Data Access and Data Use Charter for the National Registry for Gene and Cell Therapies Germany (nGCT-R)

Preamble

This Charter defines the principles and framework governing access to and use of data from the National Registry for Gene and Cell Therapies Germany (*Nationales Gen- und Zelltherapieregister Deutschland e. V.*). It ensures that all data are processed in accordance with ethical, legal, and regulatory requirements, including data protection, while promoting research and innovation. In this context, the Guidelines for Good Scientific Practice issued by the German Research Foundation (DFG)[1] as well as the principles of the Data Literacy Charter of the German Stifterverband[2] are taken into account in order to ensure scientific integrity and transparency. This Charter is intended to transparently regulate the general handling of data within the National Registry for Gene and Cell Therapies Germany; however, it does not replace the data use agreement to be concluded with each authorized data user, nor the agreement on joint data controller responsibility in accordance with Article 26(1), sentence 1 of the General Data Protection Regulation (GDPR)[3].

1. Purpose and Objectives

The National Registry for Gene and Cell Therapies Germany aims to enable a comprehensive collection of data on gene and cell therapies in Germany. The purpose is the systematic documentation of gene and cell therapy applications in Germany in order to:

- ensure and improve the quality and safety of gene and cell therapy applications, including structured exchange with regulatory authorities;
- promote and enable registry-based scientific studies and analyses;
- support public health planning and policy by providing systematic data on the use and benefits of gene and cell therapies in routine care.

Further purposes are set out in the articles of the association.

2. Legal Basis

Data processing within the Registry is carried out on the basis of the following legal provisions:

- General Data Protection Regulation (GDPR)[3]
- German Federal Data Protection Act (Bundesdatenschutzgesetz, BDSG)[5]
- Medical Devices Law and the German Medicinal Products Act (Arzneimittelgesetz)[4]
- Other applicable national and European legislation
- German Research Foundation (DFG): Guidelines for Good Scientific Practice, in particular with regard to transparency, authenticity, and the avoidance of plagiarism and falsification[1]
- Article 8 of the Charter of Fundamental Rights of the European Union[6]: Protection of personal data, ensuring that all processing of personal data takes place with due regard to the rights of the data subjects

3. Data Literacy – Promoting Data Competence Among All Stakeholders

In line with the Data Literacy Charter of the Stifterverband[2], all stakeholders involved in the National Registry for Gene and Cell Therapies Germany, including researchers and patients, are encouraged to improve their data literacy. This includes:

- **Understanding data:** All stakeholders shall be supported in accurately reading, interpreting, and contextualizing data. Key outcome data from gene and cell therapy treatments should therefore be presented in a timely and graphical manner for both treating physicians and patients. In the event of the use of pseudonymized, patient-related data, patients shall - unless a broad consent (e.g. in the form of a broad consent declaration) is in place - be offered information in plain language about the intended use of their data.
- **Critical engagement with data:** Researchers and other data users must be able to critically assess data, verify their origin and quality, and identify potential biases. As a general principle, information on the origin of the data, their completeness, and documentation quality within the National Registry for Gene and Cell Therapies Germany shall be made publicly available, for example via a public blockchain-based repository, without allowing sensitive or patient-identifying characteristics to be traceable.
- **Responsible use of data:** Data may only be used in compliance with ethical and legal frameworks and data security requirements. The data contained in the Registry are intended to improve the quality of therapy offerings and generate insights for the medical and scientific community without compromising patient privacy. The platform providing access to Registry data via a cloud-based solution shall, as a rule, store and transmit sensitive data in end-to-end encrypted form, for example through the use of the so-called Matrix encryption standard[6] of the National Agency for Digital Medicine.
- **Traceability of data entries:** The technical platform of the Registry shall, as a rule, enable the traceability of data entries (e.g. via audit trails, token systems, etc.) down to the level of individual users (patient or data-entering center) without enabling identifiability. This allows for transparent attribution of individual contributions in the event of data use, including linkage to appropriate compensation depending on the contribution to a data donation. Data entries shall be provided with an unambiguous signature that allows, in individual cases, both traceability and clear identification of the data contributor. Such unique data signatures are intended to prevent misuse of data and to enable traceability in case of doubt.

4. Types of Data

The Registry may collect the following types of data:

- Disease-related baseline data (e.g. age, sex, diagnosis, outcome predictors, treatment history, therapy outcomes, quality of life, and other subjective endpoints)
- Treatment and procedural data (including details of the applied gene and cell therapy)
- Safety and adverse event data
- Effectiveness data (e.g. therapy outcomes, quality of life, and other subjective endpoints)
- Anonymized epidemiological and cost data for analysis, research, and health-economic or macroeconomic evaluations
- Performance data on the quality and quantity of individual data sets for quality assurance and data monitoring purposes

5. Access to Data

In accordance with the purpose of the National Registry for Gene and Cell Therapies, all institutions and health-related stakeholders whose objective is the promotion of public health and public healthcare shall be granted access to the data. In line with prevailing legal doctrine, no ownership rights are asserted over the data contained in the Registry; instead, access rights to the data, including the necessary consent mechanisms, are defined.

Access to Registry data is governed by the following principles:

- **Access for authorized participants:** Only authorized users—i.e. researchers, clinical institutions, affiliated entity- or methodology-specific registries, pharmaceutical manufacturers, health insurance funds, and health authorities—shall be granted access to the data in accordance with the principles of good scientific practice, ensuring transparency and reproducibility. Approval algorithms and basic rules for each user group shall be established (see Section 8) to prevent misuse of data for commercial purposes or for purposes that do not serve the public good or scientific progress. Depending on the intended use, it shall be defined for each user group whether data are provided at individual patient level or in aggregated form.
- **Access for patients and patient representatives:** Patients have the right to access their own data and to request deletion thereof, provided no statutory retention obligations or regulatorily mandated studies in the public interest apply. Patient representatives may also be granted access to data sets depending on the research question, provided that the request is consistent with the general objectives of the Registry and serves the public good.
- **Restriction of access:** Access to sensitive data (e.g. genetic data, health data) is strictly regulated and granted only for specific purposes. The Registry generally follows a data democratization approach, i.e. the creation of regulated access to data for all stakeholder groups, ensuring timely and fair access to available data for the benefit of the community. However, any form of commercialization of the data is to be excluded as far as possible, as is any purpose of data use that is not in the interest of the solidarity-based insurance community.
- **Encryption and security:** All data must be stored with end-to-end encryption and transmitted via secure connections. Data storage within the Registry system shall be separated from secure data transmission pathways and carried out within a certified software environment. Access is granted only via authenticated, authorized channels and subject to prior approval. The Registry and/or the associated data transmission platform shall provide an eConsent mechanism to ensure transparent data use.

6. Data Use

Use of the data contained in the Registry is permitted exclusively for the following purposes:

- **Research and scientific analyses:** Data may be used for clinical research, epidemiological studies, and analyses of the long-term effects and safety of gene and cell therapies. All scientific publications based on these data must comply with the DFG Guidelines for Safeguarding Good Research Practice[1] and the principles of the Data Literacy Charter of the Stifterverband[2]. As part of a data use application, information on the planned exploitation and publication of results as well as on planned authorship, including justification, must be provided. As a rule, a prespecified statistical analysis plan shall be submitted for planned statistical analyses; its appropriate application may be reviewed on a case-by-case basis and, where applicable, subject to conditions or requested amendments.

- **Quality assurance and safety monitoring:** Data may be used for therapy monitoring and the detection of adverse events in the context of application-accompanying data collection (Anwendungsbegleitende Datenerhebung, AbD) or post-authorization safety studies (PASS). The Registry shall provide a real-time reporting system on the quality and quantity of data contained in the Registry for specific research questions.
- **Reporting and statistics:** Anonymized data may be used for public and scientific reporting and to support the interests of the solidarity-based community, subject to review of the respective purpose and completion of the relevant approval process.

7. Authorship Guidelines and Good Scientific Practice

When publishing research results based on Registry data, the following DFG Guidelines for Good Scientific Practice[1] shall be observed:

- **Honest presentation of results:** All results obtained from the use of Registry data must be presented fully and accurately. Manipulation, falsification, or selective reporting of data is strictly prohibited.
- **Transparency of sources:** All data sources used must be clearly and comprehensively disclosed, including any conflicts of interest and funding of research projects. The National Registry for Gene and Cell Therapies Germany must be explicitly named in the publication and cited in accordance with the currently applicable authorship guidelines.
- **Authorship:** Authors of scientific publications must be designated in accordance with DFG guidelines and general ethical standards. Any individual who has made a significant contribution to the research should be recognized as an author. This includes correct attribution of participating clinical institutions and researchers. First and last authorship positions must be transparently stated and justified during the data use application process.
- **Reproducibility:** All data and methods used must be documented in such a way that other researchers can reproduce the results and inspect the source data at any time for verification. This also applies to methods of data collection, processing, and analysis.
- **Avoidance of plagiarism:** All cited works and data must be properly referenced to prevent plagiarism.

The Registry reserves the right to pursue legal action in the event of violations of the above guidelines.

8. Data Use Applications

Applications for the use of Registry data must be submitted via an electronic, browser-based platform, enabling authorized users to submit requests digitally and in a traceable manner. Applications are processed by the responsible Registry body and must be completed within a maximum of four weeks. Decisions on approval or rejection are made based on the approval algorithms set out in Sections 8.1 to 8.4 and are documented transparently and comprehensibly. In the event of rejection, reasons are communicated in an understandable manner. Depending on the applicant group, i.e. inquiries from i) academia (see Section 8.1, Figure 1), ii) pharmaceutical industry/industry associations (see Section 8.2, Figure 2), iii) statutory/private health insurance funds (see Section 8.3, Figure 3), or iv) other applicants (see Section 8.4), different authorization algorithms apply. These are to be coordinated with the respective user groups in advance and may be adapted over time.

All information on approved data use applications and ongoing Registry projects shall be made publicly available on a website. Requests for collaborative projects shall be disseminated in this way and be accessible to as many users as possible.

The Registry aims to obtain a general consent regulation (auto-opt-in rule) for the provision of data for regulatorily mandated studies (e.g. PASS, PAES, AbD, or similar), both from the primary registries or gene and cell therapy treatment centers and from the included patients. In the case of regulatorily mandated studies, data use cannot be refused; the auto-opt-in rule is of an informative nature. Consent shall be obtained electronically (eConsent) and be accessible at all times.

In addition to the auto-opt-in rule, data provision for individual data use applications requires renewed, purpose-specific active consent from the data-holding primary registries or treatment centers (double opt-in rule) and - unless a broad consent is in place - informative notification of the affected patients, potentially including an active right to object (opt-out). Corresponding consent requirements may be imposed by the Supervisory Board of the Registry on a case-by-case basis. For scientific applications, a valid ethics approval must be submitted by the applicant institution as part of the data use application.

8.1 Scientific Data Use Applications from Treatment Centers, Academic Consortia, Affiliated Registries, or Individual Researchers

Scientific data use applications from individual researchers, treatment centers, affiliated registries, or academic consortia may be submitted electronically at any time. All principles set out in this Charter must be complied with. Applications must include all information specified in the online application form, including required attachments. An eConsent procedure may be requested as part of the application process.

Any fees incurred, depending on the scope of the data use application, planned duration, etc., are transparently set out in the current fee schedule of the Registry and are subject to regular adjustment. The Registry aims to provide the widest possible access to data for academic research; therefore, fees may be waived or reduced for particularly innovative research questions at the discretion of the Supervisory Board, depending on the Registry's financial situation and ongoing project funding calls.

As a general rule, all data originating from the applicant's own treatment center or independently entered and provided by the applicant shall be accessible at all times; in such cases, no application, separate consent, or fees are required.

Figure 1 illustrates the approval algorithm for fully submitted academic applications or applications from clinical treatment representatives:

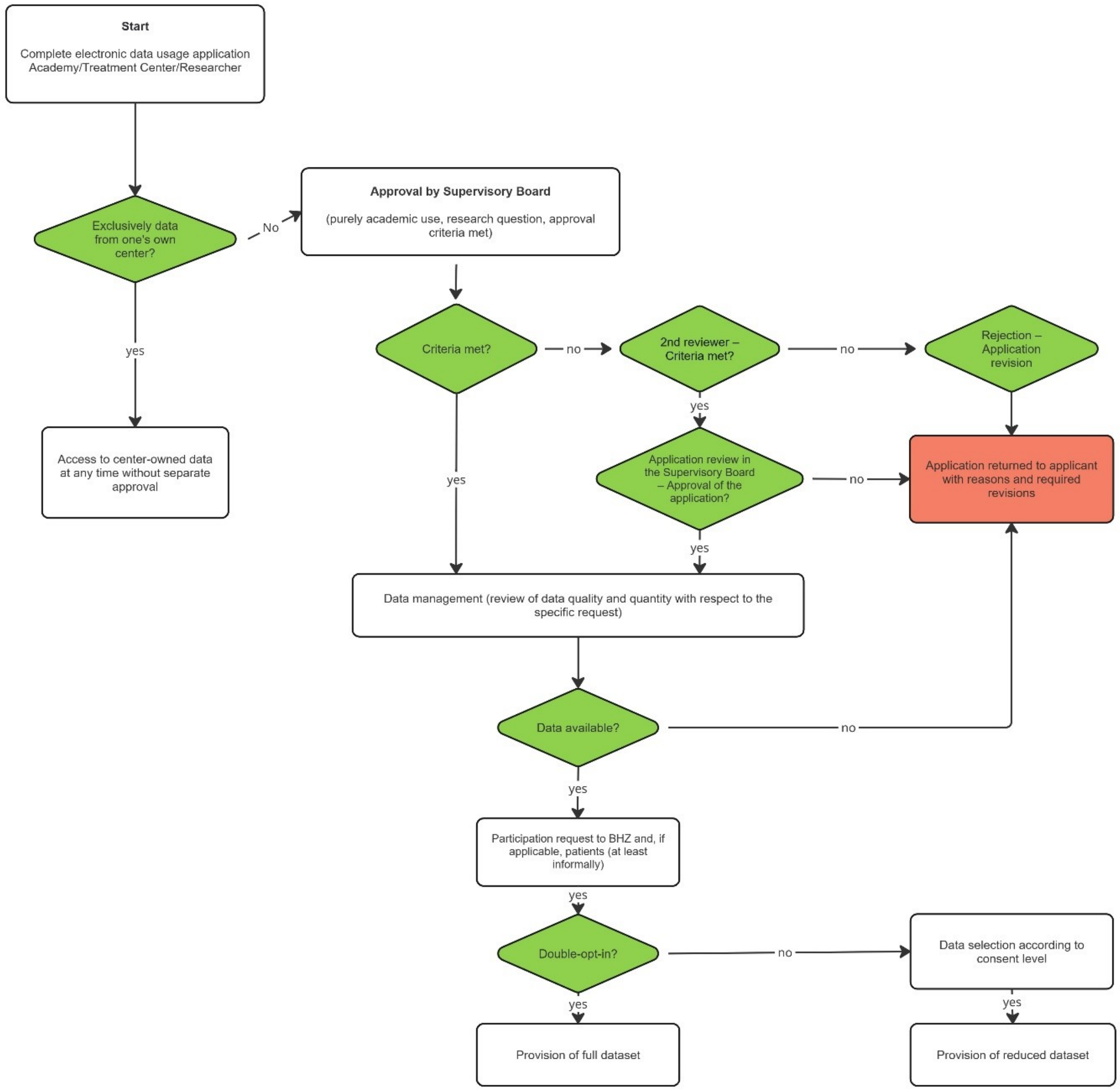

Figure 1: Approval algorithm for data use applications from academic institutions, other treatment centers, consortia, or individual researchers. Abbreviations: BHZ = Treatment Center

8.2 Data Use Applications from the Pharmaceutical Industry / Industry Associations

For data use applications submitted by pharmaceutical manufacturers or industry associations, the same principles as set out in Sections 1–8 of this Charter apply. For fully submitted applications, including those involving prospective data collection, two scenarios with different approval algorithms are distinguished:

8.2.1 Data Use Applications for Regulatorily Mandated Studies (e.g. by the European Medicines Agency (EMA) or national authorities such as the Innovation Fund of the Federal Joint Committee (G-BA, “Gemeinsamer Bundesausschuss”)

Data-entering centers/primary registries and patients participating in the Registry generally consent to the transfer of their data for regulatorily mandated studies (auto-opt-in rule). Corresponding consent is obtained electronically during onboarding of centers to the Registry and as part of patient informed consent for data donation. Consent may also be purpose-, indication-, or product-specific via eConsent. The type and scope of written consent must be documented in a traceable manner within the system and be available at any time for audits, for example via a blockchain-based model. Fees incurred for compensation of data-providing entities, ongoing Registry operation, and any analyses performed by the Registry are transparently listed in the current fee schedule and subject to regular adjustment. The applicant manufacturer must provide proof of the regulatory mandate and financing of the study; a corresponding study protocol and any required regulatory approvals must be submitted upon request. In the case of a fully submitted application for the purposes described in Section 8.2.1, the Supervisory Board of the National Registry for Gene and Cell Therapies Germany e.V. waives its right of veto. Data for regulatorily mandated studies are provided by the Registry's data management team in aggregated form based on a prespecified statistical analysis plan. Provision of single-patient-level data and any traceability of individual persons via ordering or supply chains shall not be possible.

8.2.2 Data Use Applications for Other Studies from the Pharmaceutical Industry

Figure 2 summarizes the approval algorithm for other studies from the pharmaceutical industry. Data for product comparisons involving products from other manufacturers require separate consent from the manufacturer of the comparator product. As a general principle, data from the National Gene and Cell Therapy Registry Germany shall not be used solely for commercial purposes. In doubtful cases, the Supervisory Board may require revision of the application or reject data access if the application does not primarily serve research purposes, the public interest, or medical progress._If provision of individual case data to validate outcome-based pricing models to a health insurance fund is required (see Section 8.3), the manufacturer shall be informed in a timely manner of such data transfer.

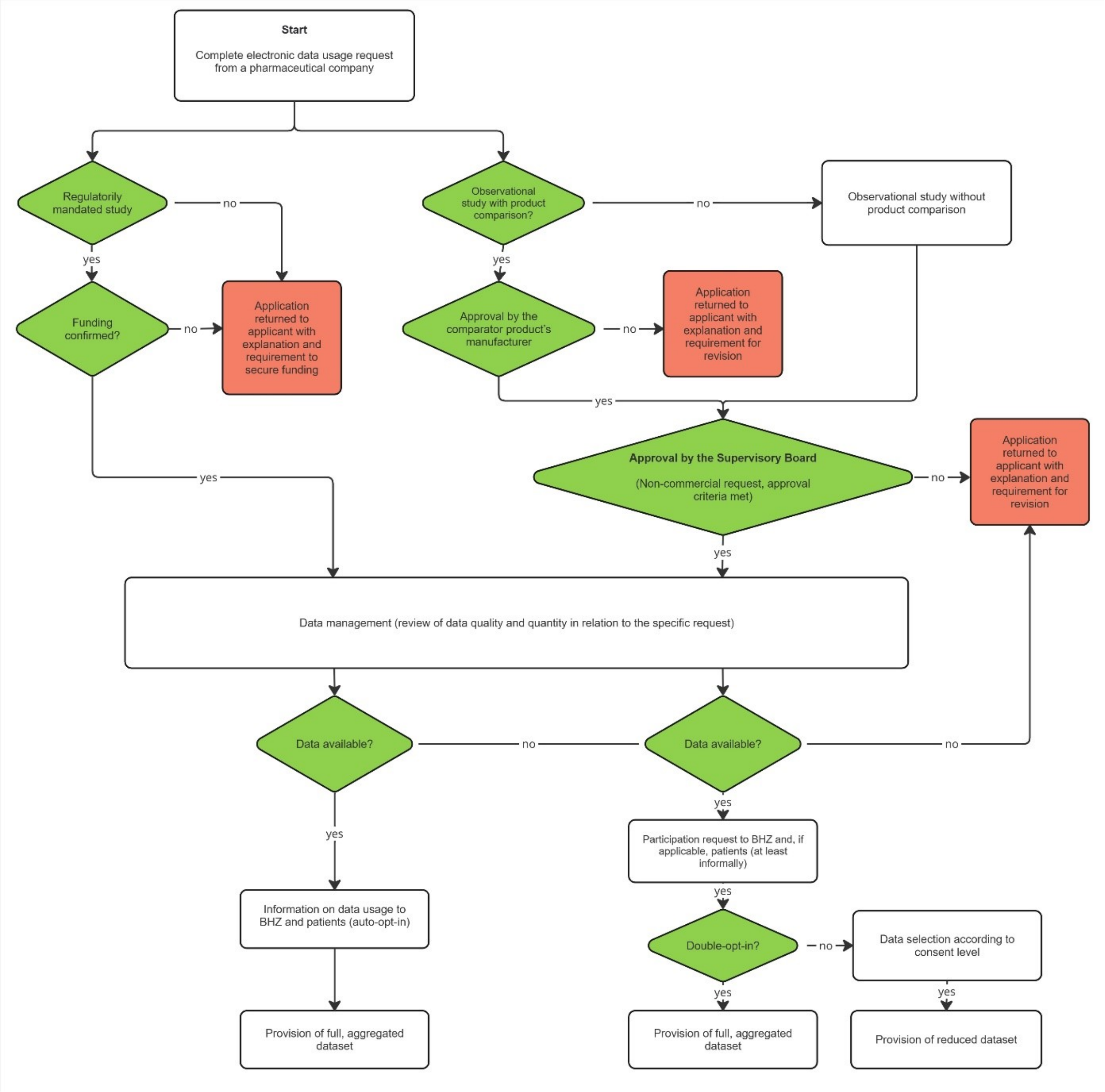

Figure 2: Approval algorithm for data use applications from the pharmaceutical industry. Abbreviations: BHZ = Treatment Center

8.3 Data Use Applications from Statutory and Private Health Insurance Funds

In recent years, outcome-based pricing models have increasingly been agreed upon for gene and cell therapies. The National Registry for Gene and Cell Therapies Germany provides health insurance funds with Registry data for the negotiated endpoints at the individual patient level, in compliance with GDPR principles and in pseudonymized form. The insurer must submit proof of the agreement with the manufacturer as part of the data use application. Data provision may only be granted if cost-covering financing for data entry by treatment centers and for Registry and platform operations is contractually secured. Other studies involving product comparisons between different manufacturers require consent from the affected manufacturers and should generally remain within the academic domain.

Figure 3 illustrates the approval algorithm for data use applications from statutory and private health insurance funds.

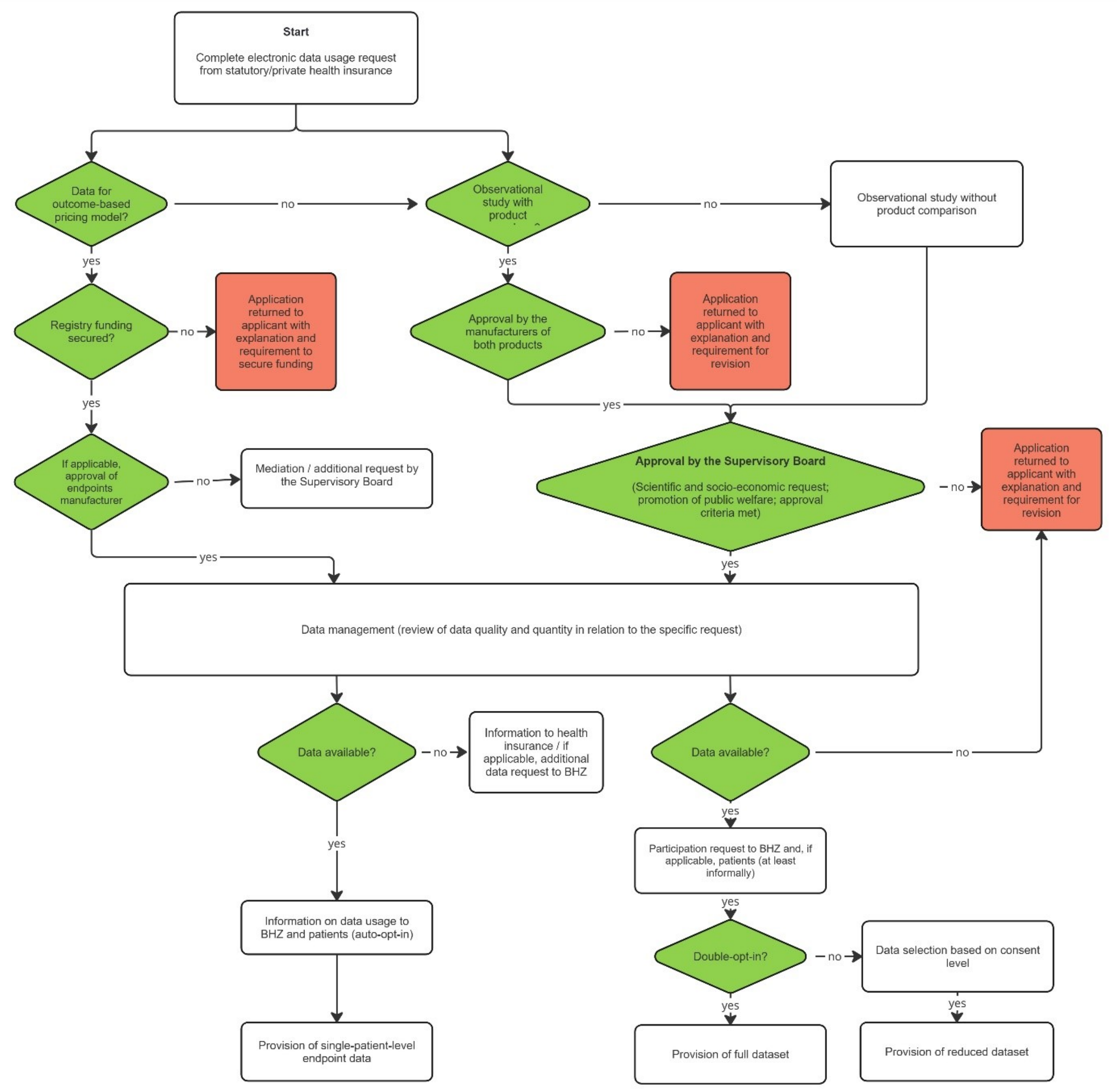

Figure 3: Approval algorithm for data use applications from statutory/private health insurance funds. Abbreviations: BHZ = Treatment Center

8.4 Data Use Applications from Other Stakeholders

For data use applications from other stakeholders, the approval algorithm described in Section 8.2.2 for other studies applies.

9. Anonymization and Pseudonymization

The National Registry for Gene and Cell Therapies Germany works exclusively with pseudonymized data. Details regarding pseudonymization procedures and the trusted third party are governed by a comprehensive data protection concept.

Prior to data transfer, Registry data are anonymized or pseudonymized depending on the data use application in order to protect patient privacy. In cases where identification of individuals is necessary (e.g. single-patient-level data in the event of adverse event reporting), all measures are taken to protect patient identity, which shall under no circumstances be disclosed. Data suitable for patient identification are never stored within the registry or its associated platform; such data are held exclusively by cooperating trusted third parties and/or primary registries and data-providing treatment institutions.

10. Consent and Patient Rights

The use of personal and medical data takes place only with the explicit and informed consent of the affected patients. Patients have the right to:

- withdraw their consent at any time;
- request deletion of their data, provided no legal retention obligations apply;
- be comprehensively informed about the use of their data.

11. Monitoring and Compliance

Independent monitoring of data use is conducted on a regular basis, for example by the scientific advisory board of the Registry or alternatively by a commissioned public health authority, to ensure compliance with this Charter, data protection requirements, and the DFG Guidelines for Good Scientific Practice. All stakeholders must comply with the defined security and data protection measures.

12. Public Communication and Transparency

The Registry shall publish regular reports on data use and progress to ensure transparency vis-à-vis the public and participating patients (at least annually; data use applications continuously). Publication shall take place online and include descriptive data on Registry performance, data quality, and data quantity. Compliance with the principles of good scientific practice and the Data Literacy Charter of the Stifterverband shall be ensured.

13. Final Provisions

This Charter may be amended and updated by the Supervisory Board as necessary to reflect legal, scientific, and technological developments. All amendments must be communicated transparently and brought to the attention of the involved parties. Responsibility for this lies with the Supervisory Board and the management of the Registry.

References

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7. **National Agency for Digital Medicine (gematik).** *Encryption Standard for Digital Medical Applications (TI Messenger / Matrix-based encryption)*. https://fachportal.gematik.de/anwendungen/ti-messenger#c4170

Note: In case of any discrepancies between the German and English versions of the Data Access and Data Usage Charter, the German version shall prevail.