National Register for Congenital Heart Defects e. V. (NRAHF)
Competence Network for Congenital Heart Defects e. V. (KNAHF)

Regulations for the Collection of Data and Samples, as well as the Use of Data and Samples and/or the KNAHF Infrastructure for Research Purposes

(Passed on the conference of the Steering Committee of the KNAHF and the Management Board of the NRAHF on 09/21/2018)

Overview

Introduction

The **National Register for Congenital Heart Defects** (hereinafter referred to as **NRAHF**) was founded in 2003 by the three German cardiac societies as a nonprofit scientific association. The statutory purpose is the *collection of data and samples of patients with congenital heart disease, as well as of their families*, and the *provision of these data and samples for research*. The NRAHF is the core project of the **Competence Network for Congenital Heart Defects** (hereinafter referred to as **KNAHF**).

The **biorepository** was implemented as a part of the NRAHF in 2009. Consent to participation in the biorepository is connected to participation in the register. The biorepository includes blood samples for the extraction of DNA, RNA, plasma and serum, saliva samples for the extraction of DNA, as well as cardiac tissue samples from cardiac surgery which were collected according to uniform standards. A uniform identity management facilitates central data and sample administration in the NRAHF.

Register data and biomaterial are used as a basis for research on congenital heart disease and heart disease in underage individuals and are to be available to interested scientists across the world.

1. Regulations Regarding the Collection of Data and Samples

1.1 Medical data and samples of register members are collected solely for research purposes as defined in the statutes of the NRAHF.

1.2 The donors grant the rights of use of the data and samples in accordance with their written consent declared towards the NRAHF.

1.3 Medical data are acquired by the NRAHF after patients' written consent ("Yellow Form") to the participation in the register, to releasing the attending physician from the obligation to secrecy (permission to require medical reports and further findings), as well as to a long-term use of the data for research on congenital heart disease.

1.4 The collection of samples is based on a specific informed consent to participation in the biorepository and is effected by two different means:
Type A - via directly contacting individuals who have already registered in the NRAHF and who have agreed to donate a sample.
Type B - via medical institutions who receive special sample kits from the NRAHF management office.
Sample donors' medical data are acquired on the basis of the consent as specified in *c)*.

1.5 The Management and the staff members of the NRAHF are responsible for the central administration, management and storage of the data and samples stored in the NRAHF; this responsibility includes adherence to ethical regulations, as well as to regulations in terms of data protection laws.

2. Regulations for Cooperating Clinics Collecting Samples for Research Purposes (Sample Providers)

2.1 The rights designated to sample providers described in these regulations are assigned to the corporate entity that is the provider of respective institution. Natural persons such as the medical director of the institution can be designated as contact persons to the *NRAHF.*

2.2 The regulations and conditions under which data/samples are collected are laid down with each sample provider in a cooperation agreement (see appendix, only in German language available).

2.3 The cooperation agreement defines the following aspects:

The sample provider commits him- or herself to

2.3.1 use the central data/sample administration, as well as the identity management of the NRAHF
2.3.2 use the electronic database systems of the NRAHF for the entry of sample data
2.3.3 send, process and/or store samples according to predefined standards
2.3.4 use the documents for patient information, patient consent and sample acquisition (sample accompanying letters) as predefined by the NRAHF.

The processing or storage of EDTA blood for extracting DNA take place centrally at a service institution collaborating with the NRAHF

The processing or storage of tissue samples, as well as blood for extracting serum, plasma or DNA, if applicable, take place ***decentrally*** *at the participating institutions with their adhering to the concerted workflows. The NRAHF can, within the means available, provide suitable logistics for the storage and preservation of the samples (sample tubes, Cryo equipment etc.).*

2.4 Samples can be used within the scope of network studies, as well as by the sample providers themselves. Sample providers' rights are also defined by the cooperation agreement:

In the case of third party use of data collected by a sample provider for scientific purposes *(see 3. Regulations Regarding the Use of Data and Samples):* If the Data Access Committee supports the performance of a study which requires use of samples that have been collected by an institution (sample provider), the following rules apply:

2.4.1 The Management of the NRAHF informs the institution in question in written form that samples collected by respective institution are intended to be provided for a research project.
2.4.2 This written information includes a copy of the application as well as further documents regarding the research project's content which the NRAHF Executive Board might have received.
2.4.3 Within a period of four weeks after receiving the written information the institution can object to the use of samples, for named research project. Objection has to be declared in written form to the Executive Board of the NRAHF. Use of samples may not be unreasonably denied.

After deadline expiration an approval is considered to be given, unless the Executive Board has received a written objection.

Sample providers may themselves also use samples that have been collected at their institution for their own research projects. *In this case, the boards of the KNAHF and the NRAHF are not involved. The Management Office has to be informed (form "**Announcement of Sample Use**"), including a description and assortment of the samples intended to be used for named study. The need for measures in terms of data protection law is assessed in collaboration with the Management Office (Material-Transfer-Agreement if external partners or companies are involved in the sample analysis)*

3. Regulations regarding the Use of Data and Samples, or the KNAHF Infrastructure

3.1 For initiating a study, the submission of an ***Application*** (see form in the appendix) is mandatory. An ***Inquiry*** to the Management Office (regarding, for instance, the availability of samples) can be made in advance. Applications are possible for register data, samples from the biorepository or the Register infrastructure (IT platform, databases, logistics) with the aim of prospective data or sample collections (e. g. sub-registers). Applications and Inquiries will be treated as confidential.

3.2 Decisions regarding the provision of data, samples or the infrastructure for a study are made by the **KNAHF *Steering Committee*** and the **NRAHF *Executive Board***. In the case that data and samples are released, both boards jointly act as *Data Access Committee.* The boards decide on the basis of recommendations of the **Review Board**. Furthermore, the use of samples that were collected by institutions (type B) requires ***the approval of the institution in question*** (see 2.4 and Fig. 1 - Decision Process).

The above-mentioned boards are not involved

- in the case of samples being used by the sample provider themselves (see 2.4)
- in the case of retrospective analyses of Register data, including, in part, also the case of surveys being initiated (decision is made by the NRAHF Executive Board/Management Office)

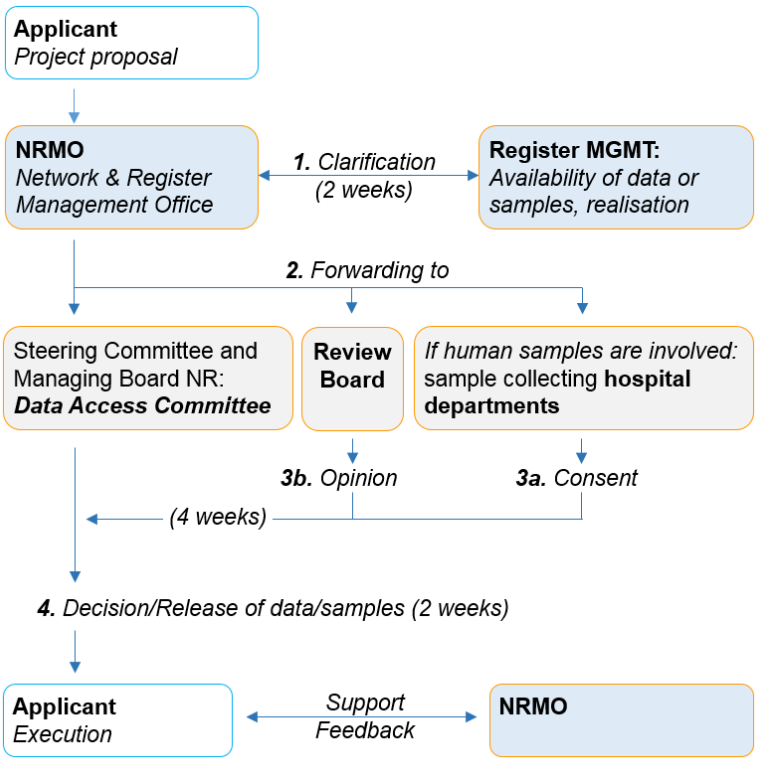

Figure 1: decision process

3.3 The application is submitted to the Management Office by the applicant. In the case of competing applications, the date of receipt is the decisive factor, or the competing parties are asked to cooperate by the Steering Committee and the NRAHF Executive Board.

3.4 The performance of a project requires sufficient financial resources on the part of the applying institution. Details regarding funding must be given in the application.

3.5 If the above mentioned boards vote in favor of a project (and, if applicable, approval is also given by the sample provider), the applicant receive the right of use of the data/samples for a defined research question and within a defined timeframe.

3.6 The project starts with transferring the samples/data to the applicant. The Management Office may charge an expense allowance for the provision and transport of the sample material.

3.7 The person responsible for the study undertakes to prepare a draft for a patient-friendly presentation of the project.

3.8 The details of data/sample use and utilization are laid down in a written agreement (*Material* or *Data Transfer Agreement, see appendix*). The agreement includes the following aspects:

3.8.1 Due to reasons in terms of data protection law, samples/data may only be transferred to third parties in consultation with the NRAHF Management Office.

3.8.2 In the case of genetic studies, data sovereignty regarding the analytical data gained from the samples remains with the NRAHF.

3.8.3 A short annual progress report has to be compiled

3.8.4 The Publication Guidelines corresponding to the ICMJE recommendations (see appendix) must be observed.

3.8.5 After completion of a project and publication of its results, the original data generated within the scope of the study (image data, sequence data from sample analyses) are to be provided to the KNAHF/NRAHF for re-use. Project managers are involved in the decision process regarding applications for the use of their data, and they are regarded in the case of resulting publications.

Appendix

Appendix 1 **Forms *"Application", "Inquiry" and "Announcement of Sample Use"***

Appendix 2 **Cooperation Agreement (template)**

Appendix 3 **Material- and Data Transfer Agreement (templates)**

Appendix 4 **Guidelines for Publications**

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