompany the development of a project plan containing the necessary development steps, infrastructure to be involved and a project timeline. It will have access to a network branching out in all directions, including experienced developers, production specialists, experts in regulatory affairs, pharmaceutical partners and public authorities. This will enable investors and scientists to proceed systematically in working through the necessary steps in a development plan. These steps include advancing swiftly and smoothly through technical and/or pre-clinical evaluation (including necessary in vitro, in vivo, toxicological and pharmacological trials); developing a suitable product prototype; establishing a reproducible manufacturing process to ensure that the components and the clinical test product are produced in line with good laboratory practice (GLP) and good manufacturing practice (GMP) guidelines; ultimately, qualification, validation and documentation of the pre-clinical and clinical proof of concept. In line with published guidelines, the PDU will work with the TTO teams and scientists to draft the respective GCT technology or product profile (TPP) as well as plans for specific requirements. In addition, the PDU will support the technology transfer using SOPs for existing processes and/or platform technologies as well as by contributing to the development of new processes. It will also aim to foster and ensure the interdisciplinarity necessary for GCT projects by collaborating with medical, biological and process engineering (research) institutes.

Timeline and resource requirements

- Short term (1 year): Secure the financial resources to establish a central PDU, set up consultancy groups and recruit qualified staff
- Medium term (2–3 years): Establish a network of external consultants (covering regulatory affairs, manufacturing and financing); engage with inter-professional TTO teams from different institutions to identify flagship projects
- Long term (4–5 years): Secure longer-term funding for the PDU, including a management with experience in industry and 3 to 4 staff members

Success indicators

- Establishment of the PDU
- Identification of the initial flagship projects and definition of milestones
- Initial projects were guided into clinical practice

Measure 2:
Create and operate jointly accessible infrastructure for GCT developers

Stakeholders required:
Political decision-makers, state and federal ministries, boards of management of academic institutions

Description:
Creating shared infrastructure would enable GCT developers from different organizations – such as universities, research associations, start-ups, pharmaceutical companies and biotech companies – to collaborate on the development of new therapies. This way, skills in different areas (e. g., medicine, biology and engineering) would be pooled at an early stage while creating an environment to foster exchange between these participants, which should simplify future clinical development and commercialization. It is particularly important to consider the manufacturing of material for pre-clinical toxicity studies and clinical studies, and the generation of data for submission of a clinical trial application (CTA) in Europe or an IND study in the USA. This requires a GMP production environment, corresponding data storage systems and suitable analysis laboratories, which should be located at a premises accessible to all partners. The shared infrastructure could support, for example, the manufacturing of material for preclinical toxicity studies and phase 1 clinical trials. Beyond improving technical skills, the PDU can also consult on translation-related topics (i. e., regulatory affairs, design and implementation of toxicity and phase 1 studies) and thereby develop GCT-specific experience over the long term. The advantage of this (partially) public funding of such hubs is improving affordability for GCT developers, for whom material manufacturing for toxicity studies is usually difficult to finance and therefore represents a bottleneck in the development of new therapies (see recommendations in Topic V, Objective 1, Measure 4 and in Topic VI, Objective 1, Measure 1).

Timeline and resource requirements

- Short term (1 year): Map all existing (partial) infrastructure capacities suitable for shared use in GCT development
- Medium to long term (2–5 years): Continuous establishment and expansion of nationwide GCT development infrastructure for academic institutions and start-ups

Success indicators

- Number of created non-competitive GCT infrastructure elements

Objective 3:
Facilitate efforts to exploit the social and/or economic potential of scientific results

Explanation:
This target focuses on utilizing the potential to benefit society and the (national) economy. The targeted social benefit is the routine treatment of patients with new, approved products. Treating a small number of patients in clinical studies is an interim target in this context. Public research institutions must transfer activities to a company, whether a newly founded start-up or an existing company, to ensure the long-term availability of new products and their market launch and distribution.

In principle, "utilization" as defined above involves a license or a transfer of rights (IP rights and/or expertise) and, in the case of a spin-off, usually requires (direct or indirect) participation in the start-up – especially to facilitate an attractive license structure for the start-up (e. g., exclusivity while still backloaded).

In life sciences, public research institutions often bear high development costs for years and facilitate cost-intensive validation processes. As a result, the transfer of patent rights or virtual shares is usually less suitable. In the case of spin-offs, it is essential to reach an agreement between stakeholders – research organizations, founders and investors – as quickly as possible. In this context, there is national and international consensus that transparent spin-off standards should be developed up front, with research organizations, existing spin-offs and investors involved in the process. In the USA, a set of guidelines has been developed in an initiative led by Columbia University, with these recommendations further refined by TenU (a collaboration of TTOs at universities in the USA, UK and Belgium) to develop the USIT Guide. National recommendations have also been derived from this in the Netherlands and Belgium. In Germany, the TransferAllianz has issued a position paper guided by the fundamental philosophy of the US recommendations and the USIT Guide. The latter is an extensive document focusing on life sciences: it addresses several aspects relevant to spin-offs and should therefore serve as the reference document for spin-offs in the context of the National Strategy for GCTs.

Measure 1 (non-GCT-specific):
Develop national guidelines for transparent spin-off standards, e. g., based on the USIT Guide

Stakeholders required:
Venture capital providers, non-university research institutes, universities, existing spin-offs (both successful and failed), TransferAllianz

Description:
A national guideline should be developed, taking into account the legal and structural circumstances in Germany, as well as internationally established approaches such as the University Spin-Out Investment Terms (USIT) Guide, by involving important stakeholders e. g., venture capital providers, non-university research institutes, universities, existing spin-offs (whether successful or failed) and the TransferAllianz. This would provide support for spin-offs, enabling them to compete patent rights. Furthermore, these conditions for licensing are known to the respective teams from the outset of the project.

Until such a national guideline is issued, however, individual institutions should draw up guidelines – at least regarding the institution's participation and licensing conditions – so that spin-off founders are no longer left feeling they must "start from scratch" when navigating an opaque environment. To achieve long-term, nationwide standardization of transfer conditions, these guidelines should be published – or at least made available to the working group developing the national guideline, as well as the TTOs at other research institutes in Germany. The model developed at Columbia University can serve as a basis for standards regarding term sheets. Further developments issued by Columbia and TenU should be used to guide national standards in the future.

Timeline and resource requirements
- Short term (1 year): 1 coordinator (human resource)
- Medium term (2–3 years): Development of guideline

Success indicators
- Creation of guidelines on participation and licensing conditions
- Completion of national guidelines

Measure 2 (GCT-specific): Clarify and improve the framework so that start-ups in the initial phase can use existing infrastructure at their (parent) research institute, especially cost-intensive GMP (Good Manufacturing Practice) infrastructure

Stakeholders required:
Political decision-makers, state and federal ministries, boards of management of academic institutions

Description:
An expert report should be composed summarizing the legal, regulatory, and organizational aspects that must be considered in the context of start-ups using existing infrastructure at their (parent) institutions. Based on this report and with input from legal consultants, and transfer experts, selected research institutes should then implement the following measures:

1. A guideline should be drawn up for research institutes, providing specific instructions for granting start-ups access to institutional infrastructure. This guideline can then serve as a starting point for academic institutions and prevent any legal disputes.
2. Efforts should be made to identify which existing legal, regulatory, and organizational regulations present the most significant risks/problems regarding start-ups' access to existing infrastructure – and how much operational freedom exists regarding the existing legal framework and particularly in the EU state aid act
3. Identify options to amend the EU legal framework on state aid and (implementing and/or supplementary) German regulations if necessary.

Timeline and resource requirements
- Short term (1 year): 1 (part-time) coordinator (human resource)
- Medium term (2–3 years): Finalization of the expert report
- Funding to engage external legal consultancy

Success indicators
- Finalization of the expert report
- Publication of the guideline with instructions

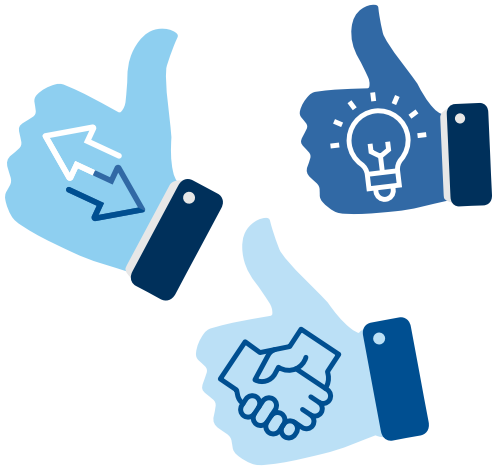
Measure 3 (GCT-specific): Conduct patent research and analysis for a small number of select and definitive key technologies

Stakeholders required:
TTOs, external patent attorneys' offices

Description:
The results of project-related patent research and FTO analyses which were enabled by federal funding should be compiled in case they concern a key technology. Building on this work, patent landscapes should be created for select, definitive key technologies (such as CRISPR/Cas9). These landscapes should identify and develop patent families that are particularly important for all projects using these key technologies. For many such projects, this measure will create an initial, robust foundation for the evaluation of third-party rights to these technologies, in turn accelerating the overall process of a later, more detailed evaluation as part of an FTO analysis. In addition, it will minimize the risk of individual errors in patent research, which is the base for evaluations of possible third-party rights.

Timeline and resource requirements
- Short term (1 year): Funding to establish and maintain a database containing the compiled results
- Medium term (2–3 years): Initial database established
- Long term (4–5 years): Ongoing updates to the database; the database should be handled and maintained by the PDU

Success indicators
- Functional and accessible database is available
- Update process is established
- Access to the database is subject to quantitative monitoring



measure and often take considerably more time than research as a doctoral candidate. The current statutory framework conditions in Germany hinder institutions from hiring a scientist for a longer term in a development project and mean that it is rarely possible for scientists to obtain longer-term employment. And, even if a spin-off is set up, financial restrictions result in a limited period of employment. This leads to a situation in which few young people can devote themselves to such projects, resulting in a high staff turnover during which knowledge and experience is lost.

Objective 4:
Establish recognition of transfer activities and successes in translation as part of individual researchers' and institutions' scientific reputations

Explanation:
To date, transfer activities have only been recognized as scientific activities in Germany under certain conditions. This sets us apart from the USA, for example, where founding a company enhances the reputation of a researcher as well as their research institutions. In Germany, however, society and academics themselves often view the act of founding a company with skepticism, believing it demonstrates a "commercial focus".

A cultural shift is required to create an environment in which innovation and entrepreneurship are explicitly appreciated, supported, and acknowledged. Successful examples of spin-offs and patent applications could be emphasized in internal and external communications, with the scientists in question presented as role models. Furthermore, an impact-oriented approach to research results should be promoted and assessed. Simultaneously, transfer activities at universities and research institutes should be incorporated as quality indicators in their assessments.

Young scientists who have grown up in an academic environment often have a keen interest in making a sustainable contribution to improving people's health and thus, society. The academic environment, however, has not yet developed any "currency" to reflect this. When it comes to obtaining a doctorate, for example, it is usually only publications that are considered, as transfer activities are difficult to

Measure 1:
Optimize academic incentive systems and project-specific employment conditions for qualified staff members

Stakeholders required:
Board of management of academic institutions

Description:
Incentives should be created for scientists who translate their research into practical applications by financial participation in the revenue from licenses or spin-offs not being limited to the inventor(s). It must be possible to employ specialist staff essential to a transfer project via fixed-term contracts until either the spin-off is financed or out-licensing is completed to avoid the loss of knowledge and skills.

It is also important to create means of recognizing transfer activities for subsequent career steps. For example, participation in patent specifications or initiation of clinical trials could be considered as relevant requirements for doctoral theses and post-doctoral teaching qualifications. An approved study protocol for an IIT or an approved manufacturing authorization should be considered equal to a peer-reviewed publication.

Timeline and resource requirements
- Medium term (2 years)
- No specific resources required, but stakeholder of the GCT initiative to lobby for this

Success indicators
- Amend collective bargaining legislation for project-specific employment in a transfer project
- Amend requirements for doctorate and postdoctoral teaching qualifications

Measure 2:
Communicate technology transfer success stories

Stakeholders required:
Communication departments in conjunction with TTOs, National Network Office

Description:
Image campaigns should be implemented to improve the reputation of transfer activities. These campaigns should feature success stories from the field of GCTs, presenting them in a manner that is readily comprehensible and creates a positive impression with students, researchers, and other interested audiences. The campaigns could cover the entire translation chain – from out-licensed patents to the founding of a company and the commercial utilization of research results.

Reports about scientists who have successfully progressed their ideas to clinical application or who have founded companies not only serve as role models but also convey an understanding of how an idea can become a product. Success stories like this have an exemplary effect and improve the standing of stakeholders who have succeeded in technology transfer in the academic community.

Timeline and resource requirements
- Medium term (2 years) for initiation and subsequent continuation of the measure
- Resources: One employee responsible for communications at the National Network Office

Success indicators
- Number of transfer projects communicated online
- Number of website visits, number of positive comments and/or shared posts
- Number of press releases
- Number of media appearances because of advertised projects

Measure 3:
Make transfer activities a quality criterion for research institutions

Stakeholders required:
German Science and Humanities Council (WR), political decision-makers, state and federal ministries, boards of management of academic institutions

Description:
To encourage research institutes to enhance support for transferring research results to the private sector, successful technology transfer activities and support for spin-offs should be explicitly established as objectives in state-level university legislation and for federal-level research institutions. These objectives should complement the fundamental duties of teaching, research and healthcare and be integrated into the criteria used for evaluations. Successful transfer activities should be weighted more heavily in academic rankings, evaluations and recommendations issued by the German Science and Humanities Council (WR), in both quantitative terms (number of spin-offs and licenses granted) and qualitative terms (number of market-ready products, unicorns, etc.). Staff who wish to support spin-offs should be given the opportunity either to work on a part-time basis or to be released from their duties for a fixed period. The corresponding legal and collective bargaining requirements should either be created or used more frequently.

Timeline and resource requirements
- Short to medium term (1-2 years)
- No additional resources required

Success indicators
- Definition of short-term and medium-term targets for successful transfer activities by each academic institution
- Adaptation of the catalog of evaluation criteria for university and non-university scientific institutes
- Evaluation of the impact of amended targets/evaluation criteria after five years
- Adaptation of indicator-based funding allocation (IMA) to incorporate translational success criteria

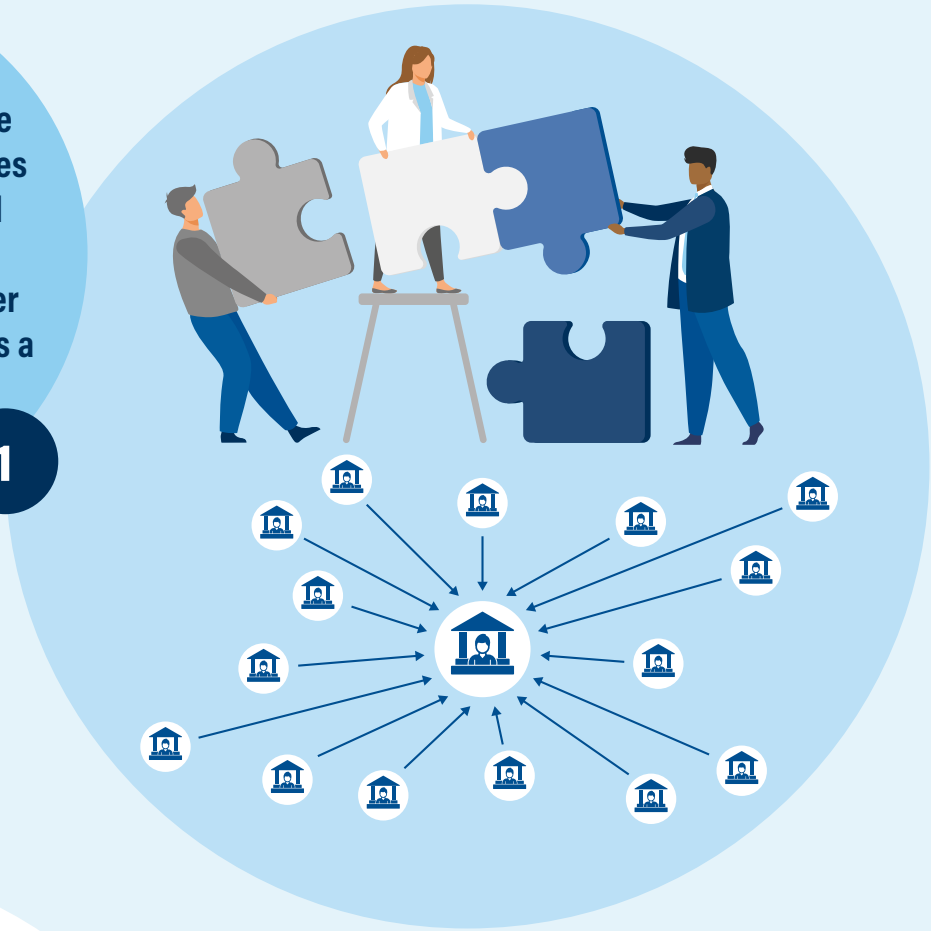
Topic IV:
Standards, norms and regulatory framework

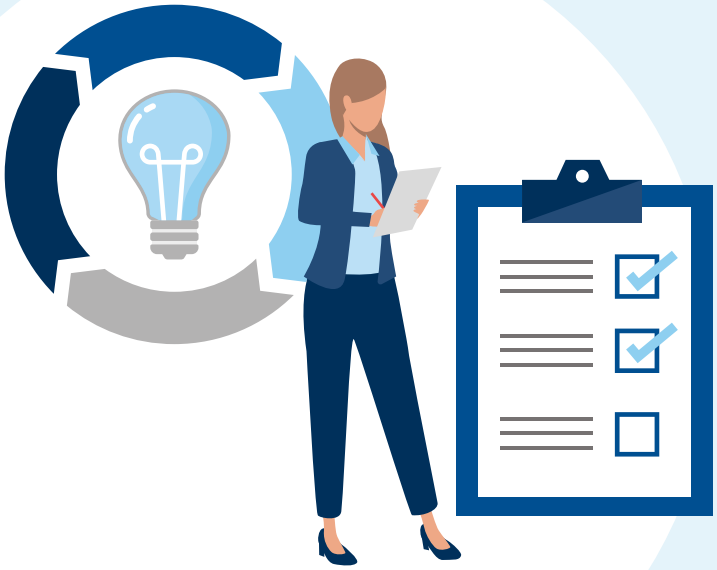
Summary

It is both possible and necessary to improve the regulatory framework to bolster innovative capabilities and strengths in Germany and in Europe. The following core elements have been identified and utilized to develop specific measures:

- **Defragment the regulatory environment for GCTs** by concentrating procedures and responsibilities, including for **manufacturing authorizations**, at the Paul-Ehrlich-Institut (PEI) and **strengthen the PEI with additional resources**
- Improve **EU legislation on clinical trials** (EU Clinical Trials Regulation (CTR) – Regulation (EU) No 536/2014) and **improve coordination of processes for medical devices and in vitro diagnostics**
- Protect, preserve and expand academic research and innovation opportunities to drive GCT developments by:
  - **redefining some medication-related terminology** and regulatory procedures in the field of GCTs
  - simplifying authorization procedures for frequently used processes and starting materials in the form of master file systems
  - introducing the **sandbox approach** as a space for innovation
- Establish a **central GCT-GMP and regulatory affairs committee** as a communication platform to continue the work of the National Strategy, taking the National Advisory Committee on Blood (Arbeitskreis Blut) as a model

1 Defragment and standardize responsibilities and processes in the clinical research and development of GCTs, and strengthen the federal higher authority and its resources as a single point of contact





2 Continuously adapt regulatory processes to developments in the field of GCTs

3 Improve the availability of low-threshold regulatory advice

Background

The development of new medications begins with well-documented research to ensure their efficiency, safety and quality-assured manufacture, followed by initial use on humans. This is where the first bureaucratic barriers emerge.

National guidelines – which do not necessarily apply to the rest of the EU – make manufacturing, research and development in Germany expensive and inefficient in comparison with other European countries. This is true even in the early phases of development, e. g., to secure approval for animal studies (see also Topic VI, Objective 3, Measure 2). The definitions of ATMPs (and therefore GCTs) and their components, which should be included in the new EU directive, are quite unsuitable for these pioneering therapeutic approaches. At the European level, submission of a master file is considerably more complicated than in the USA, as active ingredients (e. g., messenger ribonucleic acid – mRNA) and other starting materials for GCTs cannot be submitted in this format. Data must be therefore submitted on multiple occasions and IP cannot be protected.

Clinical trial applications (CTAs) and the implementation of clinical studies and clinical trials with GCTs are subject to the EU Clinical Trial Regulation (Regulation (EU) No 536/2014 – CTR) and its national implementation in the German Medicinal Products Act (AMG).

It is also not uncommon for requirements of the EU Medical Device Regulation (MDR), the German Medical Device Law Implementation Act (MPDG) or the In Vitro Diagnostic Regulation (IVDR) to complicate matters. Given their high bureaucratic complexity and the complete lack of coordination between their procedures at present, this triumvirate of EU regulations represents a concerning barrier to clinical studies in Germany and Europe. Furthermore, many aspects of these regulations are unrealistic and lack evidence in terms of their protective impact for patients and trial participants.

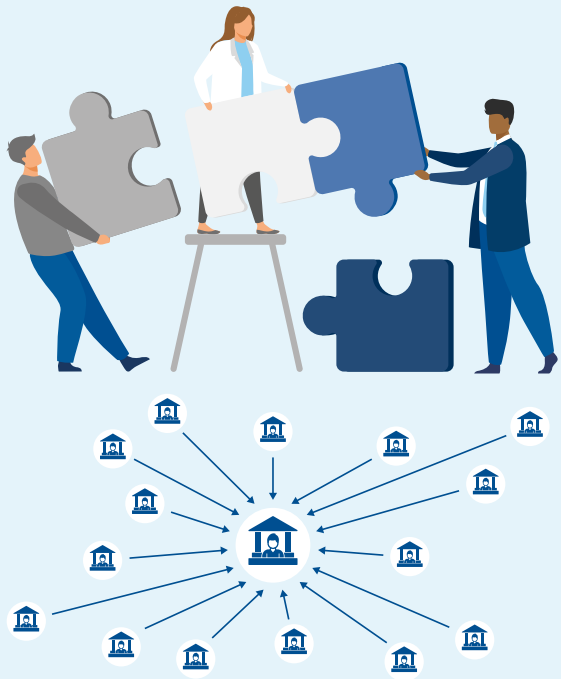
National implementation often exceeds the requirements of the EU regulations, while federal fragmentation and responsibilities can also complicate procedures and powers. The fundamentally positive idea of a standardized European application and assessment procedure for clinical studies is thwarted by the functional deficiencies of the Clinical Trials Information System (CTIS) portal. With the Federal Institute for Drugs and Medical Devices (BfArM) and PEI as the federal higher authorities, and the numerous regional governments, the complexity of the landscape in Germany is without equal in Europe. By comparison with highly developed international locations, such as the USA, it is far more difficult for patients in Germany to access studies involving state-of-the-art GCTs. In key aspects, such as FIH studies, there is already a significant number of studies moving outside of Germany. The phenomenon of international drift, in which drug studies relocate to countries with simpler regulatory procedures, has been known for some time. At present, the USA, Asia and the United Kingdom are preferred to the EU as locations for conducting studies. There has also been a decline in the number of studies initiated by academic institutions.

Germany, and Europe also lag behind in terms of further support for drug development through early scientific consultancy and accelerated authorization procedures. Scarce resources, distributed responsibilities and a lack of connection to practical applications mean that Germany is in a less favorable position than other locations.

To prevent more extensive damage to Germany and Europe as locations for such studies, this strategy paper calls for an urgent reform of the regulatory triumvirate (CTR, MDR and IVDR) by means of reasonable and practicable simplification and harmonization. National implementation must not be more complicated than required at EU level. In contrast to the previous approach, this process must involve a priori representatives of relevant groups who either conduct or are affected by studies and trials. In addition to public authorities and the pharmaceutical industry, this includes scientists, clinical investigators, members of ethics committees and patient advocacy groups.

Objectives

1. Defragment and standardize responsibilities and processes in the clinical research and development of GCTs, and strengthen the federal higher authority and its resources as a single point of contact
2. Continuously adapt regulatory processes to developments in the field of GCTs
3. Improve the availability of low-threshold regulatory advice



Objective 1:
Defragment and standardize responsibilities and processes in the clinical research and development of GCTs, and strengthen the federal higher authority and its resources as a single point of contact

Explanation:
The administrative and regulatory requirements that have grown over time at different levels of the federal and European structures are currently the most significant competitive disadvantage to investment in research and development and clinical developments in Germany and the EU. These requirements contribute to a situation in which patients in Germany and the EU do not have the same access to GCT innovations as patients in the USA, for example. The fragmentation of processes at state, federal and EU level must therefore be resolved. This means breaking down federal and national barriers in the procedures and responsibilities of state and federal authorities, thereby streamlining processes and ensuring a proportionate ratio of risks and opportunities.

Uniform regulatory structures for process development and scientific support (focusing on the federal higher authority) are preferable to federal fragmentation, especially in the context of GCT development: the German federal states' responsibility for drugs and medical devices is unique but not necessarily advantageous, because no other EU member state has a similarly decentralized structure. Manufacturing authorizations at state level should therefore be integrated into the processes operated by the federal higher authority or the European Medicines Agency (EMA) to create a single point of contact capable of communicating on all issues concerning the development of new drugs and therapies.

Strengthening the federal higher authority as a single point of contact should also create an opportunity to expand the principle of the scientific advice procedure to topic areas covered by state authorities, including the notified bodies.

As demonstrated by the example of the USA, ensuring sufficient capacity and expertise in a single, unified institution with a clear mandate to promote innovation and the authority to govern all clinical testing and approval processes involved in the development of GCTs will lay the key foundations to establish a cost-efficient, highly promising innovation landscape in Germany.

Across the EU, different national requirements exist concerning the active ingredients and critical starting materials used in the production of GCTs/ATMPs. These differences particularly pertain to the necessity of obtaining a manufacturing authorization and the corresponding requirement to have a qualified person present.

This puts Germany at a disadvantage in terms of costs and timeframe, both compared with other EU states and in an international comparison. In the future, as technical developments progress, it will be possible to produce an active ingredient or starting material by either biological or chemical means. The different production methods entail different risks. Nevertheless, this raises the question whether a manufacturing authorization for the biological method is justified or whether it would be more reasonable to distinguish between risks based on the type of application (for example the transient effects of mRNA versus the permanent effects of CRISPR/Cas).

In addition, it is vital that ethics committees are included in all such deliberations concerning defragmentation and harmonization.

Measure 1:
Implement uniform standards and processes for issuing a manufacturing authorization, particularly in the context of GCTs and their starting materials and active ingredients, by adjusting the allocation of responsibilities between local authorities and the Paul Ehrlich Institute (PEI)

Stakeholders required:
Federal Ministry of Health (BMG)

Description:
Options for the allocation of responsibilities between local authorities and the PEI include:

1. Legal examination of whether the process to issue manufacturing authorizations can be transferred to the federal higher authority
2. For clinical trials: Integrate the decision regarding a manufacturing authorization for IMPs into the approval procedure for clinical trials
3. Establish a group of GCT experts, based at the PEI, with overarching duties (see below), e. g., harmonizing procedures and requirements for manufacturing authorization applications, including for critical starting materials and active ingredients, based on applicable EU guidelines and their future amendments

Timeline and resource requirements
- Medium term (3-5 years)
- Introduction of a national committee to issue manufacturing authorizations for GCTs and monitor GMP activities, with close links to the federal higher authority
- Resource requirements: Medium staffing requirements; GMP-specific expertise must be established and expanded at the federal higher authority

Success indicators
- Shorter timeframe to obtain manufacturing authorization as well as approval of clinical trials and potentially the removal of the need to obtain a manufacturing authorization for active ingredients/ starting materials. The comprehensibility of requirements and the value of advice could be demonstrated via implementation of a feedback loop
- Number of clinical trials involving GCTs in Germany in 2030
- Number of contract development and manufacturing organizations (CDMOs) for GCT starting materials in Germany in 2030

Measure 2:
Strengthen the PEI with sufficient resources

Stakeholders required:
Paul-Ehrlich-Institute (PEI), Federal Ministry of Health (BMG)

Description:
To prevent the emigration of expertise and the loss of Germany's leading role in Europe, we recommend strengthening the resources and powers of the PEI. Approval of applications for clinical trials, assessment of GCT-related medical devices and expertise in the products of bioreactor processes (GCTs, antibodies, mRNA, etc.) should be coordinated from a single, central point of contact.

In this context, providing sufficient additional resources and expertise on these previously underserved scientific topics (GCTs, medical devices and real-world evidence) has a critical role to play in promoting GCTs in Germany. The current resources of the PEI are insufficient, the waiting times (e. g., for scientific advice) are too long by European and international comparison – and the need for such advice is particularly high in relation to GCTs. It is exceptionally important, especially for the development of GCTs, to be able to discuss topics at the interface of GCTs and medical device development (responsible: notified body) in advisory procedures. Sponsors are increasingly shifting their focus to other authorities with shorter waiting times. The accelerated assessment procedure for marketing authorization in Europe is used significantly less often than its US equivalent as national authorities lack the capacity to facilitate rapid EU-wide approval. Strengthening the PEI with sufficient resources and expertise can therefore play a decisive role for both Germany and Europe.

All in all, the interaction between the PEI and applicants should be constructive and supportive rather than characterized by delays due to in-depth examinations or limited resources. Initial advice and assessment must be binding, transparent and provided swiftly.

Timeline and resource requirements
- Short term (1–2 years)

Success indicators
- Duration until availability of scientific advice
- Number of advisory procedures per unit of time

Measure 3:
Consolidate and integrate the different approvals processes for the development of medical devices and in vitro diagnostics, including their software, into the existing application and authorization procedure for clinical trials on medicinal products in accordance with Regulation (EU) No 536/2014 (CTR) and the central authorization process set out in Regulation (EC) No 726/2004

Stakeholders required:
Federal Ministry of Health (BMG)

Description:
Upon implementation of the MDR and IVDR, a sequential application process was introduced in Germany. An application is initially submitted to the responsible ethics committee. It can only be forwarded to the responsible federal higher authority once it obtains a positive assessment from the ethics committee. A parallel assessment procedure controlled by BfArM and processed through the clinical trial application route (i. e., CTIS) would expedite the process tremendously.

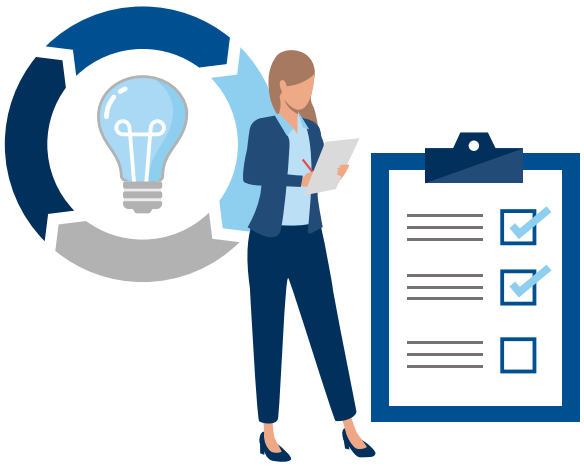
At present, when using medical devices not yet certified or not fully certified for the specific application in question, a study for the medical device must be registered separately in each individual country in parallel with the approval procedure for the medicinal product. The introduction of the EU Medical Device Regulation has created significant administrative hurdles for GCT development, which must be resolved urgently. The CTR, MDR and IVDR must be overhauled and harmonized as soon as possible. The federal government must advocate in Brussels for corresponding amendments to the EU CTR (Regulation (EU) No 536/2014) and associated implementing regulations on GMP (as well as EudraLex Vol. 4 and EMA guidelines), while also demanding the necessary GCT-specific amendments to the IVDR.

If clinical trial authorization is sought for the medical device itself (in pursuit of a subsequent certification), it would be reasonable within the European legislation (i. e., the MDR) to concentrate clinical trial authorization for medical devices in a single, central committee. The BfArM is well positioned to assume this responsibility in the EU, provided that sufficient capacities and expertise can be made available. Giving notified bodies the ability to participate in advisory processes for developers, alongside the regulators, would simplify the combined development of GCTs and accelerate their placement on the market.

Under the current regulatory framework, the development of drug-device combinations is particularly laborious. A central institution responsible for medical devices combined with drugs would be most suitable to assess both uses and their benefit-risk ratio for patients. The principles of the benefit-risk assessment for drugs should be used in this context, as most of these medical devices are either not intended for independent marketing or are already separately in use for other purposes with a declaration of conformity in the EU.

Timeline and resource requirements
- Timeline: Medium term (2–3 years)
- Resource requirements: Low: Adaptation of the process for IVDR and MDR to a procedure that already exists for drugs; parallel assessment by ethics committee following submission to CTIS
- Increased resources for a federal higher authority with experts capable of conducting the benefit-risk assessment for a simultaneous application of IVDs with GCTs
- Amendment of the MDR, IVDR and Pharmaceutical Regulation to create a standardized regulatory process for clinical trial authorization and marketing authorization for GCTs, and thus for associated medical devices and IVDRs

Success indicators
- Increase in the number of clinical trials in Germany by 2030
- Shorter duration of clinical trials and marketing authorizations via parallel assessment of GCTs and their combined medical devices/IVDRs



Objective 2:
Continuously adapt regulatory processes to developments in the field of GCTs

Explanation:
Regulatory authorities must keep pace with the rapid development of GCTs, as this is fundamental to improving patient safety and fostering trust in new therapies. For this, it is specifically necessary to broaden the scope and increase the direct involvement and engagement of experts from research and the clinical arena, as is standard practical in other EU countries. New regulatory formats should be developed and introduced to increase the efficiency and quality with which authorization applications are examined and to drive innovation. These formats should take account of the specific challenges involved in the development of GCTs. To date, no standardized procedure has been designed at EU level to protect confidential aspects of GCT production processes (e. g., the generation and quality of starting materials from a contract partner). At the same time, applicants are required to disclose these aspects so that clinical trial applications can be assessed. Furthermore, applicants must also repeatedly provide detailed information on intermediate products and, for example, their stability, along with the analytical methods used to identify them, and submit this information with each new application – even if this information is identical to previously described and authorized components of a GCT platform. By contrast, with a master file system similar to the drug master file (DMF) system used by the FDA, it would be possible (especially in the context of collaboration between academic groups and industry) to guarantee both confidentiality and protection of IP in manufacturing processes while also making the approval process for clinical trials more efficient.

In the field of GCTs, new knowledge is produced, and new technologies are developed at tremendous pace. The regulatory requirements require continuous revision. A regulatory "sandbox" should therefore be created to facilitate this process, serving as a space for development of the regulatory framework. This has also been proposed in the current drafting process for the new EU legislation.

Measure 1:
Establish a central GCT-GMP and regulatory affairs committee

Stakeholders required:
BMG, PEI

Description:
Communication can be improved through increased integration of expertise from practice, e. g., by creating a national GCT-GMP and regulatory affairs committee to contribute directly to benefit-risk assessments of clinical studies and marketing authorizations for medicinal products, following the example set by other EU countries.

A template for this committee could be the National Advisory Committee on Blood (Arbeitskreis Blut) at the Robert Koch Institute (RKI) (see also Topic V, Objective 1, Measure 1). For the PEI, establishing such a committee could:

1. strengthen its own clinical expertise with a clear practical focus, and
2. support translation activities in Germany, as the lack of regulatory knowledge in academic research has been identified as one of the key barriers to innovation translation (see also the STARS report: https://doi.org/10.1016/j.drudis.2020.10.017).

Timeline and resource requirements
- Short term (1 year): Coordination on the concept with the BMG and PEI
- Medium term (2–3 years): Establishment of a committee and corresponding office
- Medium term (2–3 years): Publishing of statements (approx. 1 year after the committee is established)
- Resource requirements: Mid-six-figure amount per year (approx. 2–3 staff positions at the office, plus material resources)

Success indicators

- Completion of an initial document with recommendations for the development of GMP infrastructure along with harmonization and risk-based streamlining of statutory and regulatory requirements
- Number of queries submitted to the office of the GCT-GMP and regulatory affairs committee (i. e. use level)
- Number of clinical studies involving GCTs in Germany in 2030
- Time from application for clinical trial to start of study

Measure 2:
Extend master file systems to GCTs

Stakeholders required:
BMG via the European Commission

Description:
Following the European Commission's Proposal for a Directive (https://health.ec.europa.eu/publications/proposal-directive-union-code-relating-medicinal-products-human-use_en) and a subsequent position paper (https://www.vaccineseurope.eu/news/position-papers/expanding-master-files-for-human-medicinal-products-in-the-eu-eea), we support the extension of the current scope of master file systems in the EU to include GCTs. Specifically, we believe the Active Substance Master File (ASMF) procedure should be applied to GCTs and cover raw materials, starting materials, additives, adjuvants, medicinal products and intermediate products. The Platform Technology Master File – currently with limited applicability – should be expanded to include GCTs. In the case of clinical trial applications, it must be possible to refer to master documents that have already been examined, approved and archived by the responsible authorities. At the same time, the IP of contract partners would be protected because such master file systems can comprise "open" and "closed" sections, with the latter accessible only to the regulators. This approach leads to standardization and streamlining of authorization documents while maintaining and safeguarding quality and, simultaneously, reducing the time and effort involved in examining applications. We recommend supporting respective proposals for amendments to EU legislation, which are currently open to comments from Member States, to ensure their prompt implementation.

Timeline and resource requirements

- Timeline: Medium term (2–3 years) with implementation of pharmaceutical legislation
- Resources are required in public authorities to expand the application of master file systems

Success indicators

- Number of applications for GCT clinical trial approvals before and after introduction of the measure
- Shorter timeframe for assessment of approval applications, leading to increased throughput of applications (quantifiable indicator: number of application assessments completed before and after introduction of the measure)

Measure 3:
Develop and introduce a regulatory sandbox

Stakeholders required:
BMG via the European Commission

Description:
The statutory regulatory environment cannot be designed to accommodate all innovations. In many cases, innovations are developed in an environment where different legal regulations overlap. Heavily-regulated countries with extensive statutory provisions are therefore at a disadvantage when it comes to innovation. In this context, a legally defined and strictly controlled "sandbox framework" would provide an opportunity to test and pilot innovations before adapting the legal framework based on experience in the sandbox. A procedure should be created to facilitate fast and flexible assessment of particularly innovative new developments, such as gene therapies, cell therapies and personalized medicine approaches, which do not fit entirely within the existing regulatory framework. These innovative therapies could then be tested under the supervision and involvement of experts, with subsequent evaluation of the experience gained. A legislative proposal has already been put forward on this topic and should be supported and swiftly implemented. [Brussels, 26.4.2023 COM (2023) 193 final 2023/0131 (COD) Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL CHAPTER IX REGULATORY SANDBOX, Articles 113–115 – Regulatory sandbox]

A regulatory sandbox for GCTs could bridge innovation and the availability of therapies to patients, while enabling sound and controlled research to safely and efficiently develop novel methods and treatments.

Timeline and resource requirements

- Medium term (2–3 years)
- Low to moderate after EU legislation is implemented: however, increased expertise for authorization processes will be required in the federal higher authorities (BfArM and PEI) from 2027, as sandbox

proposals would have to be agreed via central EU procedures with the European Medicines Agency (EMA) and adopted by the EU Commission
- Statement from the federal government as a member of the European Council and its involvement in the ongoing update on legislative acts (pharmaceutical acquis)

Success indicators
- Introduction and use of the sandbox framework
- Over the long term, the number of therapies/medicinal products in the healthcare sector that could only have been developed via this sandbox framework

Measure 4a:
Foster an open-ended discussion on the current Advanced Therapy Medical Product (ATMP) definition and relevant regulatory pathways for adoptive cell therapies with genetically modified cells (e. g., CAR T-cell therapy)

Stakeholders required:
GCT-GMP and regulatory affairs committee, PEI

Description:
Potentially, the definition of an ATMP could be updated from the infusion-ready cell product to the utilized pharmacologically definable vector. The composition of manufactured cell products prior to their administration is customized and heterogeneous, which means they are not comparable with a defined IMP. This is due to a variety of different donor characteristics (e. g., age, prior exposure to infection, record of illnesses and therapies, concurrent medications). The heterogeneous in vivo development of these living therapies after administration is another factor to consider. It must be possible, for example, to scientifically modify the composition of final cell products in an unbureaucratic process, e. g., via modifying the stimulation and duration of the production process with the aim of minimizing depletion, thereby achieving increased functional persistence in vivo, enriching or depleting certain cell phenotypes (CD4, CD8, mix ratio), adding other cell types while using certain binders as immune contributors, reinfusion plans (number, split), etc. The corresponding protocols are subject to scientific quality controls, while GMP production and product distribution can also be decentralized at the level of academia.

Timeline and resource requirements
- Medium term (2–3 years)
- No additional resource requirements

Success indicators
- White paper or position paper with input from stakeholders and regulators

Measure 4b:
Reform of the German Stem Cell Act (StZG)

Stakeholders required:
German Stem Cell Network (GSCN), BMG, PEI, Central Ethics Committees for Stem Cell Research (ZES) at the RKI and in the German Medical Association (BÄK)

Description:
The German Stem Cell Act (StZG) restricts research with human embryonic stem cells within an extremely tight framework (cut-off date regulation, restriction of use to research purposes). We therefore propose reforms for relevant aspects. This legislation inhibits research, development and therapeutic use in the field of stem cell-based cell products and medicinal product development. We refer to the Federal Government's 10th Report on Implementation of the Stem Cell Act to the German Bundestag, Document No. 20/10550 of 4 March 2024, which is available (in German) at: https://dserver.bundestag.de/btd/20/105/2010550.pdf.

Timeline and resource requirements
- Medium term (2–3 years)
- No additional resource requirements

Success indicators
- Positive research results on/approval of medicinal products that would otherwise have missed the time window

Measure 5:
Establish a register for hospital exemptions to increase transparency and success measurement

Stakeholders required:
BÄK, PEI, BMG, Federal Joint Committee (G-BA)

Description:
In addition to other pathways, such as compassionate use and individual therapy trials in accordance with Section 37 of the Declaration of Helsinki (64th WMA Fortaleza 2013) and the "extra-statutory necessity" set out in Section 34 of the German Criminal Code (StGB), a specific procedure exists for hospital exemptions in the EU and in Germany (under Section 4b of the Medicinal Products Act (AMG)). The latter safeguards therapeutic freedom for an "individual preparation for an individual patient [...] according to specific quality standards [...] in a specialized healthcare facility under the professional responsibility of a doctor".

In the face of individual, life-threatening diseases – e. g., cancer diseases and infections in immunosuppressed people (e. g., following stem cell transplants) – and rare diseases, it can be too cost-intensive and, above all, time-consuming to overcome the regulatory barriers for a CTA. Innovative therapies can be lifesaving and time-critical options for the patients in question. In such cases, the provision of a hospital exemption in the legal framework can be lifesaving. Therefore, it should be expanded (to include cell therapy, RNA therapy and gene therapy) rather than restricted. It is encouraging that the corresponding redefinition of this regulation in EU legislation barely restricts the use of the hospital exemption and will even facilitate its application across national borders. It should therefore be implemented in German law as soon as possible. We propose collecting fundamental data on the application of this instrument in a disease-specific register. The data on these applications should also be recognized by the federal higher authorities and the EMA as the basis for the design and implementation of clinical trials. The collection of this data should be integrated into a national GCT register, which is proposed as a specific measure in Topic VII (see Topic VII, Objective 4, Measure 2).

Timeline and resource requirements
- Short to medium term: See Topic VII, Objective 4, Measure 2

Success indicators
- Transparent overview of the use of this instrument

Objective 3:
Improve the availability of low-threshold regulatory advice

Explanation:
Academic projects should be increasingly prepared for advice from regulatory authorities (PEI, BfArM and EMA). Academic groups in the early stages of their projects often lack the necessary resources to develop their own regulatory strategy and make efficient use of scientific advice procedures. In addition, targeted support leading up to and following the scientific advice procedure should establish a "regulatory memory" that could help to improve interaction with regulatory authorities.

Measure 1:
Establish a low-threshold regulatory advice service

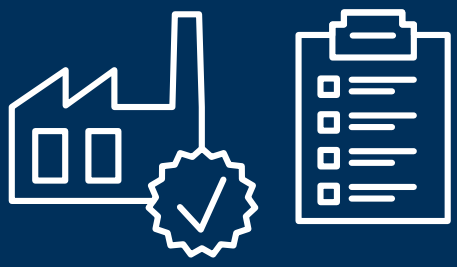
Stakeholders required:
PEI, appropriate academic institution

Description:
There is a need for national, free-of-charge regulatory advice and support for academic research groups at universities, university hospitals and publicly funded research institutes that want to test their products in the field of biological medicinal products and a focus on GCTs in clinical trials in Germany and want to access the PEI's scientific advice procedure in the respective development phase. The primary target groups are project teams that do not yet have any experience dealing with the authorities and usually also lack the financial resources needed to access this service. The service could be provided by establishing a regulatory support unit (RSU). It must be ensured that the RSU is organizationally independent of scientific structures and working groups. An alternative to this would be better equipping the federal higher authorities/the PEI to provide faster, low-threshold scientific advice to groups in academia and industry (see Objective 1, Measure 2). These measures should be considered synergistically, i. e., an upstream access point for early-stage research projects would help to relieve the burden on the federal higher authorities/the PEI while also lowering the threshold for early-stage advice, which can in turn prevent bad investments. The implementation of this measure (establishment of an RSU) is initially feasible/conceivable with funding from the National Strategy. This measure should be coordinated with creation of a PDU (see Topic III, Objective 2, Measure 1).

Timeline and resource requirements
- Short to medium term (1-3 years)
- An RSU should be established as a first point of contact, potentially with offices/contacts at different major university hospitals, to offer low-threshold advice to different groups of researchers. Networking opportunities should be examined based on the existing infrastructure at different locations.

Success indicators
- Nationwide networking and a successful scientific advice procedure at the PEI
- Regular exchange between the RSU and federal higher authorities to evaluate the performance status of time-critical submissions (e. g., 3–4 times per year)

Topic V: Quality and capacity of GMP production



Summary

The quality and safety requirements for pharmaceutical products for use on humans represent fundamental standards that apply to clinical samples as well as approved and marketed products. In the transition from laboratory testing to clinical practice, GCTs are subject to intensive product and process development in accordance with applicable guidelines on GMP. After reviewing compliance with all GMP guidelines, the responsible authority will issue a product-specific and time-limited manufacturing authorization. Given the expenditure to fulfill the various property, staffing, time, regulatory, monitoring and administrative requirements, establishing and consistently maintaining GMP infrastructure entails significant costs. This expenditure and the lack of qualified GMP professionals to operate in-house GMP infrastructure for research and development are usually prohibitive for academic institutions and start-ups with single GCT projects. In Germany, utilizing other academic and non-academic GMP contract manufacturers for innovative GCTs in the early clinical stages is only possible in limited cases, and even then, remains both time-consuming and expensive. In other European countries, and in particular outside of Europe, streamlined statutory provisions facilitate the implementation of early clinical studies. The lack of comparable regulations in Germany puts the country at a disadvantage and is a significant contributor to the loss of domestic value creation in this area. Against this backdrop, we believe there is an urgent need to improve quality standards, establish and expand GMP production capacity in Germany and optimize translational processes by streamlining structures and accelerating procedures. To achieve this in a prompt, targeted manner with due regard for the dynamics of GCT developments, we recommend four objectives:

- Promote the establishment and expansion of qualified GMP infrastructure in line with demand, for starting materials and for complex GCT products
- Secure the necessary staffing capacity and expertise for GCT manufacturing and quality control
- Increase the efficiency and speed of manufacturing processes
- Pursue development and risk-based streamlining of framework conditions

As a priority, we suggest these measures:

- Create a central GCT-GMP and regulatory affairs committee comprising all relevant stakeholders (incl. the Federal Ministry of Health (BMG), the PEI, science and industry, etc.) to analyze and continuously drive forward progress towards the objectives in this topic in a timely, needs-based manner
- Provide targeted and sufficient financial resources from the federal government, state governments and other funding providers to establish, expand and operate GMP infrastructure in line with demand, including a production facility for critical starting materials for GCTs

1 Promote the establishment and expansion of qualified GMP infrastructure (manufacturing and quality control capacities) in line with demand, for starting materials and complex GCT products

2 Secure the necessary staffing capacity and expertise for GCT manufacturing and quality control

3 Increase the efficiency and speed of manufacturing processes

4 Pursue continuous development and risk-based streamlining of framework conditions

Background

Good manufacturing practice (GMP) is the process of ensuring the reproducible quality and safety of a product for use on humans through both general and product-specific measures. GMP guidelines are also applied in the production of clinical samples and approved GCT products.

GMP describes manufacturing activities in line with frameworks such as the Manufacture of Medicinal Products and Active Substances Regulation (AMWHV), European regulations on the manufacture of medicinal products for novel therapies, the European Pharmacopoeia and various industry standards.

In Germany, the GMP-compliant manufacture of clinical samples and products is subject to regulatory supervision by the federal states. The supervisory authorities are tasked with monitoring (auditing) compliance with GMP guidelines on a regular basis and issuing product-specific manufacturing authorizations for GCT products. A GMP-compliant facility must therefore always be kept readily available and operational. Over the long term, the high operating costs involved in retaining qualified staff, maintaining building and equipment hygiene, and conducting ongoing quality management can only be covered through sufficient use and/or a minimum number of projects.

The terms **quality management**, **quality assurance** and **quality control** and their distinct definitions are used with reference to corresponding norms.

Quality management includes all activities required throughout the entire development process, including defining quality policies and quality goals, as well as processes to achieve these quality goals through quality planning, quality assurance, quality control and quality improvement.

Quality assurance is a subsection of quality management and includes all measures intended to generate trust in fulfillment of the quality requirements (in the final product).

Quality control includes all quality verification activities by means of providing objective, evidence-based proof that defined requirements have been fulfilled (e. g., through the results of tests or other forms of determination) and validation based on this objective proof that the requirements for a specific intended use or application have been fulfilled.

The manufacturing processes for GCTs differs significantly from those of conventional therapeutics. Specific GMP-compliant manufacturing processes must therefore be developed, which in turn necessitates the establishment of corresponding manufacturing and quality control infrastructure. This will require specifically trained GMP staff who are familiar with the procedures used in the context of GCTs. This applies to innovative and highly complex cell-based therapeutics, e. g., CRISPR/Cas gene-edited cell products and cell-based therapeutics from human induced pluripotent stem cells (hiPSCs). Furthermore, the existing statutory and regulatory framework – which has arisen from the manufacture of conventional medicinal products – must be adapted to meet the requirements of GCT products.

The high operating costs, the lack of specifically trained staff and the complex regulatory framework result in an insufficient capacity for GMP-compliant GCT development and manufacturing at German universities. This concerns both product-specific quality aspects (e. g., raw materials, supply chains, etc.) as well as the general field of GMP (e. g., infrastructure, staff, framework conditions, etc.). This significantly hampers the smooth transfer of successful GCT research and development to initial clinical trials and subsequent utilization, with such activities relocating to other countries as a result. Improving quality standards and expanding capacities in GMP manufacturing is therefore a decisive element of the National Strategy for GCTs.

Objectives

1. Promote the establishment and expansion of qualified GMP infrastructure (manufacturing and quality control capacities) in line with demand for starting materials and complex GCT products
2. Secure the necessary staffing capacity and expertise for GCT manufacturing and quality control
3. Increase the efficiency and speed of manufacturing processes
4. Pursue continuous development and risk-based streamlining of framework conditions

Objective 1:
Promote the establishment and expansion of qualified GMP infrastructure (manufacturing and quality control capacities) in line with demand for starting materials and complex GCT products

Explanation:
Whether for use in clinical trials or after obtaining authorization, GCT products must be manufactured in GMP-compliant conditions. To achieve sufficient capacity, it is vital to expand qualified and, if appropriate, automated GMP infrastructure, including sufficient manufacturing and quality control capacities as well as sufficient staffing capacity. This will ensure equal access to GMP infrastructure for all stakeholders, including those from research, development, patient care, academia and industry as well as start-up founders. The expansion of GMP infrastructure must be based on identified needs: a few larger, highly professionalized public contract GMP infrastructures with access for proponents from academia, industry and start-up must be able to accommodate high production volumes for late clinical phases (pivotal studies) as well as authorized GCT products. Decentralized manufacturing in GMP institutions with close links to universities must be able to ensure the development of products for early clinical phases or for rare diseases and/or particularly innovative and complex GCT products (such as CRISPR/Cas gene-edited cell-based therapeutics or therapeutic hiPSC derivatives). It is also important to make use of existing specialized GMP facilities in Europe and enable flexibility for new GMP facilities by employing a modular approach. Alternative models could include using providers from industry, such as CDMOs, and partnerships between industry and academia.

Measure 1:
Create a central GCT-GMP and regulatory affairs committee

Stakeholders required:
BMG, PEI, stakeholders from academia and industry

Description:
The development of the GCT ecosystem is dynamic and is likely to remain so in the future. This development must be continuously observed, analyzed and advanced to facilitate timely and targeted implementation of appropriate measures. A central GCT-GMP and regulatory affairs committee with a corresponding office must be established to achieve this. This committee could have a similar structure to the National Advisory Committee on Blood (Arbeitskreis Blut) at the Robert Koch Institute (RKI) (https://www.rki.de/EN/Content/Institute/Committees/NAC_Blood/nac_blood_node_en.html) or the Cellular, Tissue and Gene Therapies Advisory Committee at the FDA in the USA (https://www.fda.gov/advisory-committees/cellular-tissue-and-gene-therapies-advisory-committee/roster-cellular-tissue-and-gene-therapies-advisory-committee). (Note: This measure is also proposed in Topic IV; see Objective 2, Measure 1). We propose locating this committee within the PEI. Its tasks should include:

a. Perform risk-based harmonization and streamlining of statutory and regulatory requirements for GMP-compliant manufacturing and control
b. Continuously developing regulations for GMP manufacturing and quality control as well as for clinical studies, new technologies, etc.
c. Evaluating the demand for and provision of GMP infrastructure (including staffing) and issuing an annual recommendation for further expansion and funding
d. Supporting the coordination and efficient use of existing GMP infrastructure
e. Creating and managing a database of GMP manufacturing capacity in Germany along with a repository of manufacturing-related information

Timeline and resource requirements
- Short term (1 year): Coordination on the concept with the BMG and PEI
- Medium term (2–3 years): Establishment of a committee and corresponding office
- Medium term (2–3 years): Publish statements (approx. 1

year after the committee is established)
- Resource requirements: Mid-six-figure amount per year (approx. 2–3 staff positions at the office, plus material resources)

Success indicators
- Completion of initial recommendations for the development of GMP infrastructure along with harmonization and risk-based streamlining of statutory and regulatory requirements
- Number of queries submitted to the office of the GCT-GMP and regulatory affairs committee (i. e. level of utilization)

Measure 2:
Collect data on academic and commercial GMP infrastructure that already exists, is being planned or is under construction in Germany. Compare this against data for Europe and determine the need for GMP infrastructure for GCT manufacturing and quality control

Stakeholders required:
GCT-GMP and regulatory affairs committee, National Network Office

Description:
An analysis of existing GMP infrastructure should facilitate precise and ongoing monitoring and classification of GMP resources in Germany – corresponding to their affiliation to specific types of organization (e. g., university, research institute, industry, CDMO) and reflect their capacity, specialization, etc. (e. g., by tables detailing all their manufacturing authorizations and the number of products manufactured per year). Systematic collection and maintenance of this data will make it possible to generate up-to-date estimates of manufacturing capacity as well as future development of this capacity and relevant dynamics in Germany, thereby facilitating comparisons with other countries.

In addition, German GCT developments in academia and industry should be monitored as well as dynamics concerning short-term, medium-term and long-term demand for GMP infrastructure capacity assessed. For standard care, demand can be derived from the number of current approvals and the incidence of corresponding indications. In terms of clinical studies, demand can be derived, for example, from scientific publications, clinical study registers, scientific communications (e. g., press releases) and both public and commercial databases, with amendments made accordingly.

The assessment of demand includes both product-based and medical-therapeutic demand as well as the necessary global and individual structural requirements. This will ensure that GMP infrastructure can be built and operated in a targeted manner, thereby avoiding surpluses and shortages in regional supply.

A database for the collected data should be set up and continuously updated, potentially also serving as a matching platform between GMP infrastructure and demand (from translational scientific research, start-ups or industry). Furthermore, the data must provide an overview of manufactured end products and critical starting materials (from iPSCs to CAR effector cells, and from Cas enzymes/enzyme variants, their single guide RNAs and homology-directed repair (HDR) templates to mRNA to lentiviral and DNA vectors).

Timeline and resource requirements
- Short term (1 year): Preparation of an initial overview by the National Network Office
- Medium term (2–3 years): An employee is recruited for the central office of the GCT-GMP and regulatory affairs committee
- Medium term (2–3 years): Establishment of a database and initial functionality offered

Success indicators
- Quality control of the database by means of random checks
- Accessibility
- Number of entries
- Review to ensure data is up to date, including random samples (queries)
- Number of new matches resulting from the collected data

Measure 3:
Secure sufficient funding from the federal government, state governments and other providers to establish, expand, maintain and operate GMP infrastructure based on demand

Stakeholders required:
BMFTR, BMG, BMWE and state governments

Description:
Based on determined demand for GMP manufacturing capacity for GCTs, corresponding funding must be made available to establish, expand and maintain the necessary GMP infrastructure. The proposed GCT-GMP and regulatory affairs committee could develop appropriate proposals. The respective GMP infrastructure must cover the various demands and be accessible.

Given that GCT development and manufacturing will continue to take place predominantly at hospitals, universities and non-university research institutes, existing structures should initially be expanded and the conditions created to establish capacities that can then be tailored according to demand and future developments. Furthermore, capacity can be increased by developing GMP infrastructure (especially in an academic context) through the specific professionalization, digitalization and automation of processes (as is already taking place to some degree in industry). To facilitate this, funding designated for GMP infrastructure must be made available to research institutes. Calls for proposals for GCT projects from third-party funding providers must be equipped the appropriate financial resources; specifically, such calls should adequately consider and cover the costs of GMP development and manufacturing and, if necessary, expansion of local infrastructure. This will ensure that research institutes are increasingly able to drive forward national joint research projects and retain specialist GMP staff. In addition, the development of complementary concepts to coordinate the prioritization of technologies and indications and the production of starting materials (e. g., in the form of a national GMP network; see Topic VI, Objective 1, Measure 1) should be promoted.

Timeline and resource requirements
- Provision of investment funding for demand-focused establishment and maintenance of GMP infrastructure (a triple-digit million-euro amount)
- Continuous funding for staff and maintenance/ operation of infrastructure (single-digit million-euro amount per location per year)

Success indicators
- Proof of sustainability through designated sustainability/performance/utilization audits
- Number of manufacturing authorizations obtained and products produced

Measure 4:
Create a central national production facility to manufacture critical starting materials for GCTs

Stakeholders required:
BMFTR, BMG, PEI, stakeholders from academia and industry

Description:
In addition to a number of commercial manufacturing facilities (such as CDMOs), Germany has point-of-care manufacturing facilities in (small) university GMP facilities and start-ups as well as a handful of medium-sized academic, non-university manufacturing facilities. The availability of manufacturing capacity for therapeutically effective GCT products for early clinical studies is limited. Furthermore, the GMP-compliant production of critical starting materials, such as lentiviral and retroviral vectors and products for non-viral gene transfer (e. g., transposons, Cas enzymes/enzyme variants, their single guide RNAs and HDR templates and therapeutic RNAs) remains very difficult in Germany, as does obtaining such starting materials from abroad. While GMP facilities in Germany sometimes must wait over three years to receive supplies of these critical starting materials from abroad, these materials are essential to manufacture the necessary GCT products for an early clinical trial. Therefore, a central national production facility should be established as soon as possible with the ability to produce these critical starting materials and supply local GMP facilities. Only then will Germany be able to remain competitive and ensure the manufacture of products for clinical trials, including future direct in vivo therapies, along with their timely transfer to patients. Ideally, this production facility should be operated based on a partnership model between academia and industry. The few manufacturing facilities that already exist and produce certain critical starting materials should also be involved in this approach to ensure that all partners across Germany are supplied with the necessary critical starting materials.

Timeline and resource requirements

- Start-up phase of up to 10 years from the time of initial operations: high double-digit million-euro amount
- Annual costs for operating the facility for various critical starting materials: in the initial years, approx. €6–7.5 million per year; depending on the volume of orders received, subsequent years would see a systematic decline until approx. year 10, by which time the facility will receive sufficient orders to offset costs

Success indicators

- Number of manufacturing authorizations
- Number of critical starting materials produced per year for different partners, with a list of the total figures
- Number of clinical trials in which the GMP facility is involved (as a manufacturer)
- Number of patients to whom a GCT product is administered

Objective 2:
Secure the necessary staffing capacity and expertise for GCT manufacturing and quality control

Explanation:

Ensuring a sufficient number of specialists with specific expertise in process development, manufacturing, quality assurance, quality control and regulatory affairs is essential for GMP infrastructure to operate successfully. There is a profound shortage of specialists in these areas in Germany – not only due to the lack of education and training opportunities, but also because the field lacks the appeal and financial resources required to attract and retain qualified specialists (especially in the context of university-based research). This shortcoming must be addressed through the expansion of education and training programs with well-structured, accredited curriculums and a significant improvement in working conditions in order to attract and retain specialist professionals long term, and to prevent talented professionals from moving abroad (see also the recommendations in Topic II, Objective 1, Measure 1 and in Topic III, Objective 1, Measure 1).

Measure 1:
Expand and professionalize education and training for qualified staff in all areas in GMP production of GCTs

Stakeholders required:
GCT-GMP and regulatory affairs committee, universities, education and training sites, PEI and other authorities, lecturers and coordinators

Description:
This measure comprises the following points:

a. An overview of existing programs in Germany should be compiled and published in a database that is easily accessible for interested parties (e. g., potential program participants, GMP production facilities, authorities)
b. Clearly structured, officially accredited education and training curriculums should be developed
c. Incentives should be created to encourage educational institutions (i. e. universities, universities of applied science, education and training sites) to offer such programs

The database (a) could be established and maintained by the office of the GCT-GMP and regulatory affairs committee. For the development of curriculums we explicitly support the recommendations in Topic II (see Topic II, Objective 1, Measure 1). It is particularly important that curriculums are developed for all areas of GMP-compliant production of GCTs, including process development, manufacturing, quality assurance, quality control and regulatory affairs. In addition, options for lateral entry and protection of currently employed personnel should be devised, in order to facilitate the integration of as many qualified specialists as possible. We would also like to invite the PEI and other authorities to contribute to the development of these curriculums and to offer training workshops on the current status and development of GCTs. The activities of the FDA could provide guidance: https://www.fda.gov/science-research/scientific-meetings-conferences-and-workshops. In terms of incentives (c), specific and sufficient funding mechanisms are required – such as financial aid or tax benefits – from the state and federal governments for education and training sites along with adequate financial support for the authorities involved. The financing needs will be determined by the identified availability of GMP infrastructure and the respective demand, as well as recommendations from the GCT-GMP and regulatory affairs committee.

Timeline and resource requirements
- Short term (3–4 months): Preparation of an overview of existing education and training programs by the National Network Office; publication of findings as a database on the website
- Short term (1 year): Development of relevant programs to provide incentives and funding

Success indicators
- Maintenance and use of the database (number of visits); user survey
- Number of accredited education and training curriculums
- Continuation of programs and development of curriculums according to scientific progress
- Number of new graduates from programs with certificates in GMP-related areas for different topics (e. g., pharmaceutics, biology/biochemistry, medicine, MTAs, biotechnology, etc.)

Measure 2:
Improve the framework for employment to attract and retain qualified specialists in the field of GCTs

Stakeholders required:
GCT-GMP and regulatory affairs committee, universities, university hospitals, state ministries responsible for adjusting the allocation of funding for teaching and research

Description:
Research-focused universities and hospitals lack the necessary financial resources and adequate framework conditions to attract and retain highly educated GMP specialists and the expertise they possess. Special incentives must be created for qualified specialists to reverse this trend. Options to offer indefinite contracts to highly qualified staff in the GMP manufacturing of GCTs should be developed and the procedure then potentially even be "generalized" as part of clinical infrastructure to be able to offer long-term career prospects for specialists at university institutions. Technical expertise in GCT manufacturing should also be considered when determining pay grades – and the process simplified, if possible – to improve salary conditions. To keep pace with the rapid developments in the field of GCTs, special means of protection should be created for professional training activities for qualified staff, e. g., by specialized "educational breaks" as part of research workshops.

Timeline and resource requirements

- Establishment of competitive working conditions at academic institutions for specialist staff in GCT infrastructure (over at least five years)
- Funding of professional training activities for specialist staff in GCT infrastructure according to industry standards

Success indicators

- Number of professional training programs offered and number of specialists who successfully complete these programs for different topics (e. g., pharmaceutics, biology/biochemistry, medicine, MTAs, biotechnology, etc.)
- Number of graduates from programs with certificates in GMP-related areas for different topics (e. g., pharmaceutics, biology/biochemistry, medicine, MTAs, biotechnology, etc.)
- Number of new job appointments and retention period for specialist staff in GCT-GMP infrastructure at university institutions

Objective 3:
Increase the efficiency and speed of manufacturing processes

Explanation:

It is important to ensure data transparency and enable the exchange of proven and reliable procedures as well as their respective documentation, especially given the complexity of processes in the field of GCTs, such as raw material procurement, manufacturing, quality control, quality assurance and logistics. This transparency and this exchange of ideas and experiences will help to make processes more efficient and expedite them, thereby ensuring the consistent and timely manufacturing of GCT products.

In the context of this initiative, we wish to issue an explicit call to intensify the communication and collaboration between different GCT stakeholders to promote the increase of production capacity, expertise and capacity utilization. To achieve this, all information that can be made available should be collected and made available in a common database to which all stakeholders have access. Another goal should be facilitating the automated use of large volumes of data, which will require a standardized naming system (ontology), to keep pace with developments in this field in the long run. This database (or series of databases) should be established and managed by the office of the proposed GCT-GMP and regulatory affairs committee in close coordination with the National Network Office.

Measure 1:
Establish a clearly structured database with manufacturing-related information and documents that is accessible for all stakeholders

Stakeholders required:
GCT-GMP and regulatory affairs committee, National Network Office, GMP manufacturing facilities throughout Germany, federal higher authorities; optionally, representatives of regional governments

Description:
GCTs are developing rapidly and are significantly different to therapy approaches pursued to date, as they often involve the use of novel manufacturing and quality control methods. Consequently, it is crucial to promote transparency, collaboration and communication between stakeholders and to leverage synergies. Manufacturing-related information and documents must be collected, compiled and curated to make all relevant information available to stakeholders. This includes certified manufacturing components, documents, certifications, template contracts, audits, training and production logs, production data and metadata from the manufacturing process, document templates, a list of hospitals certified to perform biopsies, a list of treatment facilities certified to perform apheresis in accordance with the German Transfusion Act (Transfusionsgesetz – TFG) and available master files (following the standard practice in the USA). Furthermore, there should be an option to indicate where already approved protocols are included in authorization applications of a new process, thereby facilitating the review process for the regulatory authority.

Timeline and resource requirements
- Staff positions at the office of the GCT-GMP and regulatory affairs committee
- Continuous task

Success indicators
- Monitoring of database use (individual visits, unique users, number of documents input, number of downloads)
- Size of the list for materials approved by authorities
- Number of references made by applicants and authorities

Measure 2:
Create a shared basis of knowledge and communication by utilizing repositories with standardized data storage and access

Stakeholders required:
Corresponding current initiative in the field of medical data science; GCT-GMP and regulatory affairs committee

Description:
Improving the quality and increasing the capacity of GMP production requires collaborative development by different stakeholders:

1. Biologists and biotechnologists must develop a fundamental understanding of biological processes
2. System and equipment manufacturers must provide corresponding equipment and processes
3. Software developers must program IT systems for data processing
4. Data scientists and AI specialists must develop models to achieve process improvements
5. Regulatory authorities must approve new techniques

This interdisciplinary collaboration will require a shared basis of knowledge and communication. This measure therefore aims to develop repositories for the permanent and secure storage of data, information and knowledge, with standardized access for all stakeholders. For example, data from the cell cultivation process could be used to increase the quality of a GCT product. To facilitate sufficient analysis of this data and the development of corresponding data-driven models, however, this data must also be comprehensible to data scientists without a background in biology. This can be achieved through structured annotation of metadata and the creation of information models and ontologies. Already existing initiatives, such as the Open Biological and Biomedical Ontology Foundry (OBO Foundry) should be taken into account an utilized as a basis. In addition, the exchange of sensitive or confidential data between different stakeholders – e. g., hospitals, patients and service providers – must be secured accordingly. Existing initiatives to standardize data structures according to the FAIR Principles include the National Research Data Infrastructure (NFDI) and the Fraunhofer Medical Data Space.

Timeline and resource requirements

- Ongoing; IT infrastructure (e. g., IT center at a university), five staff positions (1x administrator, 2x scientific assistants for ontology development, 1x mathematical/technical software developer, 1x helpdesk specialist)

Success indicators

- Publication of an ontology for GCT manufacturing, translated into a standard (i. e. norm or guideline)
- Web-based access to repositories following prior registration
- Number of visits to the repositories; target set at exceeding 30 visits per month

Objective 4:
Pursue continuous development and risk-based streamlining of framework conditions

Explanation:
GMP-compliant GCT manufacturing requires specific raw materials and other materials that must meet strict requirements and be procured through specific distribution channels. The following measures must be taken to make raw materials procurement, quality control, quality assurance and logistics processes in the field of GCTs more effective and standardized, thereby ensuring the consistent and timely manufacture of GCT products (see also measures in Topic IV, Objective 1).

Measure 1:
Perform risk-based harmonization and streamlining of the statutory and regulatory requirements for GMP-compliant manufacturing and control

Stakeholders required:
GCT-GMP and regulatory affairs committee, relevant authorities (state hospital association, federal higher authorities, BMG)

Description:
The differences between regional and national legal frameworks significantly hinder the sustainable supply of investigational medical products (IMPs) in Germany via the various clinical GMP infrastructures. This leads to considerable delays and additional costs, which significantly impair Germany's competitiveness compared to other countries in Europe and beyond. Germany can only regain its competitiveness by utilizing a risk-based approach to harmonize regional and national requirements

and standards for GCT qualification and auditing systems, and streamline statutory requirements. Examples include: the different regulatory requirements regarding GMP-compliant manufacturing for early phase I and II trials compared to phase III trials; simplifying and harmonizing authorizations for biopsies to produce an ATMP (under Section 20b AMG); simplifying the contractual duties with the manufacturers of starting materials of human origin (Section 9 AMWHV) and enable a single audit of suppliers to be accepted by multiple GMP facilities.

Timeline and resource requirements

- Medium term (6 months after appointment of the committee): Publish statements
- Resource requirements: Establishment of the proposed GCT-GMP and regulatory affairs committee

Success indicators

- Published statements and votes
- Relevant harmonization measures and legislative amendments

Topic VI: Research and development

Summary

It is essential that ideas are recognized and supported to drive forward the development of GCTs in Germany. This happens via research and development: the driver of innovation for GCT products. They initiate the translation of pre-clinical developments into clinical trials, which ensure that the products are made available in standard healthcare. However, improvements in Germany's research and development **infrastructure** are urgently required to meet the challenges in the field of GCTs. It will be necessary to establish **decentralized hubs** that are accessible to the scientific community across Germany. In addition, the **expansion** of production capacities – and access to these capacities – should be expedited to reduce the costs of clinical studies and ensure availability. Establishing **incubators** for start-ups and biotech companies should promote innovation, while expanding **test facilities** should ensure both the efficacy and the safety of these innovations. Above all, intensive collaboration between all stakeholders involved in the development and manufacture of GCT products should accelerate **clinical studies initiated by scientific institutions**.

Identifying future topics and providing specific support requires the equal involvement of all relevant stakeholders and the development of interdisciplinary visions. In this context, implementing **novel and agile funding formats** and establishing **new collaboration models** between industry and academia will be essential. This can facilitate the swift and sufficiently funded translation of results from basic research into early clinical studies, thereby positioning Germany as an innovation leader in the field of GCTs.

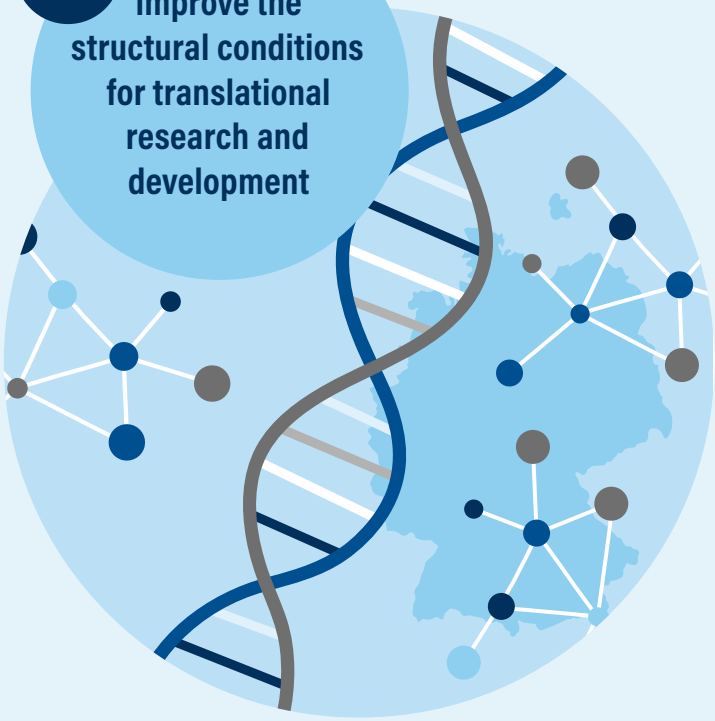
The **efficient use of financial resources**, as exemplified by international examples (the BioCanRx network, Canada; the Oncode Institute, the Netherlands; Catapult and the Medical Research Council (MRC), United Kingdom), could support this.

Considering the challenges and potential in the field of GCTs, the implementation of **GMP-light** procedures for phase I/II clinical studies should be advanced to strengthen Germany as a location for research. Furthermore, there will be a need to realistically assess the necessity for animal experiments, expedite respective **authorization procedures** and increasingly promote **alternative methods** to ensure Germany's competitive position internationally, while also meeting ethical standards. Introducing **performance indicators** is essential to promote transparency and efficiency in authorization procedures for GCTs. **Ethics committees** must be optimized and made more efficient by harmonizing standards and introducing specialist bodies with the aim of expediting authorization procedures.

Involving patients into research processes at an early stage is essential to give due consideration to their needs and perspectives, as well as to integrate this information into the design of research projects and clinical studies.

Specific **education and training programs**, grants and career-support measures in biomedical research, combined with topics such as spin-offs and translation/transfer, should encourage specialists to move to Germany and remain here. Modifications to existing education and training systems and specialized study programs can help to meet the increased demand for GCT specialists.

1 Improve the structural conditions for translational research and development



2 Identify and promote topics for the future

3 Improve the organizational and regulatory framework for pre-clinical and clinical GCT studies

4 Ensure that patients, patient advocacy groups and patients' associations are duly involved

5 Foster a change in mentality and bolster bio-entrepreneurial spirit in the German GCT community

Background

In terms of early research-initiated clinical trials, IITs and sponsor-initiated trials with industry participation in the field of GCTs, Germany has failed to keep pace with its international counterparts. While Germany risks falling further behind, countries like the United Kingdom, the Netherlands, France and Belgium have begun establishing themselves as leaders in a European context.

The fact that large biotech companies are relocating their clinical trial programs abroad demonstrates the urgent nature of the situation. The rising number of approval applications for innovative GCTs can currently be attributed primarily to foreign manufacturers.

This is due to **systemic weaknesses**, especially regarding the poor translation of the results of basic research into clinical studies. Germany must once again take on a more significant role in the value chain, which will require increased collaboration between all relevant stakeholders, from research and clinical practice to regulatory authorities, industry and venture capital providers.

In addition, the field of GCTs is subject to substantial **bureaucratic barriers** that have a significant influence on research and development processes and severely curb the **pace of implementation** of innovations.

Protracted application procedures for research funding lead to significant delays and impair the agility of research institutes. Consequently, it is essential that clear timelines are specified and strictly observed, and that unnecessary bureaucratic barriers are dismantled.

For instance, the delays in payout as well as bureaucratic monitoring of projects funded by the German federal government have dire consequences for research activities and their flexibility. Such issues impair Germany's ability to compete in research and development, thereby delaying the implementation of innovative therapy approaches. A disrupted flow of information between relevant stakeholders, which can be attributed to administrative complexity, exacerbates this problem.

Although the technical requirements for **early clinical studies (phase I/II)** and pivotal studies (phase III) are met in Germany, there is a lack of an effective **infrastructure** to enable researchers to effectively participate in these studies.

Collaboration between relevant stakeholders – such as research institutes, clinical institutions, industry, political entities, approval and assessment authorities, medical staff, patient advocacy groups and payers – is currently insufficient.

A particular challenge lies in the limited **financial support** for innovations in research and translation, as the development and application of GCTs in a scientific context requires considerable financial resources. A new balance must be struck between funding for "research" and funding for "development" to move Germany forward regarding technology and science transfer.

Another area that requires urgent attention is the **regulatory framework** for GCTs, which are currently not tailored to the specificities of these novel therapies.

In addition, **interministerial coordination throughout the entire value chain** (i. e. from invention/idea through to an approved product used in healthcare) is needed to create efficient framework conditions in the field of GCTs. For this reason, communication between the federal ministries responsible for basic research (BMFTR), business financing programs (BMWE) and market access and transfer to standard healthcare (BMG) must be intensified and optimized to secure Germany's ability to compete internationally over the long term.

Objectives

1. Improve the structural conditions for translational research and development
2. Identify and promote topics for the future
3. Improve the organizational and regulatory framework for pre-clinical and clinical GCT studies
4. Ensure that patients, patient advocacy groups and patients' organizations are duly involved
5. Foster a change in mentality and bolster bio-entrepreneurial spirit in the German GCT community

Objective 1:
Improve the structural conditions for translational research and development

Explanation:
The development of innovative GCT products – from initial idea to market launch – entails numerous steps in the pre-clinical phase, clinical translation and transfer. The availability of, and access to, critical infrastructure is a decisive factor in this process. The lack of such infrastructure, and limited access where it does exist, is currently curbing the innovative power of GCT research and development in Germany. Issues include the availability of, and access to: manufacturing facilities for gene transfer vectors in pre-clinical and clinical quality; test facilities for GLP studies on safety (including genotoxicity) and efficacy (including pharmacokinetics and pharmacodynamics); manufacturing facilities for GCT products in clinical quality for early (phase I/II) and late (phase III+) clinical studies; centers for clinical investigation of rare and prevalent diseases in the indication spectrum of GCTs, and incubators for start-ups and biotech companies. Decentralized hubs should be established to tackle these shortcomings. These hubs should have the infrastructure and expertise needed to serve as core elements in a national GCT network.

This national GCT network, with its decentralized hubs, should above all support and promote interdisciplinary collaboration between university and non-university research institutes, hospitals, companies, regulators, patients' organizations and other stakeholders. A coherent framework to define and promote this collaboration, and to integrate different disciplines, must urgently be established to pave the way for efficient progress in GCTs at national and international levels. At present, the lack of certain critical infrastructure manifests itself in the form of long and disjointed development pathways, as well as ineffective cooperation and transfer between stakeholders along the development and value chain. The low level of coordination and cooperation between research institutes, hospitals and industry results in fragmentation and unnecessary redundancy in research activities. This fragmentation in turn leads to information losses and delayed progress in the development and implementation of new therapy approaches. Consequently, hubs should be established and connected to promote the coordination of activities and initiatives. This could exploit potential relatively easily, quickly and with lasting effect.

Measure 1:
Establish a national GCT network with hubs

> **Stakeholders required:**
> Political stakeholders (at federal and state levels), university and non-university research institutes, umbrella organizations, regulators, industry, investors; moderation of this process by members of the working groups, with organizational support from the BIH

Description:
To promote the development of GCTs in Germany, it will be necessary to:

- create adequate framework conditions that meet the needs of the strong dynamics in pre-clinical and translational clinical research in the field of GCTs,
- expedite translation and transfer along the entire value chain, from basic research to research focusing on healthcare, and
- strengthen, expand and continuously develop existing expertise and infrastructure in decentralized, synergistic, harmonized and easily accessible hubs within a national GCT network, achieving last effects.

Initial approaches to the establishment of such a research structure can be found in recommendations issued by the German Science and Humanities Council (WR) (2017) and the Translation working group of the Permanent

Senate Commission on Key Questions in Clinical Research at the German Research Foundation (DFG) (2019). Building on this input, it must be guaranteed that there is open access to service structures and that synergies can be developed within the network across different locations and states. At the same time, a high level of planning reliability must be ensured to enable infrastructure expansion (especially regarding regulatory support), thus strengthening the interaction between academia, start-ups, industry and investors. The proposed GCT network and its hubs should establish extensive areas of interaction with relevant existing structures, such as the German Centers for Health Research (DZG), which focus on specific diseases. The network's structure along the entire translational value chain should be focused on academically excellent research with the aim of ensuring widely accessible, high-quality and personalized care for patients.

For this, the scientific community will require service structures that cannot be established within and for individual projects – but are essential for successful translation and transfer. These include:

a. Manufacturing facilities for gene transfer vectors (viral and non-viral vectors) in pre-clinical and clinical quality
b. Test facilities for GLP studies on safety (including genotoxicity) and efficiency (including pharmacokinetics and pharmacodynamics), omics analyses (genomics, proteomics and metabolomics, etc.)
c. Manufacturing facilities for GCT products in clinical quality for early (phase I/II) and late (phase III+) clinical studies
d. Centers for clinical trials on GCT-specific rare and prevalent diseases, including support structures for the preparation and implementation of clinical studies (with e. g., regulatory expertise, statistical and biometric expertise, clinical research organization-expertise, clinical trial offices (CTOs))
e. Incubators for start-ups and biotech companies

These hubs should be explicitly built up in a decentralized manner, i. e. they should not be limited to a single location. They should be selected according to specifically defined topics and expertise and enabled to adapt dynamically. This structure should lead to services being made available not only at specific hubs but throughout the entire national GCT network. The aim is for each hub to cover entire translational cycles regarding their respective indications, from basic research to clinical patient care to healthcare research. In addition, the individual hubs should thoroughly coordinate their activities.

Adequate public base funding will be needed to establish and operate these hubs and the GCT network. This base funding should be used to offer services for stakeholders from the GCT community. Suitable, flexible instruments and criteria must be developed to select the projects that can access a service. In addition to this base funding, PPPs will be established to continuously expand the network, its services and their availability.

The joint efforts of the federal government, state governments, industry and private investors (hence the ideal form of PPPs) can ensure the successful long-term operation of the hubs.

Timeline and resource requirements

- Short term (within 4–6 months): Detailed status overview and demand assessment; development of a concept for establishment of hubs on the core elements specified above (vectors, GLP studies, GMP manufacturing, clinical studies and incubators) and, on this basis, estimation of funding required for investment in infrastructure and staff
- Short term (within 6–9 months): Roundtable meeting with representatives of federal and state governments, university and non-university research institutes, umbrella organizations, regulators, industry and investors to discuss implementation; moderation of this process by members of the working groups, with organizational support from the BIH
- Short term (within 9-12 months): Completion of a detailed concept (including SWOT analysis) that can be used to start discussions with industry partners and investors
- Selection of hubs following transparent evaluation by international reviewers

Success indicators

- Short term (9 months): Concept for establishment of hubs within the GCT network developed and approved by public and private stakeholders in the GCT initiative
- Medium term (2 years): All hubs are established according to the concept and begin work (establishment phase completed within three years)
- Medium term (3 years): Each hub should offer services to different stakeholders in at least three projects to promote development and value creation (including at least one project focusing on technical infrastructure for the manufacture of vector-based, cell-based or combined products, e. g., bioprinting or tissue engineering, and at least one clinical study with activities at multiple sites within the GCT network)
- Long term (7 years): At least half of the hubs will be financed in part through PPPs

Objective 2:
Identify and promote topics for the future

Explanation:

Identifying topics for the future and increasingly supporting them requires a holistic approach comprising equal involvement of all relevant stakeholders and the development of interdisciplinary visions. Novel funding formats must therefore be established to give due regard to the dynamics, efficacy and innovative power of GCTs, thus facilitating innovative breakthroughs.

Identified problems and their impact: at present, topics for the future are not identified or are identified too late and addressed with inadequate funding measures. The funding currently available is far too low, too inflexible and too time-limited, as GCT-related research and development requires significant financial resources that are made available consistently over an appropriately long period. The lack of financial resources, especially at transition points (translation from pre-clinical to clinical trials; transfer from publicly funded research to the private sector) and in later phases of clinical development leads to promising projects being left unaddressed or, due to a lack of the necessary support, not being developed to the point at which they could have fully realized their innovative potential.

In terms of support for innovative ideas and projects, the long intervals between calls for applications, application submission and the start of funding (which can be up to three years for public funding providers) is highly obstructive and unreasonably long in the context of fast-moving GCT research. The reasons for these delays (incl. subsidy/ public procurement law; appointment of expert

referees; schedules for meetings of decision-making committees) must be analyzed to optimize processes, dismantle disproportionate bureaucracy and ensure prompt progress in research.

Targets: The following key points contain significant objectives for the development and implementation of new funding formats:

- The objectives should include a clear definition of needs to facilitate the development of specific, agile funding formats. A systematic approach to the identification of gaps in research, technological challenges and unmet needs could serve as the basis upon which new funding initiatives are designed.
- It is important to emphasize that new ideas often arise from public research. Funding formats should therefore be designed in a manner that preserves the creative freedom of research institutes while simultaneously facilitating effective commercial application.
- The experiences and established practices of other national centers and from previous funding initiatives should be carefully analyzed to ensure the efficacy of new funding formats. Identifying success factors and potential challenges will help to develop strategies that build on tried-and-tested approaches.
- An evaluation process for projects and funding instruments must urgently be implemented. Transparent reporting of selection criteria, project progress and outcomes will promote awareness of the benefits of research, strengthen public trust and facilitate continuous improvement of funding formats. The evaluation of SPRIN-D (Federal Agency for Breakthrough Innovation) will be essential to assess scientific and economic impacts and provide a basis for future funding initiatives.
- It is very important to create new opportunities for collaboration between research institutes and industry partners. Innovative ideas can be tested and refined in partnerships with industry. This could include producing prototypes, automating processes, conducting clinical studies and other measures that promote innovation. Integrating venture capital providers more closely should also be an objective. Creating incentives for venture capital (VC) companies to participate in innovative projects can expand the financing base and accelerate the implementation of promising ideas.
- The development of interdisciplinary visions is particularly important regarding low-wage countries. This not only means adapting technologies to local circumstances but also involves developing sustainable and inexpensive solutions. Collaboration between experts from different disciplines, such as medicine, engineering, ethics and economics, can create customized approaches to improve the availability of GCT therapies worldwide.

The following includes proposals for both conceptual and structural measures to promote innovative research projects in a dynamic, effective manner. In this context, constructive collaboration between academia and industry is highly desirable as a means of closing the gap in translation activities. This could be achieved through specific funding instruments that are tailored to both sectors' needs and promote the transfer of innovative ideas from basic research towards commercial application.

Measure 1:
Establish new, flexible funding formats, with a short lead time, which meet needs that are currently not given due consideration

Stakeholders required:
Governance structure of the National Strategy, DFG, BMFTR, third-party funding providers/foundations that support GCT projects

Description:
The scientific landscape is changing far more rapidly today than was the case just a few decades ago. Scientific breakthroughs in GCTs are occurring at tremendous pace and require swift responses in funding policy for Germany to remain competitive. Suitable mechanisms, instruments and structures must therefore be established to immediately identify cutting-edge topics for the future and propose corresponding funding. The following list contains several potential instruments and principles. However, it is important to remain fundamentally open to other suitable, innovative funding formats.

a. Develop funding formats for basic research, especially for unconventional ideas – potentially tailored for early-career junior researchers. It is tremendously important to include both experienced and early-career researchers into efforts to identify topics for the future. It is also important to draw on the potential of experienced researchers to serve as mentors in the development of new approaches. Expanding targeted funding programs and competitions would make it possible to offer financial incentives to generate pioneering ideas and test them in proof-of-concept studies.
b. Fast-track and ad-hoc project grants accelerate the availability of additional funding to previously approved publicly funded projects and thereby increase the pace of research progress.
c. Trampoline grants and hackathons could be introduced as flexible, innovative means to support creative ideas and establish an agile research environment. AFM-Telethon could be used as a model to provide initial funding to support the testing of new ideas. The trampoline grant model was developed with this in mind, allowing researchers to pursue innovative ideas without the need of extensive preliminary work when submitting their application.
d. More reasonable funding amounts are needed to support the clinical translation of effective, innovative therapy approaches, especially in the academic and start-up sectors. Combining existing funding measures could make it possible to provide higher funding amounts as well as follow-up funding for a smaller number of projects. Following the example set by MRC translational funding, higher overall funding amounts could be made available, contingent on accomplishment of specific milestones.
e. An independent, national self-help and patient fund should be established to make it easier for organizations to apply for funding regarding communication, training and support measures.
f. Funding for selected start-ups and academic groups intending to launch a spin-off in the field of GCTs, specifically to allow for use of critical infrastructure and enabling facilities.
g. Funding for research institutes to enable high-quality patenting of ideas.
h. Funding for development projects with a focus on process and production technologies, thereby creating generally accepted standards for relevant, established technologies.

Timeline and resource requirements
- Short term: Establishment of suitable structures and mechanisms to identify and prioritize topics for the future
- Short term: Establishment of suitable measures to create new, flexible funding formats with a short lead time

Success indicators
- Compilation of a list of currently relevant topics for the future and prioritization of key topics
- Continuous adaptation of the topic list to reflect current trends and developments in the research landscape
- Development of a toolbox for new funding formats and establishment of selection mechanisms and criteria

Objective 3:
Improve the organizational and regulatory framework for pre-clinical and clinical GCT studies

Explanation:
By international comparison, Germany is too slow in the pre-clinical and clinical development of GCTs. In each stage – from the idea to publication and patent (proof of concept), from patent and publication to the first patient, and from the first patient to market launch – Germany's competitors advance more quickly. There is a consensus that the existing high quality and meticulousness, particularly in regulatory assessments for late pre-clinical and early clinical studies, can be a positive aspect for Germany as a research location. Nevertheless, the international perception is that the organizational and regulatory framework for GCTs in Germany are "difficult" and have become a locational disadvantage due to the costs and effort involved. To improve these framework conditions, measures to simplify and expedite authorization procedures must be promoted. Processes at regulatory authorities – which, in their current form, are often perceived exclusively as supervisory bodies – must be reevaluated. In addition to their formal, regulatory duties, these authorities could play an advisory and strategic role (following the example set by the Office of Therapeutic Drugs – a "Super Office" in the USA).

In pre-clinical and translational research, the laborious and drawn-out authorization procedures in applications for animal experiments, and the fact that such applications are currently rejected almost as a matter of principle in certain federal states, has become a serious problem. In Germany, the authorization process for animal experimentation regularly involves supplemental claims and revisions over months and even years. In contrast, in the USA, animal experimentation applications are managed at the institutional level, resulting in a significantly faster approval process. Despite efforts to reduce animal experimentation and the growing interest in alternative methods, the use of data from animal experiments remains a fundamental requirement in the natural sciences. Such data is not only demanded by all leading scientific journals but also by regulatory authorities for clinical trial approvals as well as by investors, biotech companies and the pharmaceutical industry before licensing or acquiring GCT products. A constructive discourse is urgently needed regarding the potential of alternative models, as well as the fact that they currently remain in an early stage of development and are still not fully accepted. This discourse aims at enabling internationally competitive work in this field as well as aligning the aspired reduction in animal experiments with statutory requirements and legal framework.

Regarding clinical research, there is an urgent need to harmonize regulations between Germany's federal states, especially GMP/GLP regulations, to ensure a coherent and effective translation of research into clinical practice and healthcare. The Federal Ministry of Health (BMG) has drafted a new proposal for the Medical Research Act (MFG) containing numerous approaches that are designed to help make clinical study processes more agile. This working group supports and endorses these approaches.

Measure 1:
Facilitate the implementation of GCT manufacturing processes and their translation into early clinical studies

Stakeholders required:
National institutions for the regulation of clinical studies, BfArM, PEI, BMG, state ministries of health

Description:
Achieving these goals will require the introduction of a simplified, risk-based regulatory system for phase I/IIa clinical studies (as employed in the USA) e. g., via a GMP-light process (including rare and ultra-rare diseases) and simplified requirements regarding pre-clinical data (for example non-GLP/reduced scope). This is addressed in detail in Topic IV by targeting subjects including harmonization of GMP regulations at the national level and the introduction of sandbox systems.

Timeline and resource requirements
- Short to medium term: Development of standardized GMP regulations nationwide

Success indicators
- Establishment of a committee with members drawn from all the states' regulatory authorities to develop a draft proposal for regulations to be introduced at federal level
- Coordination between regulatory authorities, exemplified by approval of the joint proposal

Measure 2:
Promote acceptance of animal experimentation and encourage the realistic assessment of potential alternatives

Stakeholders required:
Federal Ministry of Food and Agriculture (BMEL), German Centre for the Protection of Laboratory Animals (Bf3R), German Federal Institute for Risk Assessment (BfR), governance structure from the National Strategy

Description:
The federal government's strategy to reduce the number of animal experiments must be aligned with unbiased assessments of the level of technological maturity, relevance and, above all, low international acceptance of alternative testing models. Applications for animal experiments should be processed within the statutory 40-day period, including the review of potentially necessary revisions rounds in which justified improvement proposals and criticisms are addressed. This central demand should be introduced in the planned amendment to the German Animal Welfare Act (TierSchG). In addition, the amendment should introduce a clear definition for the term "*vernünftiger Grund*" (literally: "reasonable grounds") in Section 1 TierSchG referring to sacrificing animals used in experiments, as this is currently undefined, which means that legal certainty cannot be ensured.

In parallel with this, support for alternative methods to animal experimentation must be intensified. Following the example of the PEPPER platform in France (https://ed-pepper.eu/en/), public sector stakeholders and industry should collaborate to develop a platform that facilitates the establishment and regulation of alternative testing systems. This would ensure that all relevant stakeholders nationwide have access to alternative pre-clinical in vitro testing methods.

Timeline and resource requirements
- Short term: Measures to accelerate authorizations for animal experimentation. Clear definition of the term "*vernünftiger Grund*" (literally: "reasonable grounds") in the amendment of the TierSchG
- Short to medium term: Assessment of current requirements regarding international standards and requirements for publications, clinical studies and drug authorizations, involving all relevant stakeholders
- Long term: Establishment of a national platform for validated testing systems that provide alternatives to animal models, involving public and private institutions

Success indicators
- Amendment of the TierSchG, with improvements regarding legal certainty and authorization procedures
- Reduction in processing time for animal experimentation authorizations from over 200 days at present to 40 days
- Approval of validated alternative in vitro testing systems with the aim of achieving the intended reduction in the number of animal experiments
- Establishment of a central advisory and service center regarding alternative systems for GCT stakeholders

Measure 3:
Measuring and publication of performance indicators for regulators and supervisory authorities

Stakeholders required:
BfArM, PEI, Clinical Trials Coordination Group, AKEK

Description:
At present, there is little transparency in quantitative and qualitative information on the application procedures performed by regulators and supervisory authorities at federal and state level in the field of GCTs. However, GCT stakeholders in Germany have a legitimate interest in this transparency. Performance indicators should therefore be introduced for regulators and supervisory authorities.

This would increase transparency and acceptance regarding application procedures and create "competition" to drive continuous improvement in regulators' and supervisory authorities' performance. At the same time, all stakeholders should be able to strategically plan and prioritize applications and authorization procedures (thereby relieving the burden on regulators/authorities over the medium term by reducing the submission of applications with little prospect of securing authorization). From an international perspective, "positive" performance indicators should lead to a visible improvement in Germany's appeal as a research location.

Timeline and resource requirements
- Short term: Collection of quantitative and qualitative information on application procedures and their publication in existing central registers
- Medium to long term: Constructive discourse between regulators and GCT community to determine potential means of optimizing performance indicators

Success indicators
- Publication of performance indicators by more than 80% of relevant regulators at federal and state level
- Improvement in performance indicators in a five-year and ten-year comparison
- Positive impact on the international perception of Germany as a research location through performance indicators in international comparison

Measure 4:
Optimize and refine ethics committees

Stakeholders required:
BMG, AKEK, PEI Innovation Office, German Association of Academic Medical Centers (VUD)

Description:
A central element in the translation of research results into clinical application is the assessment and approval by ethics committees. In recent years, this application and authorization process has often become a significant time burden due to protracted and complex procedures and the lack of harmonization between individual ethics committees. Indeed, this aspect is increasingly developing into a locational disadvantage. Regarding the acceleration of translation while maintaining high quality, we support the planned changes to the established system specified in the proposed Medical Research Act (MFG) – currently still in the consultation stage – which aims to simplify and expedite processes. Measures to achieve this include:

- Introduction of transparent and uniform assessment standards
- Evaluation of existing structures and procedures; scrapping of contradictory practices and processes
- Rapid and effective establishment of the "specialized ethics committee for particular procedures" proposed in the MFG

The structural implementation of these measures should take place in coordination with all relevant stakeholders in the existing system and remain open to the development or reorientation of existing structures and/or establishment of new structures.

Timeline and resource requirements
- Short term: Harmonization of standards for individual ethics committees and/or rapid introduction of the proposed specialized ethics committee for particular procedures.
- Long term: Dismantling of bureaucratic barriers

Success indicators
- Standardized ethics guidelines regarding the translation of research results into clinical practice at federal level
- Development of an accelerated authorization procedure (comparable with the EU's Green Deal for medicinal product authorizations)
- Evaluation of the number of approved clinical GCT studies in Germany (in two years' time)

Objective 4:
Ensure that patients, patient advocacy groups and patients' associations are duly involved

Explanation:
Significant progress has been achieved in recent years regarding patient participation and the involvement of patients' organizations into the development and application of GCTs. An important factor in this context is that patients who have benefited from innovative GCTs have shared their "success stories" publicly (e. g., Emily Whitehead – CD19 CAR-T). This fosters public acceptance and increases the relevance of clinical products and studies. At present, communication between researchers, doctors and patients is still hampered by several different factors. In some cases, scientific institutions and patient advocacy groups both lack the specific skills and resources needed to ensure optimal communication and collaboration.

The aim should be to involve patients more closely at specific points in pre-clinical and clinical development in a proactive and focused way. This would create added value with regard to the principles of scientific integrity, cost efficiency and acceptance in GCT development.

Patient advocacy groups can serve as a helpful peer group concerning the prioritization of funding, identification of topics for the future and recruitment of subjects for studies. Such groups could also be integrated into the analysis and evaluation of study results. Integrative collaboration between all stakeholders should therefore be pursued to generate synergies and fully exploit potential. The participation of patients and patient advocates often accounts for a significant proportion of allocated funding, especially in large-scale collaborative projects, e. g., to remunerate participants for their time and cover travel and training costs. Funding instruments must account for this aspect to meet all stakeholders' requirements.

Measure 1:
Define standards for project budgets and remuneration for patient advocates

Stakeholders required:
Federal Syndicate of Patient Interest Groups (BundesArbeitsGemeinschaft der Patientenstellen und -Initiativen, bagp), German National Association of Self-Help Groups (Deutsche Arbeitsgemeinschaft Selbsthilfegruppen e.V., DAG-SHG), Alliance of Chronic Rare Diseases (ACHSE), German Cancer Aid (Deutsche Krebshilfe, DKH)

Description:
The definition of standards for project budgets and remuneration for patient advocates should be sought to ensure that these aspects are duly considered in project funding formats. Distinguishing between non-profit and pro-profit patients' organizations would also be a useful measure to allocate both time and financial resources in an optimal and proportionate manner. This could, for example, be put into practice via a register of patients' organizations to support suitable funding models and financing. The requirements of the two types of organizations (i. e., non-profit and pro-profit) can differ significantly, e. g., in terms of whether they need expense allowances or full cost coverage for their staffing or individual appearance fees. Depending on the specific funding formats, organizations might be unable to cover the respective bureaucratic burden (non-profit) or could be ineligible for funding (for-profit).

Timeline and resource requirements
- Short term: Establishment of a roundtable meeting with all stakeholders to discuss remuneration models for patients' organizations
- Medium term: Implementation of remuneration models for GCT projects from academia and industry
- Medium term: Establishment of a national register for patients' organizations in the field of GCTs

Success indicators
- Remuneration models applied in more than 80% of GCT projects in which patients' organizations are involved (in five years' time)

- Number of GCT projects in which patients' organizations are involved increases by 25% on 2024 figures (in five years' time)

Measure 2:
Develop specific interaction concepts

Stakeholders required:
Relevant patients' organizations for GCTs – e. g., DKH, German Hospital Federation (DKG), the Cancer Information Service (KID) at the German Cancer Research Center (DKFZ), etc.

Description:
The development and implementation of improved and more specific interaction concepts between all stakeholders should help to overcome the barriers outlined above. Attending scientific conferences, which strengthen collaboration between all stakeholders via panel discussions and lecture series, represents such an opportunity for direct interaction between patients, patient advocacy groups, researchers and doctors. This form of collaboration allows for the presentation and discussion of all stages in the development of a GCT. Each GCT treatment facility will be assigned a patient participation/ stakeholder management coordinator to oversee implementation of the interaction concept.

Timeline and resource requirements
- Medium to long term: Establishment of a universal communication platform to facilitate interaction between researchers, doctors, patients' organizations and patients
- Medium term: Staff – patient participation coordinators

Success indicators
- Bedside-to-bench evaluation of the outcomes of clinical studies
- Creation of staff positions in patient-stakeholder engagement, serving as an interface in the collaboration between patients and patient advocacy groups and between researchers and clinicians

Objective 5:
Foster a change in mentality and bolster bio-entrepreneurial spirit in the German GCT community

Explanation:
To lay the foundations for the successful, internationally competitive development of GCTs, it will be necessary to maintain excellent education in monodisciplinary sciences, while also creating new opportunities for interdisciplinary education in disciplines relevant for GCTs. Universities in both the US and the UK offer study programs that convey a holistic perspective and cover topics such as commercialization, regulatory affairs and venture capital financing. A potential solution regarding topics such as patent protection, technology transfer and commercialization would be to integrate these topics more strongly into education and training for early-career researchers. Researchers should come to accept the fundamental principle that an invention or discovery can only be designated an innovation once it is made available to all affected patients as an approved product (e. g., a therapy) authorized for healthcare. This should help to foster a new generation of bio-entrepreneurs. Content from other disciplines, e. g., topics such as artificial intelligence and modern communication formats, can also be emphasized in this context. Achieving a shift in mentality will be a decisive step in this form of education to create better framework conditions for the translation of GCT research results. This includes optimizing academic incentive systems and moving away from traditional ways of thinking and towards a culture of collaboration between GCT stakeholders in the public and commercial sectors. This will promote an innovative, risk-tolerant mindset

while conveying the importance of resilience and perseverance (as not every GCT product or start-up will make it to market). Promoting entrepreneurial thinking in science and a willingness to collaborate across disciplines and accept risks will be decisive factors in accelerating the translation from research to application.

Measure 1:
Foster the necessary shift in mentality regarding GCTs

Stakeholders required:
BMFTR, state authorities for education, governance structure of the National Strategy, German Association of University Professors and Lecturers (DHV), German Association of Academic Medical Centers (VUD)

Description:
Fostering the described shift in mentality towards an increasingly holistic mindset and bio-entrepreneurial spirit will require the implementation of an array of measures:

a. Develop innovative education concepts, e. g., in the form of a School for Gene and Cell Therapy, in which experts in all disciplines in Germany can teach and train researchers and clinicians, alongside existing spring school models (for a more detailed description, see Topic II, Objective 1, Measure 2)
b. Establish further interdisciplinary professional training programs, e. g., for clinician scientists, medical scientists and translational scientists, to promote the networking of different sub-areas relevant for GCT development (for a more detailed description, see Topic II, Objective 2, Measure 2)
c. Optimize academic incentive systems by amending regulations for doctoral and post-doctoral teaching qualifications and tenure track programs to recognize clinical trials, patent applications and launching start-ups as relevant research and career achievements (for a more detailed description, see Topic II, Objective 2, Measure 1 and Topic III, Objective 4, Measure 1)
d. Intensify the direct exchange between academic research, industry and VC to support the creation of innovative concepts, projects and spin-offs (e. g., via business plan competitions, bio-entrepreneur bootcamps, public appreciation and visibility (cf. German Future Prize)) (for a more detailed description, see Topic I, Objective 4, Measure 5)

Timeline and resource requirements
- Short term: Development of a curriculum for a School for Gene and Cell Therapy; establishment of support programs for medical scientists and translational scientists
- Short to medium term: Recognition for conducting clinical studies, applying for patents or launching start-ups in academic careers and as a research achievement
- Short to medium term: Implementation of interaction formats between academia, industry and VC providers

Success indicators
- More than 250 graduates from the School for Gene and Cell Therapy (in five years' time)
- Recognition of conducting clinical studies, registering patents or launching start-ups in academic careers at more than 80% of German universities (in five years' time)
- Annual GCT bootcamp held with stakeholders from academia, industry and VC providers with over 100 participants (in three years' time)

Measure 2:
Offer natural scientists career prospects and positions as bio-entrepreneurs in the public sector

Stakeholders required:
BMFTR, German Association of University Professors and Lecturers (DHV), German Association of Academic Medical Centers (VUD)

Description:
In the public sector, natural scientists often play a crucial role as medical scientists in the design and early pre-clinical development of innovative GCTs. Clinical translation and the preparation and supervision of the transfer to biotech companies and other industry stakeholders requires considerable stamina, specific "entrepreneurial" skills and the courage to tackle projects and tasks that will not be acknowledged with the conventional academic rewards of third-party funding and impact points. Medical scientists willing to support GCT projects in the translation and transfer stages must be offered career prospects and secure positions to which they can aspire, especially in the public sector. The current version of the Academic Fixed-Term Contract Act (WissZeitVG) requires constructive reevaluation and amendment in this respect. In its current form, it creates unfavorable framework conditions for researchers and presents a genuine risk of driving medical scientists to leave the GCT sector or move abroad. A reform of the Academic Fixed-Term Contract Act (WissZeitVG) must create permanent positions for ongoing tasks because translational projects are not conducive to the academic career paths of medical scientists. Moving between positions in academia (public sector) and start-ups/ biotech companies (industry) should be made easier and encouraged to combine experience from both areas in successful projects. We advocate strengthening mid-level academic staff to allow for long-term education and training of early-career researchers and retain the innovation potential of Germany as a location for research and development.

Timeline and resource requirements
- Short term: Positions at universities and university hospitals should be increasingly made permanent as an "extension" to the Academic Fixed-Term Contract Act (WissZeitVG) with appropriate funding from federal and state governments
- Short to medium term: Establishment of senior/staff scientist positions, especially at universities and non-university research institutes

Success indicators
- Increase of >20% in the number of specialists in academic research in the field of GCTs with a permanent contract (vs. 2024 figures, in five years' time)
- Increase of >20% in the number of medical scientists at academic GCT research institutes with more than one year of industry experience (vs. 2024 figures, in five years' time)

Topic VII: Marketing authorization and transition to patient care

Summary

Early access to high-quality care with GCTs can improve the quality of life and health of the most critically ill patients. In some cases, it could even present the first and only treatment options. Challenges involved for early access to GCTs include securing approval for these new medicinal products, and applying them in practice. This requires amendments to existing provisions and possibly the creation of new structures and instruments, if necessary. The following are key measures in this context:

1. **Giving patients swift access to specialist care in terms of diagnosis, both to facilitate the start of treatment and to monitor the success of GCT during treatment.**
   - **a.** Develop and implement education and advanced training programs to ensure optimal access to GCTs and support continuous advancements in diagnostics
   - **b.** Establish interdisciplinary therapy decision boards as the gold standard in GCT diagnostics.
   - **c.** Develop nationally standardized qualification criteria, standards and reference datasets for corresponding GCT access and ongoing diagnostics.

2. **Enhance the flexibility of reimbursement and care models for GCTs while reinforcing Germany's position as a leading location for research and treatment. This includes promoting an innovation-friendly environment with high-quality patient care via efficient, state-of-the-art therapies by amending the Act on the Reform of the Market for Medicinal Products (AMNOG) and adapting care remuneration structures.**
   - **a.** Regarding therapeutic developments in the field of GCTs, it is important to allow for the necessary flexibility in the AMNOG process in terms of benefit assessments and price-setting to uphold access to, and the availability of, these vital therapies for patients
   - **b.** At the level of patient care, ensuring appropriate quality assurance measures in diagnostics and treatment for patients is a priority and requires an amendment of remuneration models

3. **Providing high-quality, safe and efficient treatment for patients with innovative therapies by establishing interdisciplinary GCT treatment facilities.**
   In this context, it will be important to establish a close structural interaction between research and healthcare, streamline qualification and certification processes for treatment facilities and streamline contract design processes between treatment facilities and manufacturers. Efficient referral and communication between treatment providers must also be ensured.

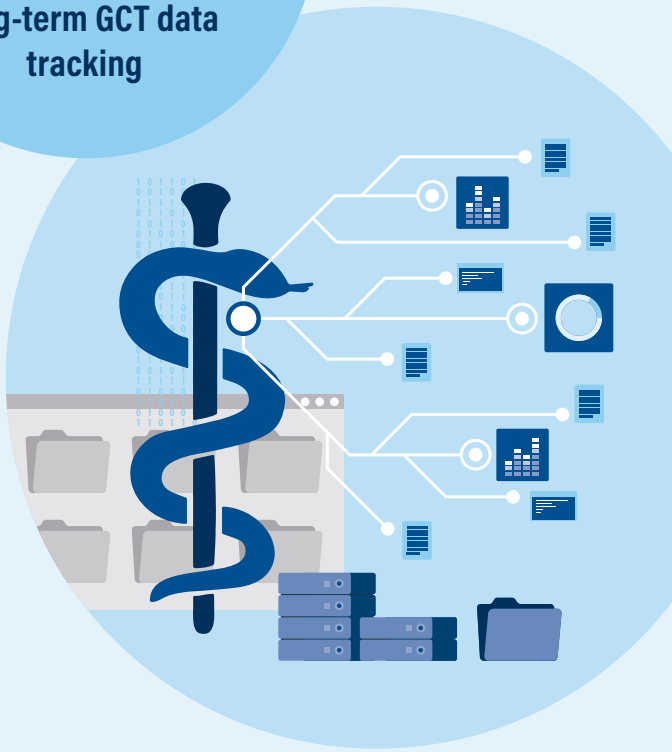
4. **Optimizing and establishing the data landscape to ensure the versatile availability of treatment data in research and long-term data tracking, regarding aspects such as the efficacy and side-effects of GCTs.**
   In this context, the recording and documentation of post-marketing data should be standardized, with a target set to maintain a method-specific national GCT register.

1 Facilitate access to patients and their targeted selection for specific GCTs

2 Increase flexibility of reimbursement and care models in the use of GCTs

3 Provide high-quality, safe and efficient treatment for patients with innovative therapies by establishing interdisciplinary GCT treatment facilities

4 Optimize and establish the data landscape to ensure the versatile usability of this data in research and facilitate long-term GCT data tracking



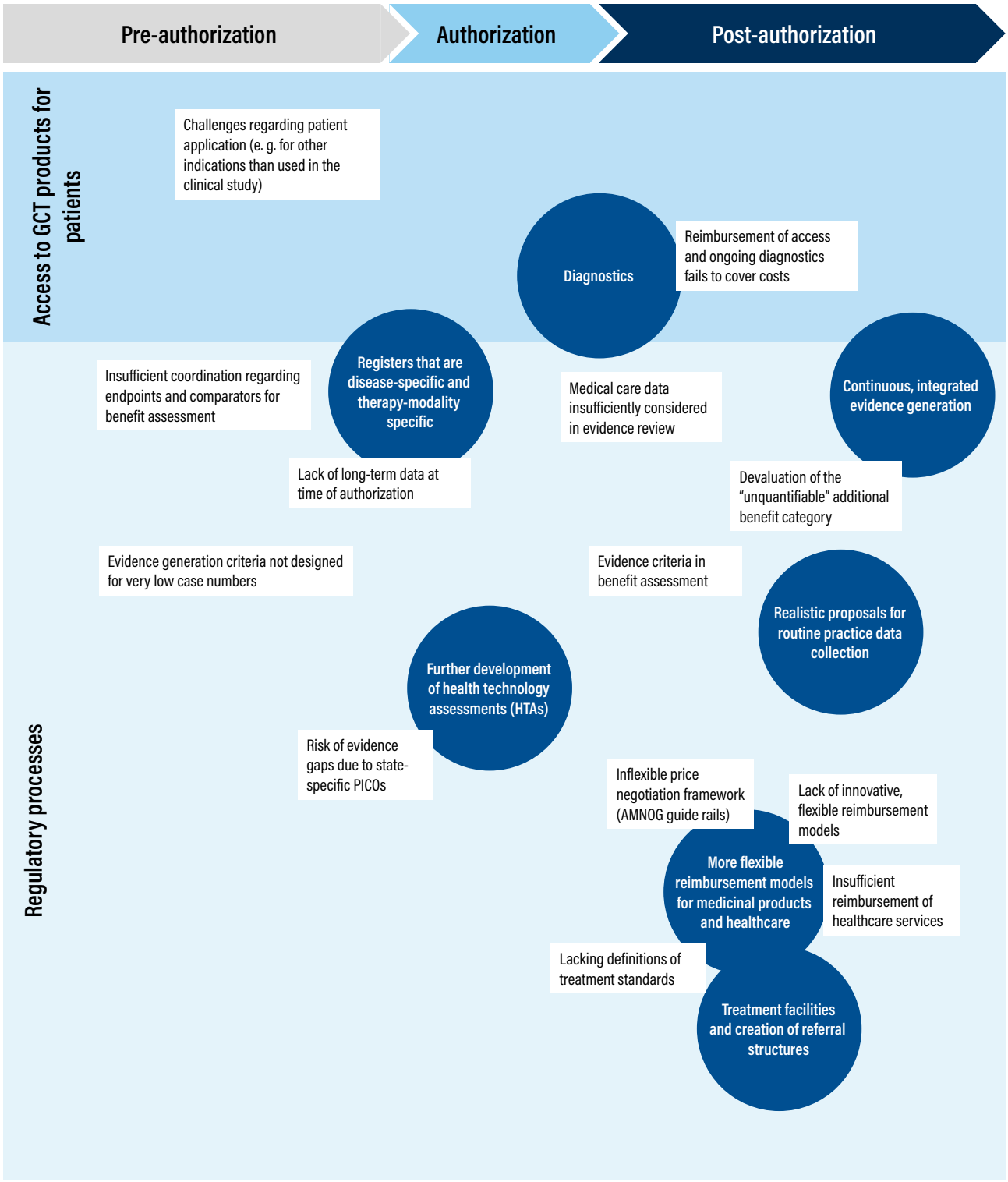


Figure 2: **Barriers to the transition of GCTs into healthcare**. Depiction of challenges to be addressed (pre-authorization, during the authorization process and post-authorization) in terms of access for patients and regulatory processes.

Background

GCTs (including ATMPs and RNA therapies) present new medical care prospects for the most seriously ill patients. As innovative and complex technologies, GCTs are subject to specific challenges in the context of the approval process as well as in the post-approval phase of translation into healthcare, including both diagnostics and treatment (see Figure 2).

This topic addresses the entire process, encompassing access and companion diagnostics, easy patient access to high-quality, safe, and efficient GCT treatments, monitoring of disease progression and forward-looking evidence generation. The goal is to ensure the sustained efficacy and quality of GCT use over time.

The objectives and specific measures proposed in this topic encompass the entire spectrum of disease entities that can be addressed with GCTs, from tumor diseases to rare and ultra-rare diseases.

Objectives

1. Facilitate access to patients and their targeted selection for specific GCTs
2. Increase flexibility of reimbursement and care models for the use of GCTs
3. Provide high-quality, safe and efficient treatment for patients with innovative therapies by establishing interdisciplinary GCT treatment facilities
4. Optimize and establish the data landscape to ensure the versatile usability of this data in research and facilitate long-term GCT data tracking

Objective 1:
Facilitate access to patients and their targeted selection for specific GCTs

Explanation:
One of the most important requirements for successful treatment with GCTs is rapid and reliable diagnostics, which allow treatment to commence quickly and monitor ongoing treatment success. Innovative multi-modal diagnostics make it possible to identify and stratify suitable patients for access to GCTs. Comprehensive, precise and sometimes patient-specific diagnostics must be used before, during and after therapeutic measures to facilitate and monitor treatment success and to identify potential adverse effects. In this context, it is important to ensure comprehensive, cross-sectoral access to diagnostics as well as mandatory, standardized reimbursement arrangements nationwide.

Measure 1:
Develop and implement education and advanced training programs to ensure optimal diagnostics to identify and stratify patients and to monitor courses of treatment for standard care facilities

Stakeholders required:
GCT treatment facilities, federal and state medical associations, Federal Joint Committee (G-BA)

Description:
Diagnostic and clinical care facilities are essential for two key aspects:

1. Identification (incl. screening) and stratification of suitable patients for GCTs during diagnostic standard care
2. Primarily clinical monitoring of courses of treatment and basic clinical and laboratory (chemical) diagnostics

Specific advanced training measures must be implemented in treatment facilities to ensure that these tasks are performed in line with the latest scientific knowledge and evolving access to GCTs.

Timeline and resource requirements

- Education and advanced training measures must be developed and implemented for treatment facilities that offer diagnostic and clinical standard care. The respective facilities shall be responsible for these measures
- Advanced training should focus on:
  - Standardized identification and stratification of suitable patients for GCTs
  - Standardized implementation and documentation of monitoring disease progression for GCTs

- Federal and state medical associations should be responsible for quality assurance as part of continuing medical education
- The costs of these advanced training measures can be covered according to regulations for centers by the Federal Joint Committee (G-BA), incl. oncological centers and centers for rare diseases

Success indicators

- Number of diagnostic standard care facilities that implement advanced training measures
- Number of GCTs incorporated in these advanced training measures
- Percentage of the treatment facilities that implemented advanced training measures and conduct corresponding GCT diagnostics according to high quality standards

Measure 2:
Establish interdisciplinary therapy decision boards as the gold standard in GCT diagnostics

Stakeholders required:
GCT treatment facilities

Description:
The indications for oncological ATMP treatment are determined by interdisciplinary tumor conferences according to Section 5(1) of Annex I of the Guidelines on Quality Requirements for the Application of Medicinal Products for Novel Therapies in accordance with Section 136a (5) of the German Social Security Code, Book 5 (ATMP Quality Assurance Guidelines). We recommend renaming these conferences to "interdisciplinary therapy decision boards", establishing them as the gold standard for determining GCT indications. Furthermore, the boards should be introduced as universal requirement into the general part of the ATMP Quality Assurance Guidelines issued by the Federal Joint Committee (G-BA) and/or into comparable guidelines for other GCTs, including those that are not classified as ATMPs. This will guarantee quality assurance for diagnostic access and qualification criteria for the specific GCTs and the respective patients. These boards will also reponsible for issues during monitoring of disease progression and decide whether to stop or continue GCT treatments.

Timeline and resource requirements

- Funding of model projects to pilot the establishment and reimbursement of interdisciplinary therapy decision boards in GCT treatment facilities (including for GCTs currently not eligible for approval) and evaluate their readiness for introduction to standard care
- A budget of roughly €1 million will be required for each of the model projects, including their evaluation. The respective funding could be provided via the German Innovation Fund or a direct project funding by the BMFTR

Success indicators

- Number of interdisciplinary therapy decision boards established at GCT treatment facilities for different GCT modalities

Measure 3:
Create nationally harmonized qualification criteria and standards for GCT access diagnostics and monitoring of disease progression

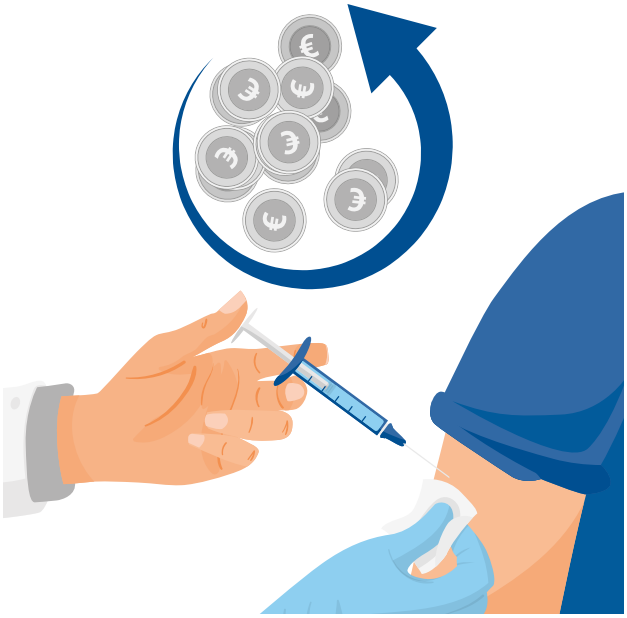
Stakeholders required:
Federal Joint Committee (G-BA), expert associations, health insurance providers, GCT treatment facilities, patients' organizations and GCT distributors

Description:
Under the coordination of the Federal Joint Committee (G-BA), expert associations, health insurance providers, GCT treatment facilities, patients' organizations and GCT distributors should work together to develop:

1. Qualification criteria and standards for GCT access diagnostics
2. Reference datasets and standards for diagnostics to monitor disease progression and treatment

Timeline and resource requirements
- The stakeholders should collectively organize and fund the process to develop these standards

Success indicators
- Existence of qualification criteria and standards for GCT access diagnostics and monitoring of disease progression for GCTs that have been approved/are eligible for approval and for GCTs that are not eligible for approval



Objective 2:
Increase flexibility of reimbursement and care models in the use of GCTs

Explanation:
It is important to provide support for innovation by strengthening Germany as a location for research and medical care – with efficient, best-possible therapies – by amending the Act on the Reform of the Market for Medicinal Products (AMNOG) along with reimbursement for healthcare services. Due to the special nature of GCTs (e. g., the fact that some only need to be administered once but have the potential to achieve very long-term effects), the AMNOG should be refined (regarding both assessment of additional benefits and creating leeway for negotiations in subsequent price negotiations). In addition, long-term data that is lacking at the time of a GCT product's market entry could be generated through a new, versatile data landscape (e. g., a register that is therapy modality-specific and/or disease-specific or telemedicine platforms with remote collection of patient-centered outcomes). Furthermore, new reimbursement models must be developed for GCTs to reflect the expenses incurred by healthcare facilities in administering these therapies (incl. diagnostics, monitoring of disease progression, providing documentation for required registers, etc.).

Measure 1:
Employ the best available evidence for the assessment of additional benefits

Stakeholders required:
Legislator (BMG)

Description:
The therapeutic paradigm of one-off therapy, which can be expected in many cases to achieve long-term efficacy in treating a disease that would otherwise require continuous treatment, demands flexibilization of the necessary evidence criteria with a focus on the best-possible evidence. During a benefit assessment as part of an AMNOG procedure, it must be routinely determined whether it is impossible or unreasonable to conduct or require studies with the highest level of evidence and/or whether this level of evidence might already exist. This assessment uses criteria that reflect the specific features of therapies and medical care, in particular patients' medical needs that are currently unmet, the severity of the disease and the size of the target population. In the legal framework of the AMNOG benefit assessment, the Medicinal Product Benefit Assessment Regulation (AM-NutzenV) acknowledges that there are therapy situations in which it is "impossible or unreasonable to conduct or require studies with the highest level of evidence". In such cases, "evidence of the best available level must be submitted". To date, however, this has not been systematically implemented. The conditions for adequate consideration of special therapy situations have been defined and require that indicated reference studies (must) be taken into consideration. The legislator should clarify this in the AM-NutzenV.

Timeline and resource requirements
- Short term (1 year): Adaptation of legal framework conditions and administrative implementing regulations (AM-NutzenV; Rules of Procedure (VerfO))
- No additional resources required

Success indicators
- An indicator of success would be the utilization of the best available evidence in medicinal product development and scientific advice (during approval) which includes a review conducted at the earliest possible stage and involves regulators and experts from science and healthcare

Measure 2:
Amend the criteria for consideration of medical care-related data in benefit assessments

Stakeholders required:
Legislator, Federal Joint Committee (G-BA)

Description:
Evidence from medical care data is assuming an increasingly significant role in the approval processes of the EMA and FDA as well as in health technology assessment (HTA) processes in many countries. This development is accelerating because of the growing data infrastructure in many countries, including Germany. Germany, too, should aim to make full use of the evidence-gathering opportunities this presents. The certification requirements for routine practice data collection are currently disproportionately high. The specific definition and operationalization of central aspects of a trial, such as the number of patients to be recruited, inclusion and exclusion criteria, outcomes and their expected assessment timepoints, confounders, adjustment procedures and the methodical approach to pre-treatment and therapy changes must be designed in such a way that the best available evidence can be gathered from routine clinical care. The degree to which routine practice data collection is appropriate and feasible must be assessed in the first procedural step and before imposition of regulatory requirements, with input from expert groups and the company in question. If limitations are identified as the process progresses, they should be acknowledged and documented with the final Federal Joint Committee resolution to perform routine practice data collection.

Timeline and resource requirements
- Short term (1 year): Adaptation of legal framework conditions and administrative implementing regulations (AM-NutzenV; VerfO)
- No additional resources required

Success indicators
- Use of routine practice data collection in suitable individual cases in accordance with the legal purpose
- Number and scope of other medical care-related data sources used in the context of HTAs
- Prompt, versatile and equal access to the Research Data Centre (FDZ) data pool at the BfArM and inclusion of this data into benefit assessments

Measure 3:
Substantiate benefit-based price-setting

Stakeholders required:
Legislator

Description:
The pricing regulations introduced as part of the Statutory Health Insurance Financial Stabilization Act (GKV-FinStG) – the price negotiation framework referred to in German as *Leitplanken* (guide rails) – represent a risk to the availability of GCTs for patients in Germany, given the specific methodological characteristics of GCTs. The reimbursement amount for medicinal products with unquantifiable or low additional benefit must not, in certain circumstances, exceed the threshold for the most economical appropriate comparative therapy, even though the Federal Joint Committee (G-BA) has identified a relevant additional benefit for patients in both cases (low and unquantifiable additional benefit). An unquantifiable additional benefit can be low, considerable or significant. As the best available evidence in specific therapies has not been recognized to date, the value of these therapies is not appropriately reflected at present. For this reason, the statutory framework on price negotiations in Section 130b of the German Social Insurance Code, Book V (SGB V) should be repealed, in particular the determination of unquantifiable and low additional benefits set out in Section 130b (3) SGB V. These changes ensure that the National Association of Statutory Health Insurance Funds (GKV-Spitzenverband) and pharmaceutical companies still have the freedom to find an appropriate price. In this context, the gradual relativization of the "unquantifiable" additional benefit category, which is incorrectly interpreted at present as the lowest category of additional benefit, should be restored to the original meaning of the category by including additional explanatory formulations in the Rules of Procedure (VerfO).

In summary, we recommend the removal of the guide rails in the price negotiation framework on both low and unquantifiable additional benefits to the legislator. This would restore the leeway that the negotiation partners need to acknowledge therapeutic improvements and give due consideration to the respective market situation. The objective to demonstrate a quantifiable additional benefit would remain unaffected.

Timeline and resource requirements
- Short term (1 year): Adaptation of legal framework conditions and, if necessary, administrative implementing regulations (AM-NutzenV; VerfO)
- No additional resources required

Success indicators
- An indicator of success would be early market access in Germany for new therapies that provide an existing additional benefit, even if this additional benefit is unquantifiable due to the therapies' long-term efficacy and/or a low number of patients

Measure 4:
Increase the use of performance-based reimbursement models in central price negotiations

Stakeholders required:
Legislator (BMG)

Description:
Due to the potentially limited evidence at the time of approval, it is important to allow for sufficient flexibility and appropriately address justifiable uncertainties regarding outcomes in specific cases. Therefore, reimbursement models based on the performance of a therapy – known as pay-for-performance or performance-based models/agreements – could be employed, extending the regulations in Section 130b SGB V. Necessary requirements for this are the willingness of both contract parties as well as the availability of an appropriate data infrastructure. Prices could then be determined to a significant degree by the actual success of a therapy in treating patients. Accordingly, reimbursement could take place via one-off payments, installments or annually adjusted payments. It is vital that such models include uncomplicated documentation for service providers.

In addition to current challenges with respect to the available data, these solutions also face barriers regarding their integration into reimbursement structures in the hospital sector, which must also be addressed. One solution could be to define an additional extra-budgetary, national fee – initially according to the sale price, later based on the reimbursement amount – if the costs of using a medicinal product are not appropriately reflected in diagnosis-related groups (DRGs). In addition, the current structure of the risk pool in morbidity-based risk structure compensation must be amended accordingly. To incentivize this, different reimbursement modalities must be available, including one-off payments and installments. In addition, the ability to track patients – according to the special report by the Federal Office for Social Security (BSS) (published October 2022) – must be established as it is still lacking.

Timeline and resource requirements

- Short term (1 year): Amendment of legal framework conditions
- No additional resources required

Success indicators

- Currently, decentralized selective contracts are used during the first year following market launch, which are concluded between individual health insurance funds and pharmaceutical manufacturers. It would be considered a success if there is an alternative option available to agree on long-term solutions with the National Association of Statutory Health Insurance Funds (GKV-Spitzenverband) in extension to the Section 130b regulations during central price negotiations. The performance-based reimbursement option can be flexibly structured in negotiations. The use of this option in suitable cases – as opposed to the status quo – is an indicator of success.

Measure 5:
Standardize and ensure cost coverage for diagnostics-related reimbursement

Stakeholders required:
BfArM, Institute for the Hospital Remuneration System (InEK), National Association of Statutory Health Insurance Physicians (KBV), National Association of Statutory Health Insurance Funds (GKV-Spitzenverband)

Description:
In terms of access diagnostics for GCTs, the model project on genome sequencing in accordance with Section 64e SGB V is likely to fill many of the gaps that exist in outpatient care.

Regarding inpatient care, advanced molecular genetic diagnostics for critically ill children (German Procedure Classification, OPS 1-944.1) are subject to unassessed additional fees, with negotiations producing very different outcomes in different hospitals, which can impair patients' access to such diagnostics at the regional level. We recommend establishing a standardized approach to national reimbursement, e. g., via an assessed additional fee.

The initiation of molecular genetic diagnostics is also not specifically covered for inpatient care of adult patients. In the case of access diagnostics for children with rare diseases, OPS 1-944.1 includes unnecessary, time-intensive and expensive preliminary diagnostics, for which there is no evidence-based justification in genetic examinations. We propose removing these preliminary diagnostics from the OPS description and limiting the requirements to conducting a case conference, in line with the recommendations of the model project on genome sequencing.

The comprehensive and necessary multi-modal access diagnostics and monitoring of disease progression must be covered in a manner that is standardized nationwide.

It must be noted that rapid whole exome sequencing (WES) and whole genome sequencing (WGS) in critically ill patients entails higher costs than standard WES/WGS. This should be reflected in the diagnosis-related groups (DRG) system.

Regarding inpatient cases, molecular monitoring of minimal residual disease (MRD) (OPS 1-991.x) is subject to unassessed additional fees, which are negotiated with very different results by different hospitals, impairing patients' access at the regional level. We recommend establishing a standardized national reimbursement system, e. g., via an assessed additional fee.

Patients with severe oncological diseases should always have access to state-of-the-art means to monitor disease progression. In addition, the reimbursement for MRD in the context of outpatient care in the doctors' fee scale (einheitlicher Bewertungsmaßstab – EBM) should be reviewed when applied to indications beyond hematological neoplasias, and with regard to reimbursement for next-generation sequencing (NGS) techniques.

Timeline and resource requirements

- The stakeholders should propose respective amendments to the OPS catalog, the DRG system and the EBM during upcoming regular revisions. The reduction of unnecessary preliminary diagnostics will save costs. Additional demands are within the overall budget.

Success indicators

- Increase in the proportion of nationally standardized reimbursement solutions for previously unassessed additional fees
- Nationally standardized reimbursement of access diagnostics and monitoring of disease progression for GCTs

Measure 6:
Create more flexible reimbursement models in the financing of quality assurance/care

Stakeholders required:
BMG, Federal Joint Committee (G-BA), pharmaceutical

manufacturers, expert associations, patient advocacy groups, federal higher authority, register representatives, representatives of GCT treatment facilities

Description:

Implementing, maintaining and ensuring compliance with current requirements results in significant costs for providers of medical care related to GCTs. These costs are not appropriately covered currently in standard reimbursement modalities for outpatient and inpatient care. The significant costs for specialized GCT treatment facilities in making GCTs available should be considered in the planned hospital reforms of the Federal Ministry of Health. We propose to bindingly determine reimbursement of healthcare models as part of a novel Quality Assurance Meeting I (QS I) of the G-BA, in which the following dimensions of quality assurance are considered (see the Innovation Fund project INTEGRATE ATMP (integrate-atmp.de) for an example):

- **Structural quality** (definition of minimum quantities of the respective product; requirements regarding infrastructure, staffing and specialist qualifications for treatment facilities)
- Process quality (definition of clinical outcomes starting from time of approval; development of structured treatment plans for pre-treatment and post-treatment as standard of care; and Delphi panel as the basis for collection of structured treatment data and definition of "necessary standards". In QS-I, specific expert representatives – selected according to product-specific requirements – are assigned to develop a treatment standard for the respective ATMP use. This treatment standard should then serve as a matrix for transparent calculation of healthcare service expenses. This must also cover inpatient treatment. Upon identification of an obvious deficit, a preliminary DRG assessed in the same way should be introduced with calculation of actual costs. The service matrix should be the basis for calculation of a nationally standardized, assessed additional fee that covers the additional expenses for ATMP administration and follow-up care. The necessary selection of patients, preparatory care and follow-up care (including continuous monitoring of disease progression) should be covered either through Section 116b SGB V (outpatient care from a specialist doctor) or via an extension of Section 132i SGB V (extension of the hemophilia regulation to an overall regulation for GCT products). This should either be ensured by adapting the respective legislation or via a regulation agreed upon by all stakeholders. In addition, the costs involved in potential routine practice data collection and/or other data collection and recording, documentation of services and entry into registers, which are not part of conventional outpatient care, must be covered (see Objective 4). The reimbursement of healthcare expenses must take place outside of a service providers' standard budget-capped reimbursement agreements and should therefore not compete with such agreements. This aspect should be added to the legal revision proposed above. In addition, it must be agreed with health insurance providers that they have an obligation to conduct negotiations regarding DRG/new examination and treatment methods (NUB) immediately and outside of existing schedules as soon as new GCTs are market approved.)
- **Result quality** (definition of the register and, if applicable, digital platforms in which data is collected following products' market approval, with categorization of the data according to the following aspects: minimum standards, definition and expansion of the data model for product-specific and patient-centered outcomes on efficacy and safety, price negotiation framework for routine practice data collection (if applicable) and joint determination of comparators).

Timeline and resource requirements

- Timeline: Adaptation of legislation immediately/as soon as possible; subsequent implementation into Rules of Procedure (VerfO) of the Federal Joint Committee (G-BA)
- Proposed composition of the new Quality Assurance Meeting (QS-I): Federal Joint Committee (G-BA) (with the power to issue rulings), pharmaceutical manufacturers, patient representatives, federal higher authority, expert associations, register representatives. Time of involvement: Following submission for approval at EMA and conclusion of the joint clinical assessment – thus approx. 6–9 months prior to approval

Success indicators

Accompanying and continuous evaluation of measures regarding their direct and indirect effects

- Short-term, product-specific success indicators are overall survival, event-free survival and disease-specific, objective outcome parameters. A medium-term success indicator is the satisfaction of all stakeholders involved (i. e., health insurance providers, healthcare service providers, patients, pharmaceutical companies and register operators), which should be systematically determined before and after the introduction of measures. In addition, the reimbursement costs calculated by healthcare service providers should be systematically evaluated via pre-post comparison

Objective 3:
Provide high-quality, safe and efficient treatment for patients with innovative therapies by establishing interdisciplinary GCT treatment facilities

Explanation:
At present, GCTs are primarily administered in departments specializing in the corresponding diseases, with input from experts of different disciplines. Accordingly, the structures for basic research, translation and the assignment, treatment and follow-up care of patients are usually aligned with specific diseases and respective therapy modalities. In light of progress in recent years, there is reason to expect the development of new GCT products for different diseases. This especially applies for rare diseases, possibly even tailored to individual (n-of-1) or very few (n-of-few) patients with a molecular or clinical profile that can be addressed through GCTs, for which conventional approval procedures are not effective. Nevertheless, a fast access to these therapeutics for patients and ensuring high-quality treatment while simultaneously utilizing resources in the healthcare system in a responsible, cost-effective manner will require the swift and continuous development and maintenance of skills and structures necessary for the use of GCTs. To achieve this, resources must be pooled via the establishment of interdisciplinary GCT treatment facilities.

Access to GCTs, both before and after they receive marketing authorization, is impaired by bureaucratic hurdles. These hurdles include long and resource-intensive certification processes and contractual negotiations between individual stakeholders (health insurance providers, marketing authorization holders and practitioners).

Adequate healthcare structures and pathways must be established and refined, involving all relevant sectors. This will require interdisciplinary treatment facilities with a corresponding focus on GCTs, including the establishment of corresponding assignment structures along with structures for post-marketing monitoring and follow-up care for patients. Furthermore, a continuous dialog should occur to explore ways to facilitate access to therapies prior to marketing authorization (low threshold) to ensure the safety of these therapies but also to give patients early access to them.

Measure 1:
Establish close structural interaction between research and healthcare

Stakeholders required:
Federal Joint Committee (G-BA), expert associations, GCT treatment facilities

Description:
Patients should be treated exclusively in structures that are associated with current treatment facilities (as defined by the G-BA). Some of these treatment facilities will be focused exclusively on medical care, while others will serve as hubs in the proposed National GCT Network (see Topic VI, Objective 1, Measure 1). Those hubs will target both high-quality medical care and excellent research. Optimal networking and interaction between both types of treatment facilities will be essential to ensure medical care that meets all patients' needs. Treatment facilities should be established and developed with an interdisciplinary nature and a focus on GCTs. In the future, the quality guidelines for treatment in these facilities should not be newly defined after each individual authorization – as has been the case to date – but rather according to the G-BA resolution for authorization groups. Here, it is essential that stakeholders (especially practitioners) are included at an early stage to define criteria for the selection and certification of treatment facilities.

Timeline and resource requirements
- Resources will be required to establish and support the National GCT Network (in line with Topic VI, Objective 1, Measure 1)

Success indicators

- The degree to which this structure influences the development, translation and application of GCTs in Germany can be determined by the number and quality of treatments performed with GCTs. This can be compared with historical numbers and data from other countries

Measure 2:
Streamline the processes necessary for qualification and certification to administer GCTs in treatment facilities

Stakeholders required:
Patients, practitioners, health insurance providers, pharmaceutical companies, Federal Joint Committee (G-BA)

Description:
The certification processes currently conducted by pharmaceutical companies (marketing authorization holders – MAHs) and the Medical Service (Medizinischer Dienst) should not focus solely on individual therapies and indications but on therapy groups, where possible. Treatment facilities should be able to obtain a qualification to administer treatments using individual therapies/for individual indications or for corresponding therapy groups. For the addition of new GCTs to the portfolio of treatment facilities, we propose the extension of current qualification processes to specifically focus on technical innovations.

Highly detailed regulations that increase the need for documentation in treatment facilities without demonstrating a noticeable impact on the quality of results should be avoided. Practitioners should be involved appropriately, for instance through collaborations with medical expert associations (e. g., committees on novel therapies) and with distributors possessing knowledge of the necessary infrastructure. The feasibility and necessity of regulations should be pragmatically reviewed on a regular basis by a committee consisting of different stakeholders.

If a facility successfully requalifies without notable issues, a reduction of follow-up inspections by the Medical Service could be employed (from annually to every two or three years). The topics and content of existing certification processes in treatment facilities that are already being certified in similar areas should be considered before each further certification procedure. The overall aim must be to reduce the frequency and redundancy of certification procedures.

Timeline and resource requirements

- Implementation could be achieved by expanding the scope of the QS-I conducted by the G-BA. The relevant stakeholders must be included into the process. Otherwise, no specific resources are required

Success indicators

- Certification procedures become significantly less time-consuming and resource-intensive within two years of the measure's implementation

Measure 3:
Streamline contract design procedures

Stakeholders required:
Practitioners, pharmaceutical companies, political stakeholders

Description:
Contracts concluded between distributors and treatment facilities (e. g., quality assurance contracts, supply agreements) both before and after marketing authorization, should not exclusively focus on individual therapies and indications but also on therapy groups, where possible. To simplify and accelerate new contracts, standardized model contracts and a standardized procedure should be introduced. These should be reviewed and amended on a regular basis by a committee made up of different stakeholders. The decision-making basis for the allocation of GCTs should be nationally standardized.

Timeline and resource requirements

- Establish and coordinate a working group of stakeholders to revise current model contracts
- This could be achieved by continuing Working Group VII in the National Strategy for GCTs. Otherwise, no specific resources are required.

Success indicators

- Certification procedures become significantly less time-consuming and resource-intensive within two years of the measure's implementation

Measure 4:
Ensure efficient assignment and communication between the personnel and institutions involved in treatment

Stakeholders required:
Federal Joint Committee (G-BA), healthcare service providers, patient advocacy groups

Description:
For treatments to be successful, excellent interaction between the doctor assigning a patient to a therapy and the doctor administering the treatment is crucial. Therefore, the following points must be considered:

- Ensure prompt diagnosis and assignment of patients to a GCT treatment facility, if necessary
- Avoid preliminary treatments that could impair the efficacy of other, potentially more effective therapies such as GCTs (see Objective 1, Measure 2 regarding therapy decision boards)
- Ensure treatment (e. g., using bridging therapy) and monitoring during disease progression or preparation of the GCT product
- Ensure follow-up care
- Ensure thorough documentation in patients' files and registers

These points should be incorporated into G-BA guidelines to ensure their implementation. Structures and processes must be established or optimized to simplify the flow of information between assigning doctors and treatment facilities. Processes and the distribution of responsibilities between GCT treatment facilities and assigning doctors (experts in disease entities and diagnostics) must always be clearly defined. In addition to the bi-directional exchange of information and data (ideally digitally), it is also important to ensure and facilitate patient mobility between GCT treatment facilities and the assigning doctors. Perhaps, this can include a simplified method to cover travel expenses and overnight stays for patients and possibly an accompanying person.

Timeline and resource requirements
- Resources are needed to establish, optimize and operate digital communication platforms that are data protection-compliant to ensure an efficient exchange of information between assigning doctors and GCT treatment facilities
- These communication platforms can be established by GCT treatment facilities, in cooperation with assigning doctors
- Additional resources for board meetings and register documentation are discussed elsewhere in this document

Success indicators
- Patient satisfaction regarding their interactions with their treating doctors and relevant institutions
- Evaluation of the proportion of patients who receive indicated GCTs and the time between diagnosis and GCT treatment

Objective 4:
Optimize and establish the data landscape to ensure the versatile usability of this data in research and facilitate long-term GCT data tracking

Explanation:
This goal aims to enable evidence generation for efficacy and safety of GCTs, which is initiated as soon as a new GCT enters the market and is then continuous implemented in an integrated approach ("evidence available at the touch of a button"). The necessary conditions must therefore be created to facilitate systematic acquisition and storage as well as controlled access to semantically and syntactically interoperable datasets.

Measure 1:
Standardize the acquisition and storage of treatment data

Stakeholders required:
Data access and coordination office – as specified in the recently adopted Health Data Use Act (GDNG) – located at the BfArM, Federal Joint Committee (G-BA), GCT treatment facilities, National Network Office, federal higher authorities, register representatives

Description:
Existing data infrastructure must be updated to ensure the quality-assured acquisition and storage of GCT treatment data in the long term. For this, developments at the European (e. g., European Health Data Space – EHDS) and national (e. g., National Research Data Infrastructure – NFDI) levels must be considered. We propose the following specific measures:

- Expand the authority of the central data access and coordination office, which is proposed in the Health Data Use Act (GDNG) to include GCT products. The PEI and relevant treatment facilities or respective representatives have to be involved in the necessary discussions and decisions.
- Develop a data access and usage charter for GCTs, which integrates the Research Data Centre – Health (FZD Gesundheit), register operators and expert associations. We propose altruistic register operator models with "neutral" data custody and management, e. g., through a coalition of academic expert associations or in cooperation with federal higher authorities.
- In the future, the gold standard for the collection of post-marketing data in the context of GCT administration should be registers that are disease- and sub-modality-specific (e. g., cell therapies). However, standardized requirements for data models and for the registers' minimum technical equipment should be developed and continuously updated in line with national/European developments (e. g., by the data access committee created in accordance with the Health Data Use Act (GDNG)). The aim is an increasingly automated data collection.
- Establish a standardized testing and possibly a certification process to facilitate the transparent examination of register standards during the Quality Assurance I (QS-I) meeting. This examination should be done by the G-BA or the Institute for Quality and Efficiency in Healthcare (IQWiG). In the future, this can serve as the basis for te decision prior to marketing authorization, whether there are sufficiently qualified

and interoperable registers or whether post-marketing data collection should occur via through the GCT umbrella register instead (see Figure 3).
- Establish a standardized advisory and examination process to determine the data and evidence for non-authorizable GCTs that must be collected to be reimbursable (e. g., in accordance with the Nikolaus decision | 1 BvR 347/98). This process should be jointly established and implemented by the IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; Institute for Quality and Efficiency in Health Care) and academic developers.

Timeline and resource requirements

- Financing: The establishment and long-term operation of register structures entail constant expenses and require the necessary refinancing to cover these costs. Given that post-marketing data on GCT administration is relevant in the context of health policy as well as economically, we recommend refinancing ongoing register costs from public-sector budgets in the future. Alternatively, the expenses could be refinanced from statutory health insurance funds. We propose separating this refinancing into the two main types of occurring costs:
  - The costs of data entry and validation by GCT treatment facilities as part of new overall fees for GCTs by health insurance providers (new legal regulations required; see Objective 2, Measure 6 regarding reimbursement of healthcare costs)
  - Refinancing of running costs for involved registers and the new GCT umbrella register. Proposal: Financing via resources from public funds, which are provided for this purpose.
- It is also expedient and necessary to substantively involve the affected pharmaceutical companies. Additionally, the precise conditions and potential financial contribution from these companies could be discussed, possibly during the Quality Assurance I (QS-I) meeting, proposed above.
- Register experience and data expertise: Representatives from academic medicine with long-standing experience in establishing and/or operating corresponding register solutions should be included and consulted while implementing the specified measures. Ideally, the altruistic operator models should be managed independently.

Success indicators

- The success and long-term development of the specified measures should be monitored and evaluated on an ongoing basis, e. g., through the Research Data Centre (FDZ) or an independent evaluation institution
- Indicators are an increase in lasting data quality, the number of interoperable registers, and the satisfaction of healthcare service providers and patients with remote data acquisition. We recommend conducting a health economic evaluation regarding the success of cost-covering refinancing of data entry by healthcare insurance providers and/or register operators.

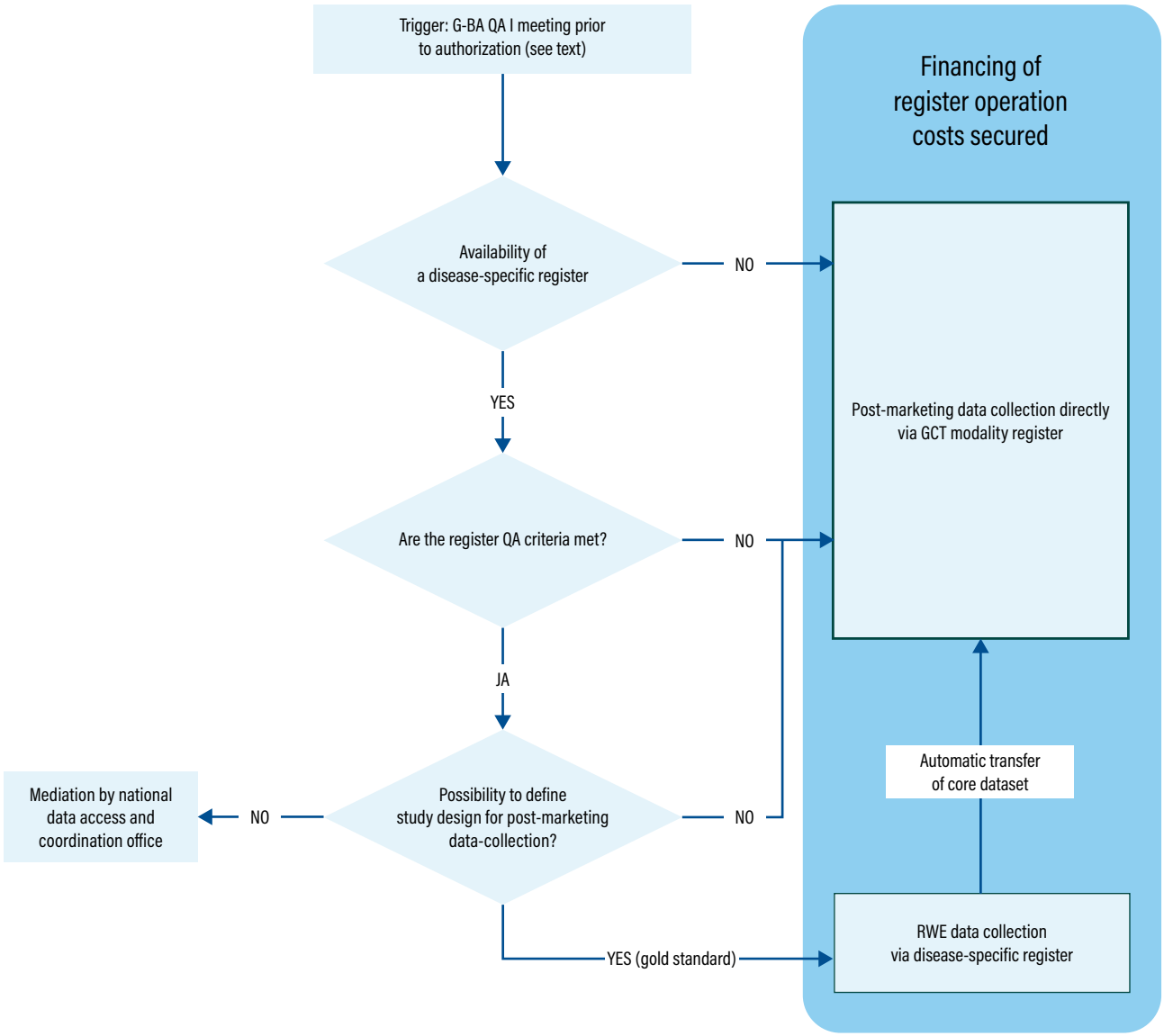


Figure 3: **National GCT register (with submitted authorization application)**. Proposal for an algorithm for collection and integration of data in a central GCT therapy modality register (to be established) to implement qualified post-marketing studies in Germany.
(Case 1: GCT therapeutic with submitted authorization application)

Measure 2:
Establish a method-specific national GCT register

Stakeholders required:
Federal Joint Committee (G-BA), INTEGRATE-ATMP consortium, various expert associations, Technology, Methods, and Infrastructure for Networked Medical Research (Technologie- und Methodenplattform für die vernetzte medizinische Forschung, TMF), National Network Office

Description:
In addition, and complementary to the previously described gold standard for disease-specific and sub-modality-specific register data acquisition, we recommend establishing a national GCT register as a modality register. Models and blueprints have already been developed. This should explicitly include application of the hospital exemption, which is regulated in the EU and in Germany (under Section 4b AMG) for specific procedures. In organizational terms, it could take the form of a registered association (*eingetragener Verein* – e. V.) or a non-profit company with limited liability (*gemeinnützige Gesellschaft mit beschränkter Haftung* – gGmbH). Potential benefits of such a method-specific meta-register include:

- Usability for overview projects on methods as well as for economic aspects (e. g., international benchmarking, etc.)
- Identification of overarching class effects on the efficacy and/or safety of different products, e. g., T-cell lymphoma risk in the use of CAR T-cell products, AAV safety class effects, safety and efficacy of n-of-few/n-of-1 antisense oligonucleotide (ASO)
- Transparency of GCT use in healthcare practice, across all treatment facilities and diseases
- Quality assurance: Avoidance of excessive fragmentation of the register landscape, as individual registers must be subject to ongoing quality and suitability reviews
- Prevention of reporting bias (so-called "black holes") that could develop in monocentric register systems
- Particularly in the case of hospital exemptions: The data from these applications should also be recognized by the federal higher authorities and the EMA as the basis for the design and implementation of clinical studies

In terms of its content, the new GCT modality register should comprise two key areas of data:

- Meta core data on the post-marketing use of GCTs in Germany: In the future, these datasets must be submitted from disease-specific and sub-modality-specific registers on a mandatory and automated basis (ensuring interoperability). This will help to automatically comply with European requirements of registers for post-authorization efficacy studies (PAES) and post-authorization safety studies (PASS). This explicitly includes developments in GCT application in individual cases outside of standard marketing authorization-oriented development paths (Figure 4). The core dataset should be developed and continuously updated by academic treatment facilities and the responsible federal higher authorities. For this purpose, digital platforms must be expanded and supported, incorporating datasets from different sources.
- Data for potential post-marketing studies: This area substitutes for disease-specific and sub-modality-specific registers in case such registers do not exist or are not suitable for post-marketing studies in terms of their content or technical features.

Timeline and resource requirements
- A sustainable and altruistic operator structure for a long-term GCT meta-register should be established and consolidated (see above; already in progress, next steps should build on this). The reimbursement logic described above should be embedded in this structure. In this context, we recommend establishing a transparent governing committee, combining academic treatment facilities, the federal higher authority, the-BA, the National Association of Statutory Health Insurance Funds (GKV-Spitzenverband), pharmaceutical manufacturers' associations, existing register operators (e. g., German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST), European Society for Blood and Marrow Transplantation (EBMT), etc.) and political representatives.
- Implementation could be achieved in the short term through the following project proposal: In a model project, the existing, publicly funded ATMP register should be made data-interoperable with other GCT-disease (group)-specific registers and subsequently be supplied with a modality-specific core dataset. This would include the DRST and EBMT sub-modality registers along with digital remote recording of patient-centered outcomes through a complementary telemedicine healthcare platform. The aim would be to continue developing the umbrella register model outlined above as well as the accompanying platform for GCTs. Specific registers to be connected could include the hemophilia register and/or the Pediatric Register for Stem Cell Transplantation (PRST) along with other suitable ones. (Project timeframe: 2 years. Timeline: as soon as possible. Financial estimate: approx. €2 million).

Success indicators

- Short term: Successful establishment of an altruistic operator structure and method-specific core dataset
- Medium term: It is reasonable and necessary to outline and employ key benchmarking indicators, e. g., number of patients treated and number of treatment facilities, along with success indicators such as individual and patient-centered clinical outcomes at a national and international level.

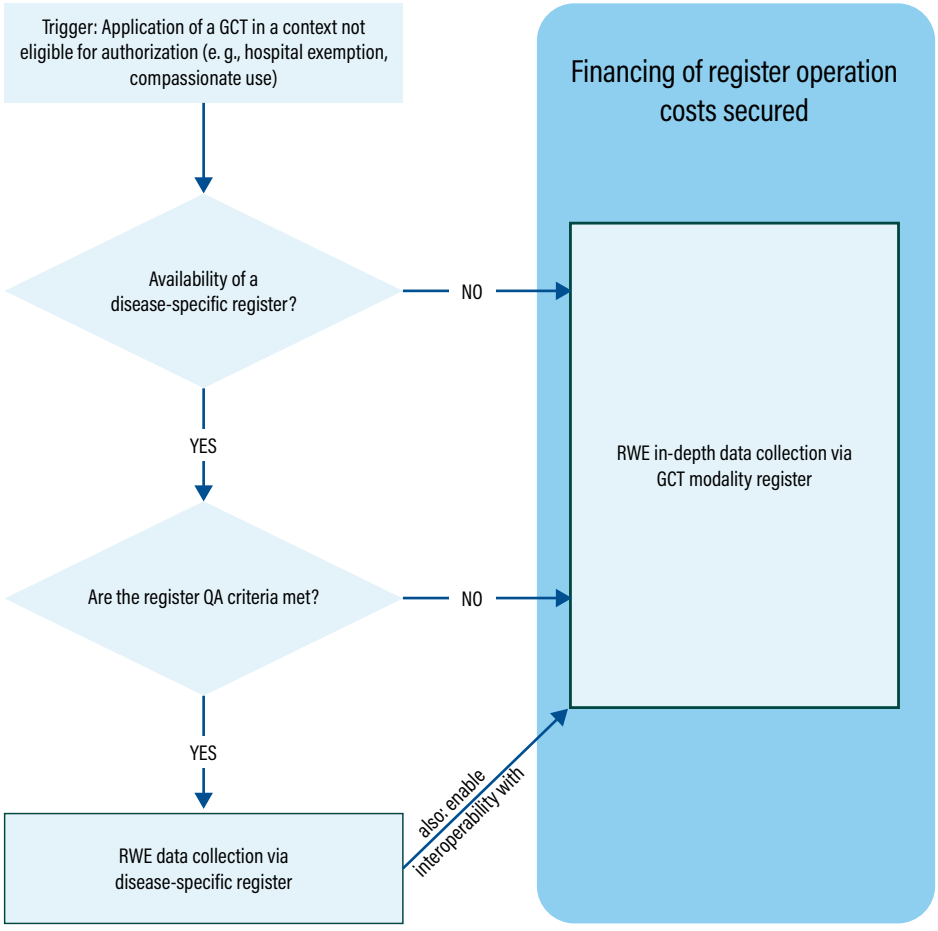
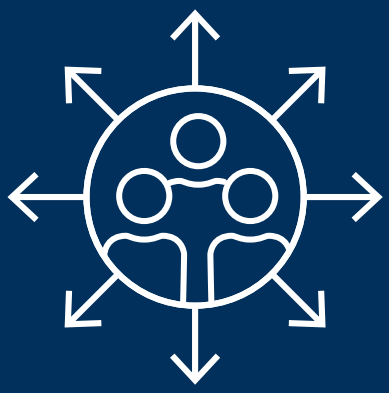


Figure 4: **National GCT register (without expected authorization).** Proposal for an algorithm for collection and integration of data in a central GCT therapy modality register (to be established) for products not expected to obtain authorization. (Case 2: GCT not eligible for authorization)

Topic VIII: Interaction with society



Summary

The developments in the field of GCTs continues to be dynamic with particularly high needs regarding engagement with different target groups and stakeholders in society – both today and for the foreseeable future. We have therefore defined the following **objectives** for Topic VIII:

- **Inform society about GCTs** by providing reliable, target group-specific information
- Support/advise decision-makers by **strengthening engagement with politics** as well as initiating/maintaining an open-ended humanistic/social discourse
- **Implement targeted measures to promote the potential benefits of GCTs** through intensified involvement and participation of research funding organizations, foundations and parts of civil society willing to donate

Achieving these targets will require a lasting governance structure from the National Strategy and should attract widespread public attention using visible and credible ambassadors. The following **measures and resources** will therefore be required in the short to medium term:

- Establishment of a **central communication platform** with an online presence to provide information for different relevant target groups. **Target group-specific services** should be compiled and created for the general public, as well as specific offers for media/journalists, patients and patients' organizations, medical expert associations, pupils, students and teachers. All should be available via a single platform.
- Regular reports should be made in relevant committees (i. e. science, health, economy) to support long-term **engagement with political stakeholders** and the provision of **information for parliamentarians** (at federal and state levels). As part of a **discourse with wider society**, an open-ended human discussion should be promoted and reviewed with all stakeholders in society.
- Appropriate **research funding organizations, foundations and supportive private individuals** should be **identified**, provided with specific information material to organize high-profile public events that will encourage donation to raise additional funding.

The measures listed here interlink synergistically and are based on the stakeholders in this topic interacting closely with the National Network Office. Implementing these measures will require personnel at the National Network Office (information/political engagement/social discourse), project funding for short-term agency contracts (research, graphics, events) and networking funding to help stakeholders in the GCT network interact with the specified groups in society. We estimate annual funding requirements in the six-digit euro-range, depending on the intensity of these interactions.

1

Inform society about GCTs by providing reliable, target group-specific information

2

Support/advise decision-makers by strengthening engagement with politics and facilitating/ maintaining an open-ended humanistic/social discourse

3

Implement targeted measures to promote the potential benefits of GCTs through increased involvement and participation of research funding organizations, foundations and parts of civil society willing to donate

Background

In recent years, GCT has evolved into a very dynamic field. While this previously focused on treatments for severe and rare monogenetic diseases, their range of applications has since expanded from oncological diseases to more widespread conditions. As a result, the development and authorization of new therapeutics is increasingly relevant to growing proportions of society. Local centers have already been established at several sites across Germany, bringing translational aspects of modern GCTs to clinical practice. Regarding engagement with society, various initiatives have already been launched with the aim of introducing the scientific principles, opportunities, risks, limitations and social implications of the use of GCTs into public discourse. At present, these initiatives are not particularly well connected and this is especially the case with the perception of new knowledge. A notable example was knowledge gained during the COVID-19 pandemic, which underlined the importance of new scientific insights being presented in generally comprehensible terms. Furthermore, scientists and other communicators explaining these insights (e. g., public figures from the healthcare sector) have to be perceived as highly credible. These are key factors in helping to shape public opinion in a pluralistic society by providing balanced information. The problem, however, is that sensational reports, alleged scandals and polarized disputes between scientists generate many times more (media) interest than solid, factual, scientific content.

Our knowledge of GCTs is constantly increasing. Therefore, a long-term communication strategy is required – from the education system to specialist institutions to the general public – to provide society with comprehensive, up-to-date and trustworthy information in the field of GCTs. This strategy should be developed with input from all relevant stakeholder groups. There is an urgent need for measures that make it possible to provide balanced information for broad sections of society and facilitate continuous humanistic and social scientific support regarding current developments. Also important are measures that connect and expand local activities (e. g., in engagement with schools) to spark the interest of new aspects of GCT in as many pupils as possible and provide them with knowledge of GCTs.

Existing structures (e. g., expert associations and network associations) are not sufficiently equipped to conduct all public relations work necessary to support the National Strategy. Nevertheless, it will be essential to involve and leverage existing structures in subsequent processes and make use of their experience regarding strategic interaction between stakeholders from the fields of research, development and clinical trials with society as a whole.

Objectives

1. Inform society about GCTs by providing reliable, target group-specific information
2. Support/advise decision-makers by strengthening engagement with politics and facilitating/maintaining an open-ended humanistic/social discourse
3. Implement targeted measures to promote the potential benefits of GCTs through increased involvement and participation of research funding organizations, foundations and parts of civil society willing to donate

Objective 1:
Inform society about GCTs by providing reliable, target group-specific information

Explanation:
It is important to provide well-founded, reliable, generally comprehensible information for different target groups and stakeholders in society. In addition to specific content for patients, information should also be compiled for political stakeholders, the media, funding providers and expert associations. Furthermore, tried-and-tested information and teaching materials should be made available for large sections of education, targeting both adolescents and adults (e. g., upper secondary education), study programs (e. g., medicine, biology and biotechnology). Content should also be incorporated into tertiary education curriculums and training curriculums in health-related professions, including learning platforms and formats involving citizen science and, if appropriate, media partners. In this context, it will be particularly important to consider, incorporate and use existing materials.

Measure 1:
Establish a central communication platform with an online presence to provide information for different relevant target groups

Stakeholders required:
Coordination by National Network Office in conjunction with WG VIII

Description:
A central website must be created and maintained as a central starting point. This website can provide different types of information, which must either be compiled from existing sources and/or created prior to publication. Existing information materials should be identified and a collaboration with their providers should be established where possible. The following key aspects must be considered and tailored to the respective target groups:

- Clear messages: Develop concise, readily comprehensible messages that illustrate the efficacy, risks and ethical aspects of GCTs. Compare with symptomatic treatment approaches. Avoid, or clearly explain, technical terminologies and focus on generally comprehensible language.
- Scientific education: Convey fundamental information about GCTs and their areas of application, including an emphasis on the scientific background.
- Use international case studies: Specific case studies that clearly illustrate the use of GCTs, taking due account of the opportunities and risks they present. If appropriate, quantify the chances of success in relation to the risks.
- Co-create the structure and content of this information with relevant stakeholders (i. e. patient advocacy groups, scientists and communication experts).
- Integrate a survey tool on patients' experiences (using their experiences and expectations as quality indicators).

Timeline and resource requirements
- Short term (12–18 months)
- Resource requirements must be discussed with a communication agency; funding may also be required for long-term projects

Success indicators
- Website developed through a co-creative process and launched
- Editorial board appointed to contintue to develop content
- Number of unique visitors (with an annual target TBD)
- Engagement level (i. e. sharing on social media)

Measure 2:
Create or refer to target group-specific information resources for the general public

Stakeholders required:
Coordination by National Network Office in conjunction with WG VIII

Description:
Interactive formats and dialog: Using different media formats – i. e. infographics, webinars, etc. – to make complex information more comprehensible. Experts should be involved into communication activities to foster a dialog with the general public and answer questions.

Timeline and resource requirements
- Short term (12–18 months), continuous process
- Travel costs

Success indicators
- A staff member of the National Network Office has begun to coordinate this work
- Pool of experts is assembled and engaged in this project

Measure 3:
Create or refer to target group-specific information resources for media representatives/journalists

Stakeholders required:
Coordination by National Network Office in conjunction with WG VIII

Description:
Using the media as multipliers: Targeted collaboration – e. g., with media representatives, journalists and communicators – to promote balanced, transparent and factual reporting. Provision of precise information via press releases, interviews and background information. Network of experts for interviews: Establish a network of experts comprising subject matter experts and patients' advocates, who stand by for interviews and informal discussions. This will promote high-quality reporting and enable journalists to better understand complex topics. Press conferences: Organization of press conferences to give journalists direct access to experts, researchers and patients' advocates. Informal discussions and exclusive insights: Offer informal discussions and exclusive insights for journalists to facilitate more comprehensive reporting. Media collaborations and guest essays: Engage with media companies (specialist media, mass media, etc.) to arrange guest essays by experts and researchers on the topic of GCTs. Press releases and background information: Regularly publish press releases and supply background information to provide journalists with up-to-date and well-founded facts about GCTs. Establish a board of speakers (i. e. subject experts, patient experts) which is available for a range of formats (e. g., talks, presentations, interviews, talk shows, guest essays, etc.).

Timeline and resource requirements
- Short term (12 months)
- Low resource requirements

Success indicators
- Creation of an information services concept
- Establishment of a board of speakers
- Number of contributions per month

Measure 4:
Create or refer to target group-specific information resources for patients and patients' organizations

Stakeholders required:
Coordination by National Network Office in conjunction with WG VIII

Description:
Navigated access to easy-to-locate, transparent, comprehensive, patient-centered and evidence-based information regarding potential therapies. Corresponding information also include the possible side effects and success rates as well as directions for a subsequent course of action for patients (e. g., potential ways to access clinical studies, advice and support services, etc.). In this context, it is critical to identify patients' organizations that are willing to collaborate on and co-create these information services. A collaboration model will be developed that clearly defines processes, ensures the independence of all participating stakeholders, and provides full transparency regarding the contributors and their contributions.

Timeline and resource requirements
- Medium term (approx. 18–24 months) for 2–3 exemplary diseases

Success indicators
- Identification of partner patients' organizations
- Development of code of conduct/framework of rules
- Navigation system developed
- Corresponding materials created (perhaps in the context of BMFTR-funded projects)
- Collaboration opportunities with the Federal Institute for Prevention and Education in Medicine (BIPAM) have been examined

Measure 5:
Create or refer to target group-specific information resources for pupils, students and teachers

Stakeholders required:
Coordination by National Network Office in conjunction with WG VIII

Description:
Establish a multidisciplinary editorial board with teaching staff from lower and upper secondary education levels (representatives from the following subject areas could be included: biology, chemistry, German, ethics/religion, English) and, if appropriate, representatives of educational textbook publishers. Develop competency-frameworks tailored to each school level. Develop digital guidelines for teaching staff, referring to existing materials. Distribute this competency-framework using suitable channels.

Timeline and resource requirements
- Medium term (18–24 months)
- Fees/expenses as required for development of the guidelines

Success indicators
- Establishment of a multidisciplinary editorial board
- Development of a GCT competency framework
- Guidelines for teachers are developed
- Materials made available in a central information platform
- Number of visits per year
- Examples for GCT applications are used in teaching and made available on the information platform

Measure 6:
Create or refer to target group-specific information resources for medical expert associations

Stakeholders required:
Coordination by National Network Office in conjunction with WG VIII

Description:
Create an overview of patients' organizations, focusing on diseases for which GCTs are particularly relevant in the near future (e. g., oncological diseases, rare genetic diseases). Connecting with European and international structures. Offer to organize symposiums for congresses. Create and distribute exhibition/information material for "patients' information days" and similar events.

Timeline and resource requirements
- Medium term (18–24 months)
- Costs for coordination/agency

Success indicators
- Overview provided on website
- Letters of support signed with a specified number of European and international structures

Measure 7:
Offer a regular newsletter for patients/ organizations/expert associations on relevant GCT publications and activities

Stakeholders required:
Coordination by National Network Office in conjunction with WG VIII

Description:
Make use of the overview of relevant patients' organizations. Collaborate with patients' advocates to develop content to convey the potential benefits of GCT research. The focus has to be to communicate the needs of people living with a serious illness in a comprehensible manner and from the patients' perspective.

Timeline and resource requirements
- Short term (12-16 months)

Success indicators
- Completion of mapping of relevant patients' organizations
- Assembly of co-creation group with patient advocacy groups
- Creation and publication of first newsletter
- Number of subscriptions, engagement level (e. g., social media posts) and degree to which newsletter content is used in media (incl. media published by patients' organizations)

Objective 2:
Support/advise decision-makers by strengthening engagement with politics and facilitating/maintaining an open-ended humanistic/social discourse

Explanation:
Article 2 of the German Basic Law (GG) states that every citizen has the right of life and physical integrity. Section 12 of the German Social Insurance Code, Book V (SGB B) gives insured persons a comprehensive and extensive promise of healthcare where economically reasonable. This also applies to life-threatening and terminal diseases, for which new GCTs offer the prospect of a cure, or a substantial improvement in the progression of a patient's disease. This leads to challenges for politicians and decision-makers in society regarding the implementation of these new GCTs in standard healthcare. Those challenges will need to be resolved.

The normative and regulatory framework for these new GCTs will be the result of discussions with society as a whole, which serve as the basis for political decisions. Regional, state and federal political aspects must be considered in this context, ensuring interaction between all three levels. In terms of ethical, legal and social aspects (ELSAs), structured concomitant research and continuous political dialog should be established to integrate current aspects of genome-based medicine and reflect them in political decision-making and regulatory affairs.

For this reason, it is important to inform and engage with parliamentarians, ministries, (federal and state) authorities and decision-makers in society regarding

the promise of healthcare set out in the Basic Law (GG) and Social Insurance Code (SGB) in terms of new GCTs – with the aim of creating a healthcare landscape in Germany that does justice to this promise.

This will require political stakeholders to create the necessary legal conditions, such as standardizing regulatory frameworks concerning GCTs at federal and state levels, updating the German Stem Cell Act (StZG), establishing reliable reimbursement structures and expanding manufacturing capacities for GCTs in Germany. An open-ended discussion must therefore be facilitated within the well-informed section of the public to achieve the broadest possible consensus within society and with decision-makers in society.

Measure 1:
Improve the targeted communication of information to political stakeholders

Stakeholders required:
Moderation through the governance structure of the National Strategy and/or the National Network Office in conjunction with WG VIII, scientists, relevant politicians at state and federal level in Ministries of Science, Health and for Economic Affairs (i. e. ministers, state secretaries, levels of parliamentarians)

Description:
Establishment of long-term engagement and exchange of information with policymakers and parliamentarians (at federal and state levels), by submitting regular reports to committees (science, health, economy). A secondary option is for interaction formats such as "parliamentary evening" events to be organized. For the exchange, strategic key topics should be addressed and recommendations for action developed.

Credible ambassadors with a strong reputation must be identified and recruited to facilitate this interaction (potentially drafted from experts who developed the National Strategy and, for example, integrating patient advocacy groups). Additionally, the following measures also need to be implemented:

- Creation of white papers and the involvement of the German Gene Technology Report (https://www.gentechnologiebericht.de) as a measure for monitoring and information
- Address concerns regarding advanced scientific research at public events (e. g., gene manipulation, ESC, viral transfer, CRISPR/Cas, enhancement)
- Provide a well-founded view of successes, including a reflection on failures in advanced scientific research
- Emphasize the importance of advanced scientific research for Germany as a location for business
- Integrate politicians into scientific conferences (e. g., in panel discussions)
- Offer regional information events, with attendance of politicians

Timeline and resource requirements
- Short to medium term (1-3 years)

Success indicators
- Number of events in which politicians attend

Measure 2:
Establish/maintain an open-ended humanistic/social discourse

Stakeholders required:
Moderation through the governance structure of the National Strategy and or the National Network Office in conjunction with WG VIII

Description:
Both branches of science – natural and social – face the challenge of deploying their respective skills to engage with a very specific, highly technical and thoroughly complex field that also features demanding ethical, legal and social aspects. The following measures should therefore be implemented to affix the current state of knowledge and related ethical implications in discussions within society as a whole:

- Research programs that simultaneously consider humanistic, ethical and technical aspects (ELSA projects), which are supported through specific funding mechanisms, e. g., via the BMFTR or the DFG (such as accompanying research integrated into current calls for research consortia in the field of GCTs)
- Fellowships or similar programs for direct exchange/interaction with humanities scientists at GCT institutes, taking the form of sabbatical/visiting fellow positions for a sufficient period to facilitate substantive and long-term interaction. Where possible, this should culminate in a joint publication

- Interaction with Leopoldina and state academies on GCTs along with ethics institutes, university chairs in the field of medicine and bioethics, academies run by churches and religious communities, and contributions to position papers regarding the field of GCTs

Timeline and resource requirements

- Medium term (18–24 months)
- Project funding
- Travel costs

Success indicators

- Projects are launched; publication of initial results
- A defined number of fellowships awarded
- Publication of a defined number of articles/papers/etc.

Objective 3:
Implement targeted measures to promote the potential benefits of GCTs through increased involvement and participation of research funding organizations, foundations and parts of civil society willing to donate

Explanation:
Public research funding organizations, foundations and individuals willing to donate have identified the need to provide increased support for research and development in the field of GCTs and are intensifying their support.

Measure 1:
Identify and map research funding organizations, foundations and private donors

Stakeholders required:
Moderation through the governance structure of the National Strategy and/or the National Network Office in conjunction with WG VIII

Description:
As potential funding providers and supporters are not a homogeneous group, they must be addressed through communication depending on the specific target group. Potential funding organizations and private donors interested (or potentially interested) in the development of GCTs and/or the transfer of knowledge into society should be identified and mapped in a database according to their thematic/regional focus areas. This will provide a foundation for effective engagement with them.

Timeline and resource requirements

- Short term (1 year): Analysis of international and national examples, e. g., the Telethon Foundation and compilation of a list/database of potential private donors and supporters in Germany. Establish contact with them and determine the kind of information that is relevant for them regarding the National Strategy
- Medium term (2–3 years): Implementation of targeted events for foundations and private donors, exploration of opportunities for PPPs, e. g., establishment of a special fund for GCTs, and initiation of funding alliances for GCT development (following the example of vaccine alliances)
- Long term/continuous (5 years): Information for interested funding organizations, foundations and private donors regarding the current state of science in the field of GCTs

Success indicators

Level of total public and private funding for the National Strategy and for individual GCT measures and projects (both central and regional)

Measure 2:
Develop specific information material for foundations and private donors willing to contribute and organize high-profile events to attract donations by securing funding specifically dedicated to knowledge transfer

Stakeholders required:
Moderation through the governance structure of the National Strategy and or the National Network Office in conjunction with WG VIII, scientists, media experts, journalists, academics

Description:

Establish a continuous knowledge transfer with different and specifically targeted formats to secure funding from foundations and private donors willing to contribute.

Timeline and resource requirements

- Short term (1 year): Creation of tailored information materials for foundations and private donors willing to contribute
- Medium term (2–3 years): Based on mapping of potential funding providers and foundations, and focusing on knowledge transfer in particular, specific support should be acquired from relevant foundations to create information materials on GCTs. Specific funding (e. g., from regional foundations with a focus on social cohesion) should be used, for target groups with specific information needs (e. g., people with reservations regarding the prevention and treatment of diseases, and educationally disadvantaged groups).
- Medium to long term (3–5 years): Organize high-profile events to raise awareness and secure donations (e. g., via telethons, "Ein Herz für Kinder" events, etc.)

Success indicators

- Level of funding
- Extend of knowledge transfer

Measure 3:
Strengthen established and/or planned funding measures and their synergistic development together with foundations and private donors willing to contribute

Stakeholders required:
Moderation through the governance structure of the National Strategy and or the National Network Office in conjunction with WG VIII, research funding organizations

Description:

In the context of implementing the National Strategy, specific support should be given for measures to develop synergies with existing funding measures for GCTs (e. g., implemented by the German Centers for Health Research (DZG), regional centers, etc.) with foundations and/or private donors willing to contribute, e. g., through matching funds.

Timeline and resource requirements

- Short term (1 year): Mapping of existing regional structures in the field of GCTs with description of focus areas and capacities. Afterwards, it should be determined which foundations and sponsors have specific regional and/or thematic focus areas to potentially connect with them. It will also be important to actively engage with new foundations with relevant missions at the regional level regarding existing funding measures and structures.
- Long term (5 years): Establishment of a network of foundations/sponsors and GCT research institutes

Success indicators

- Number and scope of funding measures and collaborations between institutions and foundations
- Establishment of networks and collaboration projects

Overview: Objectives and measures

Topic	Objective	Measure
I Stakeholder networking and support	1) Ensure coordinated implementation of measures in the National Strategy	1) Establish a governance structure to implement the National Strategy
	2) Strengthen political accountability for GCTs – a key topic for the nation's future	1) Prepare an annual progress report on the National Strategy for GCTs
		2) Implement intra-annual measures to convey successes of the national network for GCTs to political stakeholders at federal and state level
		3) Organize information events for policymakers at innovation locations
		4) Establish and maintain contact with German representatives on EU bodies and committees
	3) Strengthen national networking structures	1) Establish a central point of contact (GCT website) with structured information about all stakeholders
		2) Design and compile a national GCT map depicting relevant stakeholders, structures and other parties, along with their functional interactions
		3) Conduct analysis of network components and the links between them, plus subsequent SWOT analysis
		4) Raise profile of GCT network-related issues in the national science community; organize network events
	4) Establish and expand national and international networking activities	1) Provide information for national and international patient advocacy groups
		2) Provide information for patients
		3) Provide information for international/European clinical research groups
		4) Establish an exchange of information with national and international regulators
		5) Appeal to national and international investors and funding providerss
		6) Exchange and cooperate with public-private partnership (PPP) initiatives, especially the EU's Innovative Medicines Initiative (IMI)
		7) Provide targeted information for scientific organizations and associations
		8) Raise the profile of the GCT initiative at international scientific congresses
		9) Establish an exchange of information with medical service providers and health insurance funds
		10) Integrate international entities into the GCT value chain
II Training and development of skills	1) Establish training and development programs for early career professionals and specialists, and improve the necessary infrastructure for training and development	1) Create and implement a concept for multi-track, modular additional training
		2) Establish extra-occupational, interdisciplinary Master's and doctoral programs at universities and universities of applied science (FHs) along with training programs for all occupational groups in the field of GCTs
		3) Establish national GCT education and training centers to strengthen academic, non-academic and industrial skills
	2) Develop adequate career concepts, bonus concepts and interaction concepts	1) Create incentive systems, bonus systems and career concepts
		2) Develop an interaction concept to support training and career development for relevant stakeholders

Topic	Objective	Measure
III Technology transfer	1) Improve the framework for early identification and utilization of innovative potential of scientific results	1) Education, training and development
		2) Strengthen technology transfer offices (TTOs)
		3) Establish structures for the targeted implementation and market preparation of GCT projects
	2) Ensure comprehensive consultancy and assessment of transfer projects, incorporating the entire development process from production of an IMP to its use in patient care	1) Establish a product development unit (PDU) to support project planning and implementation
		2) Create and operate jointly accessible infrastructure for GCT developers
	3) Facilitate efforts to exploit the social and/or economic potential of scientific results	1) (non-GCT-specific): Develop national guidelines for transparent spin-off standards, e. g., based on the USIT Guide
		2) (GCT-specific): Clarify and improve the framework so that start-ups in the initial phase can use existing infrastructure at their (parent) research institute, especially cost-intensive GMP infrastructure
		3) (GCT-specific): Conduct patent research and analysis for a small number of select and definitive key technologies
	4) Establish recognition of transfer activities and successes in translation as part of individual researchers' and institutions' scientific reputations	1) Optimize academic incentive systems and project-specific employment conditions for qualified staff members
		2) Communicate technology transfer success stories
		3) Make transfer activities a quality criterion for research institutions
IV Standards, norms and regulatory framework conditions	1) Defragment and standardize responsibilities and processes in the clinical research and development of GCTs, and strengthen the federal higher authority and its resources as a single point of contact	1) Implement uniform standards and processes for issuing a manufacturing authorization, particularly in the context of GCTs and their starting materials and active ingredients, by adjusting the allocation of responsibilities between local authorities and the Paul-Ehrlich Institute (PEI)
		2) Strengthen the PEI with sufficient resources
		3) Consolidate and integrate the different approvals processes for the development of medical devices and in vitro diagnostics, including their software, into the existing application and authorization procedure for clinical trials on medicinal products in accordance with Regulation (EU) No 536/2014 (CTR) and the central authorization process set out in Regulation (EC) No 726/2004
	2) Continuously adapt regulatory processes to developments in the field of GCTs	1) Establish a central GCT-GMP and regulatory affairs committee
		2) Extend master file systems to GCTs
		3) Develop and introduce a regulatory "sandbox"
		4a) Foster an open-ended discussion on the current ATMP definition and relevant regulatory pathways for adoptive cell therapies with genetically modified cells (e. g., CAR-T-cell therapy)
		4b) Reform of the German Stem Cell Act (StZG)
		5) Establish a register for hospital exemptions to increase transparency and success measurement
	3) Improve the availability of low-threshold regulatory advice	1) Establish a low-threshold regulatory advice service

Topic	Objective	Measure
V Quality and capacity of GMP production	1) Promote the establishment and expansion of qualified GMP infrastructure (manufacturing and quality control capacities) in line with demand, for starting materials and complex GCT products	1) Create a central GCT-GMP and regulatory affairs committee
		2) Collect data on academic and commercial GMP infrastructure that already exists, is being planned or is under construction in Germany. Compare this against data for Europe and determine the need for GMP infrastructure for GCT manufacturing and quality control
		3) Secure sufficient funding from the federal government, state governments and other providers to establish, expand, maintain and operate GMP infrastructure based on demand
		4) Create a central national production facility to manufacture critical starting materials for GCTs
	2) Secure the necessary staffing capacity and expertise for GCT manufacturing and quality control	1) Expand and professionalize education and training for qualified staff in all areas in GMP production of GCTs
		2) Improve the framework for employment to attract and retain qualified specialists in the field of GCTs
	3) Increase the efficiency and speed of manufacturing processes	1) Establish a clearly structured database with manufacturing-related information and documents that is accessible for all stakeholders
		2) Create a shared basis of knowledge and communication by utilizing repositories with standardized data storage and access
	4) Pursue continuous development and risk-based streamlining of framework conditions	1) Perform risk-based harmonization and streamlining of statutory and regulatory requirements for GMP-compliant manufacturing and control
VI Research and development	1) Improve the structural conditions for translational research and development	1) Establish a national GCT network with hubs
	1) Identify and promote topics for the future	1) Establish new, flexible funding formats, with a short lead time, which meet needs that are currently not given due consideration
	3) Improve the organizational and regulatory framework for pre-clinical and clinical GCT studies	1) Facilitate the implementation of GCT manufacturing processes and their translation into early clinical studies
		2) Promote acceptance of animal experimentation and encourage the realistic assessment of potential alternatives
		3) Measuring and publication of performance indicators for regulators and supervisory authorities
		4) Optimize and refine ethics committees
	4) Ensure that patients, patient advocacy groups and patients' associations are duly involved	1) Define standards for project budgets and remuneration for patient advocates
		2) Develop specific interaction concepts
	5) Foster a change in mentality and bolster bio-entrepreneurial spirit in the German GCT community	1) Foster the necessary shift in mentality regarding GCTs
		2) Offer natural scientists career prospects and positions as bio-entrepreneurs in the public sector

Topic	Objective	Measure
VII Marketing authorization and transition to patient care	1) Facilitate access to patients and their targeted selection for specific GCTs	1) Develop and implement education and advanced training programs to ensure optimal diagnostics to identify and stratify patients and to monitor courses of treatment for standard care facilities
		2) Establish interdisciplinary therapy decision boards as the gold standard in GCT diagnostics
		3) Create nationally harmonized qualification criteria and standards for GCT access diagnostics and monitoring of disease progression
	2) Increase flexibility of reimbursement and care models in the use of GCTs	1) Employ the best available evidence for the assessment of additional benefits
		2) Amend the criteria for consideration of medical care-related data in benefit assessments
		3) Substantiate benefit-based price-setting
		4) Increase the use of performance-based reimbursement models in central price negotiations
		5) Standardize and ensure cost coverage for diagnostics-related reimbursement
		6) Create more flexible reimbursement models in the financing of quality assurance/care
	3) Provide high-quality, safe and efficient treatment for patients with innovative therapies by establishing interdisciplinary GCT treatment facilities	1) Establish close structural interaction between research and healthcare
		2) Streamline the processes necessary for qualification and certification to administer GCTs in treatment facilities
		3) Streamline contract design procedures
		4) Ensure efficient assignment and communication between the personnel and institutions involved in treatment
	4) Optimize and establish the data landscape to ensure the versatile usability of this data in research and facilitate long-term GCT data	1) Standardize the acquisition and storage of treatment data
		2) Establish a method-specific national GCT register
VIII Interaction with society	1) Inform society about GCTs by providing reliable, target group-specific information	1) Establish a central communication platform with an online presence to provide information for different relevant target groups
		2) Create or refer to target group-specific information resources for the general public
		3) Create or refer to target group-specific information resources for media representatives/ journalists
		4) Create or refer to target group-specific information resources for patients and patients' organizations
		5) Create or refer to target group-specific information resources for pupils, students and teachers
		6) Create or refer to target group-specific information resources for medical expert associations
		7) Offer a regular newsletter for patients/organizations/expert associations on relevant GCT publications and activities
	2) Support/advise decision-makers by strengthening engagement with politics and facilitating/ maintaining an open-ended humanistic/social discourse	1) Improve the targeted communication of information to political stakeholders
		2) Establish/maintain an open-ended humanistic/social discourse
	3) Implement targeted measures to promote the potential benefits of GCTs through increased involvement and participation of research funding organizations, foundations and parts of civil society willing to donate	1) Identify and map research funding organizations, foundations and private donors
		2) Develop specific information material for foundations and private donors willing to contribute and organize high-profile events to attract donations by securing funding specifically dedicated to knowledge transfer
		3) Strengthen established and/or planned funding measures and their synergistic development together with foundations and private donors willing to contribute

List of Abbreviations

5qSMA	spinal muscular atrophy on chromosome 5
AABB	Association for the Advancement of Blood and Biotherapies
AAV	adeno-associated virus
AI	artificial intelligence
ACHSE	Allianz Chronischer Seltener Erkrankungen / Alliance of Chronic Rare Diseases
WG	working group
AMG	Arzneimittelgesetz / Medicinal Products Act
AMNOG	Arzneimittelmarktneuordnungsgesetz / Act on the Reform of the Market for Medicinal Products
AMWHV	Arzneimittel- und Wirkstoffherstellungsverordnung / Manufacture of Medicinal Products and Active Substances Regulation
AM-NutzenV	Arzneimittel-Nutzenbewertungsverordnung / Medicinal Product Benefit Assessment Regulation
ATMP	advanced therapy medicinal products
BÄK	Bundesärztekammer / German Medical Association
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte / Federal Institute for Drugs and Medical Devices
BMBF	Bundesministerium für Bildung und Forschung / Federal Ministry of Education and Research
BMFTR	Bundesministerium für Forschung, Technologie und Raumfahrt / Federal Ministry of Research, Technology and Space
BMG	Bundesministerium für Gesundheit / Federal Ministry of Health
BMWE	Bundesministerium für Wirtschaft und Energie / Federal Ministry for Economic Affairs and Energy
BMWK	Bundesministerium für Wirtschaft und Klimaschutz / Federal Ministry for Economic Affairs and Climate Action
BvR	Beschwerdeverfahren des Bundesverfassungsgerichts / complaints procedure of the Federal Constitutional Court
CAR	chimeric antigen receptor
Cas	CRISPR-associated protein
CDMO	contract development and manufacturing organization
CRISPR	clustered regularly interspaced short palindromic repeats
CTA	clinical trial application
CTIS	Clinical Trials Information System
CTO	clinical trial office
CTR	EU Clinical Trials Regulation
DFG	Deutsche Forschungsgemeinschaft / German Research Foundation
DKH	Deutsche Krebshilfe / German Cancer Aid
DMD	Duchenne muscular dystrophy
DRG	diagnosis-related group
DRST	Deutsches Register für hämatopoetische Stammzelltransplantation und Zelltherapie / German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy
DZG	Deutsche Zentren für Gesundheitsforschung / German Centers for Health Research
EBMT	European Society for Blood and Marrow Transplantation
ELSA	ethical, legal and social aspect
EMA	European Medicines Agency
EORTC	European Organisation for Research and Treatment of Cancer
ERN	European Reference Network
ESC	embryonic stem cells
EU	European Union
FIH	first in human
FDA	U.S. Food and Drug Administration
FDZ	Forschungsdatenzentrum / Research Data Center
FTO	freedom to operate
G-BA	Gemeinsamer Bundesausschuss / Federal Joint Committee
GCT	gene- and cell-based therapy
GKV	gesetzliche Krankenversicherung / statutory health insurance
GLP	good laboratory practice
GMP	good manufacturing practice
hiPSC	human induced pluripotent stem cell
HDR	homology-directed repair
HTA	health technology assessment
IIT	investigator-initiated trial

IMA	indikatorgestützte Mittelallokationen / indicator-based funding allocation
IMI	Innovative Medicines Initiative
IMP	investigational medicinal product
IND	investigational new drug
IP	intellectual property
iPS cell/iPSC	induced pluripotent stem cell
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen / Institute for Quality and Efficiency in Healthcare
IVDR	In Vitro Diagnostic Devices Regulation
MRC	Medical Research Council
MDR	EU Medical Device Regulation
MRD	minimal residual disease
mRNA	messenger ribonucleic acid
MTA	medical-technical assistant
NGS	next-generation sequencing
n-of-few	small number of patients
n-of-1	individual patients
NUM	Netzwerk Universitätsmedizin / Network of University Medicine
OBO Foundry	Open Biological and Biomedical Ontology Foundry
OPS	Operationen- und Prozedurenschlüssel / German Procedure Classification
PAES	post-authorization efficacy studies
PASS	post-authorization safety studies
PCSK9	proprotein convertase subtilisin/kexin type 9
PDU	product development unit
PEI	Paul-Ehrlich-Institut
PPP	public-private partnership
QP	qualified person
QS-I	Qualitätssicherungsmeetings I / Quality Assurance Meeting I
RKI	Robert Koch-Institut / Robert Koch Institute
RNA	ribonucleic acid
RSU	regulatory support unit
SGB V	Sozialgesetzbuch Fünftes Buch / German Social Insurance Code, Book V
SOP	standard operating procedure
SPRIN-D	Bundesagentur für Sprunginnovationen / Federal Agency for Breakthrough Innovation
SWOT	strengths, weaknesses, opportunities, threats
TenU	international collaboration formed to capture effective practices in research commercialization
TierSchG	Tierschutzgesetz / Animal Welfare Act
TPP	target product profile
TTO	technology transfer office
UK	United Kingdom
USA	United States of America
USIT Guide	University Spinout Investment Terms Guide
VC	venture capital
VerfO	Verfahrensordnung / Rules of Procedure
WES/WGS	whole exome sequencing/whole genome sequencing
WIPANO	Wissens- und Technologietransfer durch Patente und Normen / Knowledge and Technology Transfer through Patents and Standards
WissZeitVG	Wissenschaftszeitvertragsgesetz / Academic Fixed-Term Contract Act
ZLG	Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten / Central Authority of the Länder for Health Protection with regard to Medicinal Products and Medical Devices

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