General Description of Codex4SMEs

The Interreg project Codex4SMEs (Companion diagnostics expedited for small and medium-sized enterprises) plans to improve healthcare by enhanced adoption of Personalized Medicine in North-West Europe. The objective is to establish a network, which supports SMEs along the value chain of Companion diagnostics (Cdx) development.

Companion diagnostics (Cdx) are an indispensable tool for optimum application of Personalized Medicine: they allow tests to determine the molecular causes of a disease before treatment has started. However, thus far the development of companion diagnostics has been highly time-consuming and costly, so at present it is only used in the context of very few treatments.

Codex4SMEs is establishing a transnational network of nine partners and two sub-partners from seven countries (DE, FR, NL, UK, IE, LU and AT) and expedite the development of the SMEs' products in the field of Cdx. There is a need to improve SMEs' innovative capabilities and raise both international competitiveness and the impact of North-West Europe SMEs in this global market as the USA are far ahead - Codex4SMEs will directly address this challenge.

Biobank Graz (BBG): Lead partner for Sample Access within the Codex4SMEs network

Biobank Graz (BBG) of the Medical University Graz is the largest academic and clinical biobank in Europe and member of the European biobanking network BBRMI-ERIC and the Austrian network BBMRI.at. Biobank Graz offers its services not only to scientists at Medical University of Graz, but also to scientists from academia and industry worldwide. Due to its leading position in automation of collection and storage of samples, the maintenance of highest sample quality is one of the key features of Biobank Graz.

Biobank Graz has been specifically designed to support the needs of biomedical research in the fields of human diseases, drug discovery and public health. Advanced modern biomedical research that aims at improved therapeutic and diagnostic methods and strategies eventually culminates in personalized medicine and requires an integrated infrastructure which links biobanks with the required IT-infrastructure, analysis platforms, systems biology and other biological resources.

Biobank Graz currently contains approx. 20 million samples from approx. 1.2 million donors representing a non-selected patient group characteristic of Central Europe from patients treated at the LKH University Hospital Graz during the last 30 years. Biobank Graz comprises both population-based and disease-focused collections of human biological material. Samples include a large number of FFPE blocks stored at room temperature, fresh frozen cryo samples stored in the vapour phase of liquid nitrogen as well as a large variety of body fluids (e.g. serum, plasma, whole blood, buffy coat, urine and liquor) stored at minus 80°C. Collection of fluid samples as well as all storage facilities are based on innovative automated or semi-automated systems. Biobank Graz is serving approximately 300 projects requests each year.

Contact information

Regional partners for application related questions:

- University of Leicester (and subpartner),UK
- BOM Holding BV, NL
- WestBIC, IE
- Innovation Quarter (and subpartner),NL
- Medicen Paris Region, FR
- BioRegio STERN Management GmbH, DE
- CÙRAM, IE
- Integrated Biobank of Luxembourg, LU

Point of contact for Sample Access related questions:

Biobank Graz: E: codex4smes@medunigraz.at

General Workflow of Sample Access

Applicant requirements:

European SMEs in the field of (Companion) Diagnostics for Personalized Medicine may apply to participate in the project via the regional partner network of the Interreg NWE Codex4SMEs project. They are welcome to submit an application.

As a **North-West-Europe (NWE) approach**, SMEs from all over NWE and especially from one of the **participating partner regions** (see table of partners below) will receive preferential treatment for the offered biobank services.

Region/Country	Partner	Contact email address
Regions of Stuttgart, Tübingen, Reutlingen, Neckar Alb | Germany	BioRegio STERN	codex4smes@bioregio-stern.de
North Brabant | The Netherlands	BOM Business development & foreign investment BV	codex4smes@bom.nl
Zuid-Holland | The Netherlands	InnovationQuarter	codex4smes@innovationquarter.nl
France	MEDICEN Paris Region	codex4smes@medicen.org
Ireland	WestBIC	codex4smes@westbic.ie
Ireland	CÚRAM Centre for research in Medical Devices	codex4smes@curamdevices.ie
United Kingdom	University of Leicester/Medilink	
Luxembourg	Integrated Biobank of Luxembourg	codex4smes@ibbl.lu
Austria	Biobank Graz at the Medical University of Graz	codex4smes@medunigraz.at

SMEs can't apply for the same support scheme twice if they received access to the relevant service already. However, they can apply for different services and combine them.

If access to samples is required for the applicant's research project the respective documents and application forms described later in this guideline

have to be submitted directly to Biobank Graz (BBG) which is the responsible partner for sample access within the Codex4SMEs network.

Sample material from up to 20 patients is available per project application. (If this number remains below the specific needs for your research project please describe your specific needs and the requested number of samples in the project application form).

To assess if the required sample material is available before starting the project application you may request an initial availability status directly from Biobank Graz for a sample availability statement.

- The localization of requested sample material and accompanying requested data are internally reviewed by Biobank Graz. This review process can take more than one month. (The Codex4SMEs Jury will review incoming applications on a weekly basis).

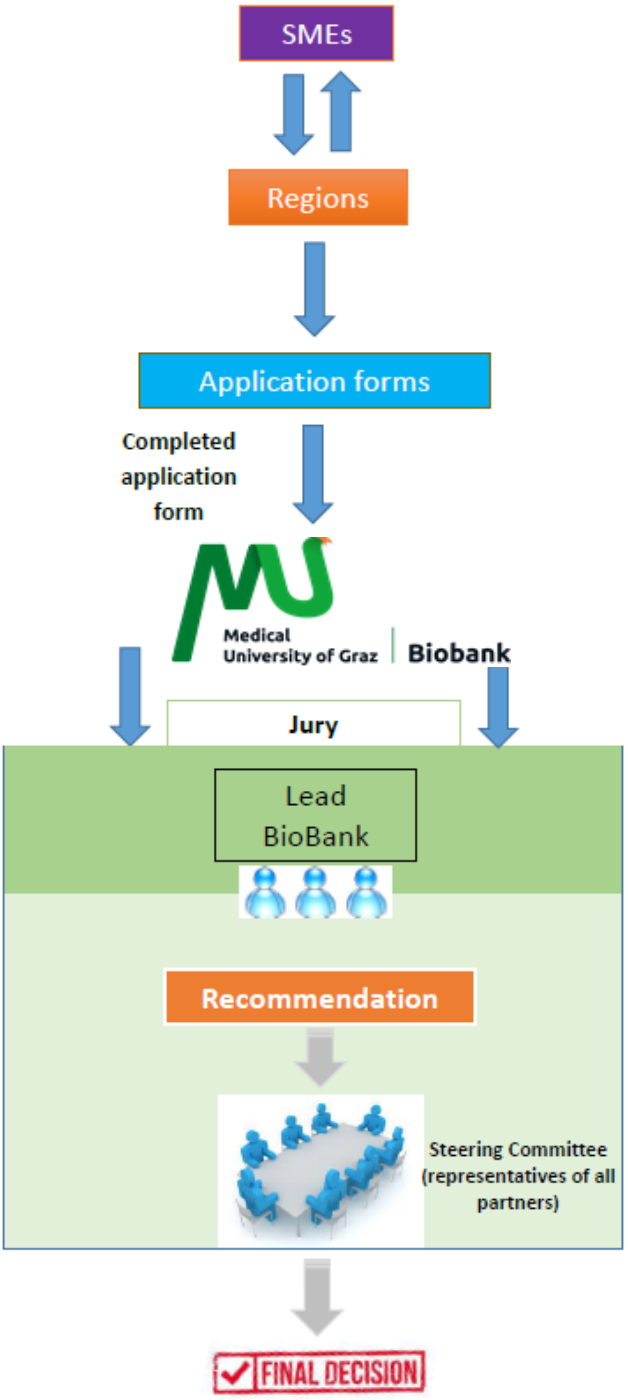
- If sample material is available from Biobank Graz the submitted project applications are reviewed on a weekly base.
- The Codex4SMEs Jury is consisting of three staff members of each biobank (IBBL and BBG) and of the members of the Steering Committee, composed of representatives of each partner institution of the Codex4SMEs project.
- The Jury approves applications based on the input given by the evaluation of the two biobanks.
- Please note: Project partners are already bound to secrecy by a partnership agreement.

Applicants have to agree to this procedure during the application process. Agreement to this procedure is given through the respective application form.

Data Protection Regulation

All data submitted to a respective project partner of the Codex4SMEs consortium will be treated according to the EU General Data Protection Regulation (GDPR).

General Workflow Overview



How-To Access Samples from the Biobank Graz:

Sample materials available from the Biobank Graz consist of body fluids and tissue, such as formalin-fixed paraffin-embedded (FFPE) slides, cryo-conserved tissue and liquid samples (blood, plasma, serums, etc).

For further information regarding available sample material please contact Biobank Graz directly via the application process or take a look on the BBMRI Catalog (link below) where sample collections of BBG are listed. For further information regarding Biobank Graz please visit our homepage.

Links:

BBMRI CATALOG
http://catalog.bbmri.at/biobank.html?_cachebust=2.6.2&bbid=MUG

BIOBANK GRAZ
http://biobank.medunigraz.at/en/

Principle Sample Access Application types:

- **Project type I: Project request for a pilot study**
- **Project type II: Project request for a research project**

Project type I

- **Project request for a pilot study**

Pilot studies are projects including samples from a maximum number of five patients. Per patient only one kind of sample material can be provided.

This type of project allows the applicant to test or establish a new method. An ethics vote is not needed for this type of projects as the number of samples is very limited. Results gained from a pilot study must not be published!

1. An applicant has to fill and submit the project application form for primary project initiation. The availability of samples and additional requested data is evaluated by Biobank Graz (This review process can take more than one month depending on the project's complexity).

2. If required samples and data are available from the Biobank Graz the applicant has to fill and sign all required forms and declarations listed in the project application form.

All required forms and documents have to be submitted to initiate the project application process:

Summary:

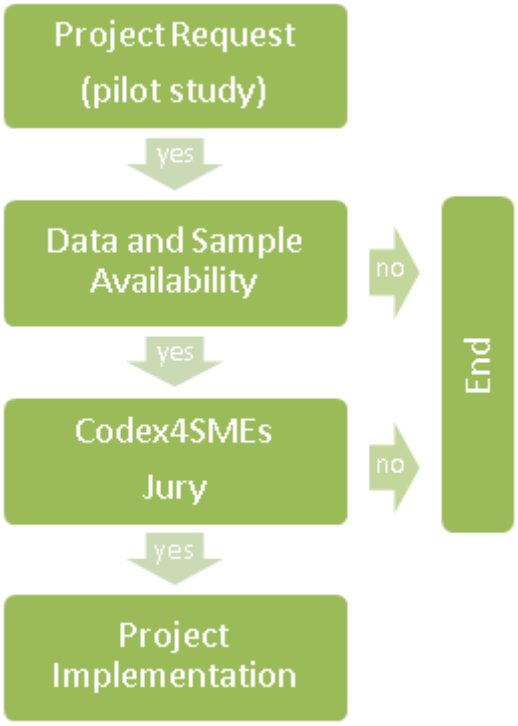
A complete research project application includes:

- Project application form including De Minimis declaration

3. Approval of the project
   3.1. After submission of all relevant forms and meeting the listed requirements, the Codex4SMEs Jury will evaluate the project application.

4. An approval of the Codex4SMEs Jury allows the implementation of the project. As a prerequisite for sample transfer the Material transfer agreement (MTA) of the Biobank Graz has to be accepted.

Pilot study Workflow



Project type II

- ## Project request for a research project

Research projects include samples from more than five patients and require several steps to be approved.

1. An applicant has to fill and submit the project application form for primary project initiation. The availability of samples and additional requested data is evaluated by Biobank Graz (This review process can take more than one month depending on the project's complexity).

2. If required samples and data are available from the Biobank Graz the applicant has to fill all required forms and declarations listed in the project application form.

3. A positive ethics vote or a finalized application for ethics approval (approval has to be positive for project initiation) is a prerequisite for a successful project application. The ethics vote has to include a statement that declares the usage of samples from Biobank Graz and a declaration if samples with or without informed consent (IC) will be used for the research project. (Please note, applications for ethics approval can be submitted to the local ethics committee in Graz with support of BBG).

4. The study protocol of the research project has to be submitted to the Biobank Graz.

5. Contributing partners of the research project have to be declared

6. De Minimis declaration has to be filled and signed if applicable.

7. Employees in charge of samples adoption, signing delivery notes etc. have to be listed

All required forms and documents have to be submitted to initiate the project application process:

Summary:

A complete research project application includes:

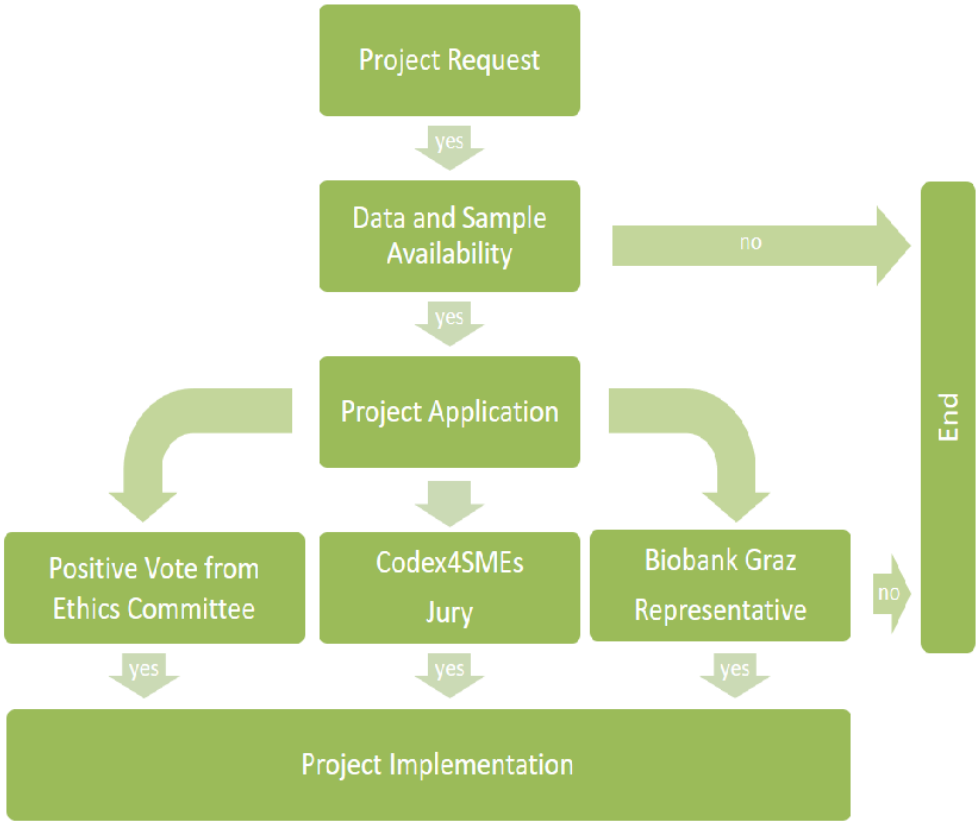
- Project application form
- Ethics proposal
- Ethics vote (if available)
- Study protocol
- De Minimis declaration
- List of contributing partner
- List of employees in charge of sample adoption, signing delivery notes etc.

8. Approval of the project

8.1. After submission of all relevant forms and meeting the listed requirements, the Codex4SMEs Jury and the Biobank representative will evaluate the project application.

8.2. An approval of both Codex4SMEs Jury and the Biobank representative allows the implementation of the project. As a prerequisite for sample transfer the Material transfer agreement (MTA) of the Biobank Graz has to be accepted.

Research project Workflow



Sample Transfer

If an applicant is granted access to samples via the Codex4SMEs project the requested and available sample material can be transferred to the respective applicant. All cost for samples are covered by the Codex4SMEs project.

Please note, that shipment cost for sample transfer is not included. The SMEs may use a transport service of their choice or if there are no preferences an adequate transport service will be chosen by BBG. Shipment costs have to be refunded by the SMEs. If shipment of samples for a biomarker validation at IBBL is needed all samples will be directly transferred from BBG to IBBL.

Post Project "De Minimis" Processing

After the service has been finalized the beneficiary SME will receive a notification letter by its regional contact person of the project. Additional information regarding De Minimis Regulation can be found in the next section.

Additional information on De Minimis regulation

1 *De minimis*[1]

The *de minimis* rule allows for State aid relevant activities, but only those that are of minimum financial importance, up to a threshold in a rolling three year period, subject to certain administrative steps being taken. The amounts of *de minimis* aid granted to a single undertaking within the last 3 financial years cannot exceed €200,000[2].

1.1 Single undertaking

Single undertaking means all enterprises having at least one of the following relationships with each other:

(a) one enterprise has a majority of the shareholders' or members' voting rights in another enterprise;
(b) one enterprise has the right to appoint or remove a majority of the members of the administrative, management or supervisory body of another enterprise;
(c) one enterprise has the right to exercise a dominant influence over another enterprise pursuant to a contract entered into with that enterprise or to a provision in its memorandum or articles of association;
(d) one enterprise, which is a shareholder in or member of another enterprise, controls alone, pursuant to an agreement with other shareholders in or members of that enterprise, a majority of shareholders' or members' voting rights in that enterprise.

Enterprises having any of the relationships referred to in points (a) to (d) through one or more other enterprises shall also be considered to be a single undertaking.

Please note that enterprise means here any undertaking performing economic activity.

1.2 Exclusions

De minimis granted by NWE Programme (both direct and downstream) does not apply to:

(a) aid granted to undertakings active in the fishery and aquaculture sector,
(b) aid granted to undertakings active in the primary production of agricultural products;
(c) aid granted to undertakings active in the sector of processing and marketing of agricultural products, in the following cases:
i. where the amount of the aid is fixed on the basis of the price or quantity of such products purchased from primary producers or put on the market by the undertakings concerned;
ii. where the aid is conditional on being partly or entirely passed on to primary producers;
(d) aid to export-related activities towards third countries or Member States, namely aid directly linked to the quantities exported, to the establishment and operation of a distribution network or to other current expenditure linked to the export activity;
(e) aid contingent upon the use of domestic over imported goods.

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[1] Commission Regulation (EU) No 1407/2013 of 18 December 2013 on the application of Articles 107 and 108 of the Treaty on the Functioning of the European Union to *de minimis* aid Text with EEA relevance, http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1458746162354&uri=CELEX:32013R1407

[2] In the road freight transport sector this threshold is decreased to €100,000 and will not apply for acquisition of road freight transport vehicles.