Guideline for application of materials
Bio- and Genome Bank Denmark

Background

Bio- and Genome Bank Denmark (RBGB) is a nationwide/cross-regional infrastructure for biobanks in Denmark. Overall, the biobanks in RBGB are clinical biobanks, but biobanks for other health scientific purposes are also accommodated by the infrastructure. The purpose of RBGB is to secure biological material for the citizens' own current and future treatment, to support Danish health research as well as national and international cooperation and promote personalized medicine in the Danish healthcare system. For further knowledge on the principles of RBGB please see "RBGB Principals PIXI".

All information concerning the biological material (metadata) in RBGB can be accessed by contacting the secretary of RBGB, while clinical data (e.g., treatment) must be accessed through other registers. By default, both wet data and information concerning the biological material can be used by all publicly employed researchers and is to contribute to the development of personal medicine, amongst others.

This document describes the guidelines for retrieval and use of biological material from RBGB to publicly employed staff (clinicians, researchers etc.), and is a politically approved document. For guidelines regarding retrieval of biological material or metadata for private companies, please see "RBGB Principals PIXI".

General guidelines for retrieval and use of biological material

RBGB consists of several clinical biobanks, one donor biobank for other health scientific purposes, and one research biobank. Regarding the clinical biobanks, retrievals for clinical use/genetic investigation always have the highest priority. Regardless of material amount or project reservations, materials for clinical purposes will always be retrieved. Once the clinical use is catered for, the aim is for the collected material to benefit as much research as possible. This means, only the specific amounts or molecules needed by the project, is handed over. It is the professional staff associated with the biobank center, who is responsible for pipetting and other physical handling of the material. All use and handling of material and information concerning the biological material (metadata) must always happen according to current legislation. Retrieval is not possible until all the relevant regulatory approvals and documentation hereof have been presented to the RBGB secretariat or the regional biobank center. The project manager (Principal Investigator (PI)) is responsible for obtaining the necessary approvals.

It is not up to the RBGB secretariat to conduct a scientific evaluation of the projects. On certain occasions, several applicants may wish to perform comparable projects on sparse material. In such cases, RBGB encourage the projects to cooperate. RBGB cannot choose between projects or favor certain projects at the expense of others. In case of a rejection of a requested retrieval, the rejection must be substantiated in writing by the RBGB secretariat, the local biobank center, or by project-reserving researchers as well as be submitted and evaluated by the steering committee of RBGB (see figure 1). If there is any intention to appeal the decision, the steering committee of RBGB must be addressed through the RBGB secretariat.

Application of data and materials from Bio- and Genome Bank Denmark (RBGB)

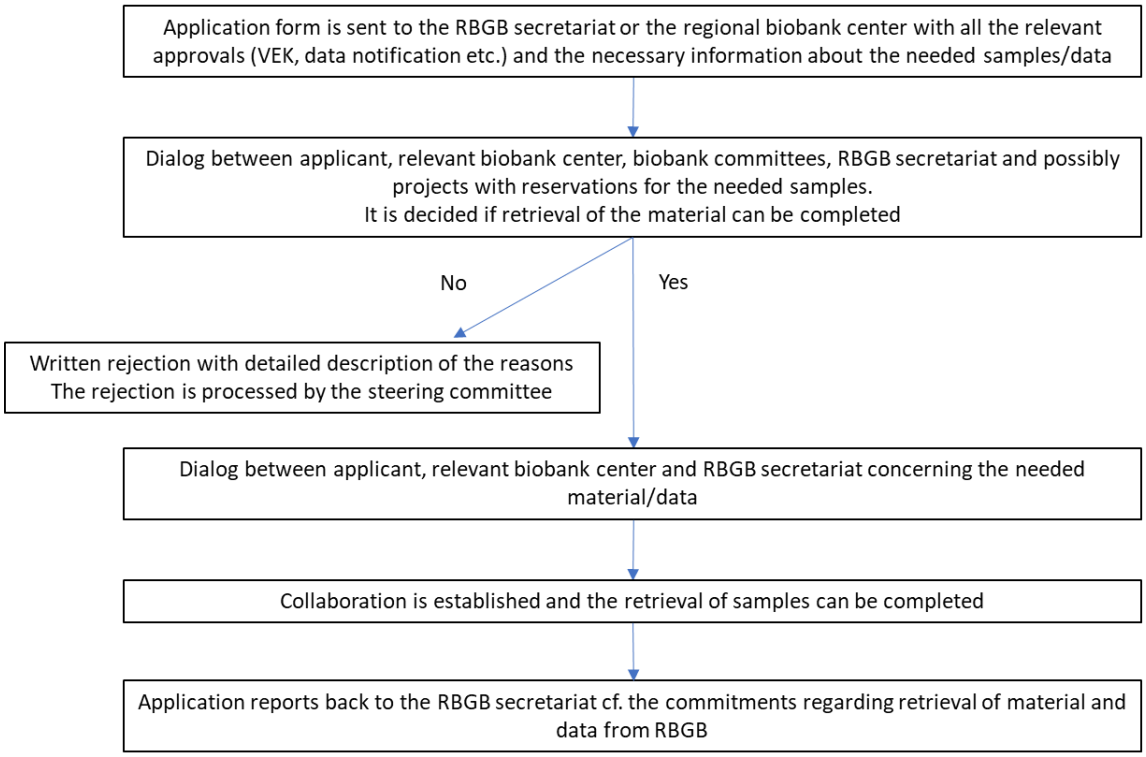

Figure 1. Process of applying for data and material from RBGB. The figure describes the process of applying for already collected data and material (retrospective studies) in RBGB.

Guideline for requesting data and materials

The applicant should always be the one responsible of the project which material is applied for. The application requires a completed approved application form, either to the RBGB secretariat (national retrievals) or to a regional biobank center (regional/local retrievals). The relevant application form as well as any associated instructions are provided by the RBGB secretariat or the local biobank center but are also available on RBGB's webpage: http://rbgb.dk/.

In general, data and material can be retrieved through three scenarios:

A. Retrieval of biological material and data for clinical use/genetic investigation:

Biological material and data concerning materials (material-type, fraction-type, processing time, diagnosis etc.) are, on request, handed out to the healthcare personnel, that are to conduct the analyses. The treating department/doctor is responsible for gathering, storing, and documenting consent to clinical use of biological material, from the patient. The applying department/doctor is asked to document the need for a retrieval by forwarding a copy of the requisition to the RBGB secretariat or the concerned biobank center. No further legal authorizations or documents are required to apply for this type of retrieval. The material must solely be

used for the individual patient's own medical diagnosis or treatment, or in relation with genetic examination for hereditary diseases. This service is free of charge.

B. Preliminary inquiry of data about materials for research:

If the applicant wishes to use already collected biological material from RBGB for a retrospective research project, the applicant can apply for data on a group level. This may include information about the number of unique patients within certain search criteria or the number of materials/fractions of a certain type and their geographical placement. All data retrieved on preliminary inquiry will be on a group level, meaning no personally identifiable data is included. If there are fewer than 5 persons in a group (n<5), this is specified as personally identifiable data. If the applicant has the relevant clearances to request data on specific CPR-numbers, this request can be met. This might occur, if the applicant is already in possession of data from other registers which includes CPR-numbers, and therefore want an overview of data from several registers, before the biological material is obtained. This service is free of charge.

C. Retrieval of biological material and data for research projects:

This type of retrieval requires, that all relevant approvals have been gathered by the PI. It may be approval from a Danish Medical Research Ethics Committee (regional Videnskabsetisk Komité) or the Danish National Committee on Health Research Ethics (National Videnskabsetisk Komité) and could also include approval from Danish Medicines Agency (Lægemiddelstyrelsen) and other instances. The project must have a validated version according to GDPR article 30 of the records of processing activities at the chosen represented data processor in the specific region.

Apart from this, there must be consent from the specific patients/donors, or an obtained dispensation for consent. If a request is made for material from a clinical biobank in RBGB, it must always be verified, that the concerning patients are not registered in 'Vævsanvendelsesregisteret' (VAR). Upon registration in VAR, the biological material cannot be retrieved for research studies.

If the applicant has gathered the samples prospectively (ongoing over time) in context of RBGB, no patients are registered in VAR, and the necessary documentation (legal approvals) are accounted for at project initiation, the material can be retrieved by request of the project manager. If a patient is registered in VAR or has withdrawn their consent for the project, please see RBGB's current guideline concerning the matter.

On requests concerning already collected material in RBGB (retrospective studies), the applicant must be able to document, that all necessary approvals have been gathered before material or data on material can be retrieved. In research projects where clinical data are a fundamental prerequisite, a pledge on retrieval of clinical data from the relevant source must be provided (such as a clinical quality database or other registries).

In context of RBGB, the material is in a clinical biobank, and therefore prioritized for clinical use/genetic examination. When the material is retrieved by a research project, it is handed over to the project's own research biobank (or the research biobank in RBGB). The PI is responsible for the establishment of a research biobank, or– in the case where no research biobank is needed/established – to document, that the retrieved material will be analyzed within 1 week.

From 01.06.2019, projects with prospectively collected material in RBGB have one free retrieval per sample/material available. All project reserved material can be retrieved at once or it can be retrieved from a subset of materials at a time at the request of the project. The cost of additional retrievals is settled for the

individual project. Projects where the collecting of materials was initiated before 01.06.2019 can retrieve materials free of charge cf. the terms of the prior RBGB agreements. When these projects expire, the agreement ceases unless the project has applied for and received an extension of the project. In the event of a project extension, the project transfers to one free retrieval per sample/material from all materials collected throughout the project.

Projects, which retrieve material for a retrospective study, must pay for the retrieval themselves cf. the applicable price list in RBGB or according to individual agreement, unless otherwise agreed. All retrieval for clinical/genetic use is free of charge, and this also applies to retrieval to projects that are part of clinical studies. Projects that receive material for a retrospective study must pay for the retrieval cf. the current RBGB price list or by individual agreement, unless otherwise agreed. The transport expenses are paid by the project, unless otherwise agreed. The individual centers/hospitals might have local guidelines for retrieval and application of materials, which must be followed.

The obligations of the applicant when receiving material and data from RBGB

When receiving biological material and/or data from RBGB, the applicant obliges to the following:

- To only utilize the material for what has been agreed upon with RBGB according to the project description as well as the RBGB agreement and/or the application form. In general, only the amount of material necessary for the planned analyses will be handed over to the project. PI is responsible for the destruction of any excess material. When this is not possible an individual agreement can be made, to return the excess material to RBGB for destruction. The retrieved material must **never** be passed on to others without permission from the Danish Data protection Agency and the contact person of the project.
- To inform which analyses will be conducted on the material. Analyses that are to be performed on the material in the specific project should be indicated in the application form but results on individual level achieved in connection with the analyses, are not registered by RBGB.
- To report back whether performed analyses could be completed. This is done to continuously ensure that RBGB is delivering materials of high quality for current and future analyses.
- On request, to contribute with a short project description (layman's description) for publication in the newsletter of RBGB both initially and when results can be presented.
- To consider co-authorship to any relevant collaborators in RBGB according to the Vancouver rules or mention the relevant person in *Acknowledgements*.
- To mention the relevant biobank in the paragraphs *Materials and methods* and *Acknowledgements* in articles, that the material is part of, by writing, for example:
  "Bio- and Genome Bank Denmark (Danish Cancer Biobank/Danish Rheumatologic Biobank/Danish Diabetes Biobank/Danish Blood Donor Biobank) is acknowledged for biological material and for data regarding handling and storage".
- To inform the RBGB secretariat about publications, wherein material from RBGB is used. Information about publications is published on RBGBs webpage, in newsletters, and in the annual report.

Rejection of request of data and material

In cases where material cannot be retrieved for a research project, the RBGB secretariat or the regional biobank center must provide a written justification hereof. Rejections are sent to the applicant with a copy to the chairman of the scientific advisory board of the actual biobank and the steering committee of RBGB. If the applicant wishes to appeal the decision, the steering committee of RBGB must be addressed through the RBGB secretariat.

Advice and guidance in connection with the application

The RBGB secretariat is always available if guidance and counseling on the retrieval procedures or other relevant affairs in RBGB is needed. The secretariat can be contacted at:

Tel.: +45 38 68 91 32 or +45 38 68 98 12

E-mail: RBGB.sekretariat.herlev-og-gentofte-hospital@regionh.dk

We also refer to our webpage for RBGB, http://rbgb.dk, where the relevant application form and an accompanying instruction can be found.

Information about Bio- and GenomBank Denmark (RBGB):
The Bio- and GenomBank Denmark secretariat, Department of pathologyi, Herlev Hospital, Borgmester Ib Juuls Vej 73, Opgang 7, 4. etage, L5, 2730 Herlev. Phone. (+45): 3868 9132/3868 9812, E-mail: RBGB.sekretariat.herlev-og-gentofte-hospital@regionh.dk