Guide to Biobanks in Sweden

–Access to Samples for Research and Clinical trials
Foreword

The information in this guide is aimed at research that requires access to samples – research initiated by a medical technology or pharmaceutical company, a county council/region or a university.

Sweden has good conditions and a good climate for research and clinical trials including human biological samples (hereinafter referred to as samples). There are national quality registers, national health data registers and biobanks with millions of samples that can be linked for research, upon approval from an Ethics Review Board. Samples are important for the development of diagnostic markers, new pharmaceutical drugs and personalized treatments for a variety of diseases, such as rheumatic disease, inflammatory disease, diabetes, cardiovascular disease, psychiatric disease and many more. By combining collected samples with information on the patient, care in Sweden has been improved. In addition to the immediate benefit for patient care and treatment, there is awareness that access to samples provides opportunities for research generating new knowledge of causes of diseases, diagnoses, diagnosis classifications, improved treatments, new pharmaceutical drugs and vaccines. In cancer research, stored tissue samples have enabled cancer care to develop significantly, through better characterisation of various cancer tumours, and how these characteristics affect prognosis and need for treatment. This has led to improved diagnostics and new pharmaceutical drugs and treatments as well as personalized therapies. An association between certain HPV viruses and cancer was found by comparing stored samples collected in gynaecological healthcare for cervical cancer. This insight led to changes in the cervical cancer screening program and the development of the HPV vaccine, which today is included in the child vaccination program. Within healthcare and universities, there are comprehensive and well-defined sample collections for care and research, scientific and clinical competence, established service functions for administrative, regulatory and operational support in planning and implementation of different types of studies, as well as joint enforcement of the Swedish Biobanks in Medical Care Act. An important prerequisite for Sweden’s successful biobanking is the positive attitude to research on part of the public and patients. A collaboration has been established between county councils/regions, medical universities and industry organisations regarding a national infrastructure for biobanks to facilitate research and development.

ABOUT THIS GUIDE
This guide describes biobanks in Sweden and how samples can be used in research and clinical trials. The document provides guidance on what researchers and companies should do to get access to existing samples in Swedish biobanks, as well as requirements for collecting new samples from persons in Sweden. It also provides guidelines for researchers and companies regarding biobank services available for the collection of new samples and the release of samples. The purpose of this guide is to contribute to making shared resources available and ensure that support is used optimally and with respect for the integrity of patients and donors.
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In the spring of 2017 a new agreement was reached between county councils/regions with university hospitals and universities with a medical faculty, for enhanced collaboration to support biobank infrastructure for healthcare, academia and industry (medical/technical/pharmaceutical). To implement the agreement, the association “Biobank Sweden” was established (former National Biobank Council and BBMRI.se).

The agreement originates from the county councils/regions responsibility for healthcare, and the universities responsibility for research and education, as well as the universities need to collaborate with healthcare in order to fulfil their responsibilities. The goal of the extended collaboration is to build a joint, improved and sustainable national biobank infrastructure for healthcare, academia and industry with the best conditions for both national and international collaboration. The enhanced collaboration aims at producing science based on biobank samples for the benefit of public health and the individual patient. Biobank Sweden also aims to facilitate the enforcement of the Swedish Biobanks in Medical Care Act.

In May 2017, the industry organisations Läkemedelsindustriföreningen (LIF), Swedish Medtech, Swedish Labtech and SwedenBIO also joined the main agreement with the purpose of increasing the competitiveness of Swedish medical research and development, and with the aim to promote the development of healthcare. A good collaboration between industry, healthcare and universities promotes coordination of resources made available through the existing collaboration between biobanks, on both a national and local level, as well as within the healthcare regions.

Biobank Sweden consists of a National Steering Committee, with representatives appointed by the county councils/regions and universities with a medical faculty and with representation from industry organisations, a strategic preparatory group, two working committees for regulatory and operative biobank service and a national network with the county councils’/regions’ biobank coordinators (Swedish: “Biobankssamordnare”). In Biobank Sweden, which is supported by the Swedish Association of Local Authorities and Regions, representatives from patient organisations are also included.
2. Biobanks in Sweden

In Sweden, there are 7 universities with a medical faculty and 21 county councils/regions, each being their own principal. Together, they have nearly 250 biobanks containing over 150 million samples and approximately 3-4 million samples are added each year. The most extensive biobanks and largest quantity of samples are stored in the county councils’/regions’ 200 biobanks (estimated 90% of all stored samples). In these biobanks, there are sample collections stored from the early 1900s, but it was not until the mid-1960s that samples began to be collected to a greater extent. In addition to biobanks at county councils/regions and universities, there are biobanks at private healthcare providers, private laboratories, medical and medical technology companies as well as biobanks at some authorities (approximately 200 in total). Several of the biobanks that are not included in the healthcare sector are so-called e-biobanks (or virtual biobanks), implying they contain only sample data and no samples. The e-biobanks are established with the purpose of following the requirements of the Biobanks in Medical Care Act regarding clinical pharmaceutical trials.

Sweden has a uniform healthcare system consisting of 21 county councils/regions, where of 7 have university hospitals (university county councils/regions). Through agreements, there are established collaborations between the 7 university hospitals and the 7 academic universities with a medical faculty. In
the healthcare sector, a well-established infrastructure for the handling of samples and information, as well as biobanking for care, has long been established. When the same infrastructure is used for research, it is cost-effective, patient safe, quality assured, and in accordance with the regulations covering the healthcare sector, provides increased accessibility across the country. Therefore, universities and the healthcare sector collaborate on biobanking of research samples, which means that samples for research often, but not always, are stored in the county councils/regions biobanks with a university hospital. The latter also applies to the 14 county councils/regions that do not have a university hospital. Sweden’s 21 county councils/regions are divided into six healthcare regions within which there is extended collaboration and joint functions, such as the Regional Biobank Centre (RBC Swedish “Regionalt biobankscentrum”).

Register of biobanks

The Health and Social Care Inspectorate (IVO) is the authority that supervises the Swedish Biobanks in Medical Care Act and manages a register of all biobanks in Sweden. Principals (the legal entity responsible for a biobank) who decide to establish a biobank must notify the decision to IVO. When biobanks are registered at IVO, they are assigned a unique number that is important for traceability and should be stated in biobank applications for access to samples. The registry does not contain data on individual samples, but contains administrative information about the biobank, such as who the principal is, who the biobank custodian is (person responsible for the biobank) as well as the purpose of the biobank.
3. Existing sample collections in Swedish biobanks

Samples collected for healthcare purposes

The largest sample collections consist of samples collected in the healthcare sector for care, diagnostics and treatment (approximately 95% of all stored samples). They are stored in the county councils/regions biobanks or in the biobank of a supplier of laboratory services with which the county council/region has an agreement. The largest sample collections for healthcare purposes are within clinical pathology and cytology (approximately 90%), followed by clinical microbiology, the PKU biobank (approximately 5% in total) and clinical genetics, immunology, and chemistry. Materials primarily stored are tissue (blocks and sections), cells/smear cells, blood/plasma/serum and cerebrospinal fluid (CSF). These are materials used for analysis/diagnostics in laboratories for healthcare purposes. These samples can be used for follow-up of an individual’s diagnosis and course of disease, quality assurance, development work and education. They are also important in the investigation of genetic diseases. Stored samples are also valuable in research and clinical trials.

In order to gain access to samples in any of these sample collections, an approved biobank application, approved ethical vetting and consent from the donor in accordance of the approval from an Ethics Review Board are required. See heading 7. “Biobank application”.

For information on healthcare samples, contact the biobank coordinator (Swedish “Biobankssamordnare”) in your county council/region (contact information can be found at www.biobanksverige.se).

What information is registered about healthcare samples?

Information about samples collected for healthcare purposes is stored in the Laboratory Information System (LIS) of the county council/region in question. The LIS information is a part of a patient’s medical record. The content of LIS may differ depending on the type of IT system and the clinical discipline. A LIS for clinical pathology/cytology can contain data regarding: donor’s identity linked to the internal ID number of the laboratory, data regarding consent linked to samples, date of sampling, when samples arrived at the laboratory, at what clinic samples were taken and what clinic the results should be sent to, type and quantity of sample material, what examinations and analyses as well as routine-, special and immunostainings have been made, who has sought samples in the IT system, who has handled samples and what they did, diagnosis as well as entity responsible for diagnosis.

The county councils/regions are in the process of establishing a joint register for traceability of stored samples, called the Swedish Biobank Registry (SBR). The purpose of the SBR is to find samples for the purposes of: changed consent, patient care, and research and clinical trials. The SBR is under construction and estimated to be available for use from 2020.

Samples collected for research purposes

In Sweden, there are several large sample collections and cohorts that specific researchers or research groups have completely or partially collected. These sample collections can be based on geographical areas, specific age groups and/or diseases or conditions. In some of the sample collections, persons or patients are monitored over time, which is of great value since it enables detection of risk factors or disease markers. The research sample collections mainly consist of blood/plasma or serum, but may also include RNA/DNA, urine, saliva or tissue. Consent from patient/donor is collected during sampling, and approval from an Ethics Review Board is also required for the samples to be used for research. Samples may also be available for research groups and companies that have not been part of the collection of the samples. In order to gain access
to samples that are part of research collections, approved ethical vetting and obtained consent is required in addition to the biobank application, and the applicant also has to obtain permission from the group or committee granting access to the respective samples. See heading 7, “Biobank application”. The Ethics Review Board will also decide if new consent from the research participant is required before an existing sample can be used in the specified research project. Using existing samples for research has practical advantages. It may shorten the start-up time of the research project and the samples have already been characterized and quality controlled.

Information about existing cohorts can be found at www.biobanksverige.se. Biobank coordinators (Swedish “Biobankssamordnare”) or biobanks with operative services can also provide guidance on

existing cohorts (contact information can be found at www.biobanksverige.se)

**What information is registered about samples collected for research?**

Information on samples collected for research purposes initiated from a research institution or a healthcare provider can be stored in the laboratory information management system (LIMS). LIMS exist at almost every university hospital/university and in some healthcare regions. Data registered in LIMS regards handling of samples from sampling until storage. There is usually no data on analysis results or diagnostics, as such data is stored in another system by the researcher.
4. Collecting new samples

In healthcare clinics, samples are taken and managed daily within the framework (often with requirements of standardisation) of a specific research project or clinical trial according to the instructions of each individual project/trial. This is particularly important in international studies where samples need to be collected in the same way regardless of which country the sample is taken in. For more information on advisory functions and support in planning clinical studies, see www.kliniskastudier.se.

Collecting new samples with known and high quality

A routine for the collection and handling of liquid-based research samples has been implemented in the infrastructure of the routine healthcare for collecting and handling samples at a number of hospitals in Sweden. This existing high-quality and long-term infrastructure with competent staff around the clock, standardisation, traceability and documentation ensures that samples collected for research purposes maintain the same high quality as samples collected in the routine healthcare. Regardless of what purpose samples are collected for, they automatically receive traceability of the handling, as well as information regarding how and when the sample has been handled. In other words, the routine, called healthcare integrated biobanking for research (SIB) means that the collection and handling of research samples use existing structures in the routine healthcare.

The routine means that sampling can be ordered in the electronic referral at the examining clinics, which allows sampling to be made by qualified personnel on site when a patient is in for care. Each step is automatically recorded and the time from sampling to freezing is 0–4 hours. The samples are frozen in smaller aliquots; thereby the whole sample does not have to be thawed when analyses are to take place. This ensures the quality of the remaining materials. Sampling and biobanking are done in accordance with the Swedish Biobanks in Medical Care Act and the Ethical Review Act, and with the patient’s or donor’s consent. For more information about what hospitals have implemented SIB, see www.biobanksverige.se.
5. National registers and quality registers

Because Sweden has population-based registers with personal data, there are many reliable data sources for register research in Sweden. Sweden's system of unique personal identity numbers (Swedish: “personnummer”) gives the opportunity to link data about individuals from different data sources. Registries of interest for research can be divided into public governing registers, quality registers in healthcare, biobanks and research generated data.

Information about registers in Sweden

Registerforskning.se

The Swedish Research Council has compiled information about different registers, current legislation, and how data for research is requested. The information is aimed at researchers who want to use data from registers in their studies. For more information, see www.registerforskning.se.

Register Utiliser Tool (RUT)

The Register Utiliser Tool (RUT) has been developed to show register information on a meta-level to simplify register research. The work is in accordance with the Swedish Research Council's mission from the government and has been done in close cooperation with Swedish authorities holding registries.

The purpose of RUT is to facilitate the identification and evaluation of registers and their variables and provide structured information about variables with associated metadata in the registry linked to the tool.

RUT is currently being expanded, with the goal of getting every governing register, quality register, biobank, and research database frequently used in register-based research linked to this tool.

National governing registers

National governing registers of great interest for research are population and socioeconomic registers, health data registers as well as population based surveys and studies based on interviews. Most of these registers are available at Statistics Sweden (SCB) and the National Board of Health and Welfare (SoS). There are also registers of interest for research e.g. at the Swedish Public Employment Service (Arbetsförmedlingen), the Swedish National Council for Crime Prevention (Brottsförebyggande rådet), the Swedish Social Insurance Agency (Försäkringskassan) and the Swedish Defence Recruitment Agency (Rekryteringsmyndigheten).

The register authorities need to be contacted to get register data for research. Some register authorities have a dedicated point of contact for data requests, whereas others have none. The register service of the National Board of Health and Welfare provides support for researchers who wish to order statistics or individual data for research purposes. The micro data unit of SCB helps researchers who want to order micro data.

If a researcher needs data from several authorities, Statistics Sweden (SCB) can provide registers for certain other authorities, which can interact regarding release of samples.

The rules of the Public Access to Information and Security Act determine whether register data can be released. Each authority takes an independent decision to release data for which they are responsible.

Registers in universities

Research databases/cohorts

There are registers created within specific research projects, so-called research generated registers. There are also large research databases, which can be considered a kind of infrastructure. The purpose is to serve several research projects, sometimes even within different scientific disciplines. From an international perspective, Swedish cohorts are very useful as outcome events can be obtained from public registers, such as the Prescribed Drugs Register, the In-Patient Register, the Swedish Cancer Registry and the Cause of Death Register, whereby a complete follow-up of all individuals can be obtained. The same principles as for samples collected for research purposes usually apply for access to these data. Information about some of
these registers is available at the Swedish National Data Service (in Swedish, SND) (www.snd.se). Information about several larger cohorts is also available at the Swedish Cohort Consortium (www.cohorts.se).

Registers in County Councils/Regions

National Quality Registers
Today, there are 108 National Quality Registers operating under the healthcare system with an authority in a county council/region as the personal data controller (CPUA). These registers have been established in specific areas to systematically and continuously develop and ensure the quality of healthcare. The registers are used for improvement work and follow-up of healthcare as well as for research. The quality registers contain personal data regarding healthcare, such as diagnosis, treatment, and results of treatment.

The registers differ in quantity and setup and therefore differ in suitability for research. Therefore, it is recommended to contact the register manager or other representative of the steering group of the register as early as possible. To access data from a national quality register, it is required that the CPUA decides that data may be disclosed. For more information, see www.kvalitetsregister.se.
6. Rules and regulations for biobanks

Samples and associated data to be used in research are covered by the Ethical Review Act (2003:460), the General Data Protection Regulation, GDPR (2016/679), and the Swedish Biobank in Medical Care Act (2002:297) as well as related regulations.

A requirement for identifiable samples to be used in research is an approval from a regional Swedish Ethics Review Board in accordance with the Ethical Review Act. The ethical vetting also involves a review of whether processing of personal data in the project takes place in accordance with the provisions of the GDPR (Article 9).

The Swedish “Biobank in Medical Care Act”

The Swedish Biobank in Medical Care Act makes it possible to use samples in healthcare and treatment, national or international research, and development in a way that guarantees the patient's or donor's integrity.

What samples does “Biobanks in Medical Care Act” apply to?

It applies to all samples in Sweden, with the following exceptions,

- **Routine samples** for medical care (activity operating under the provisions of the Health and Medical Service Act or the Dental Care Act) stored for < 2 months after analysis. Please note, this exception does not apply to samples taken within healthcare with the purpose of research or clinical trials.
- If the donor takes samples outside the healthcare sector.
- **Anonymized** samples (samples that neither directly nor indirectly can be linked to the sample donor).
- Samples that are a result or a product.
- Samples taken outside the borders of Sweden.

What does “Biobank in Medical Care Act” entail?

The Swedish Biobank in Medical Care Act regulates how samples taken within a healthcare provider’s operations may be used in research and in clinical trials. Among other things, the law entails;

- A biobank is established by a decision by a principal owner (a legal entity, e.g. a healthcare provider, a unit for research or diagnostics, a public research institution or a pharmaceutical or a medical technology company). The principal designates a biobank custodian (person responsible for the biobank) and reports the decision to establish a biobank to IVO. IVO then assigns the biobank a unique number.
- Every sample taken within a healthcare provider's operations is included in the primary sample collection in the healthcare provider's biobank. This applies regardless of whether the collection takes place on behalf of another principal’s operations or if the samples will be discarded directly after analysis.
- Samples in a biobank must be coded and safely stored so that there is no risk of samples being accidentally destroyed or accessed by anyone unauthorised.
- A regional Swedish Ethics Review Board must approve research projects (if applicable, including research participant information and consent form) in accordance with the Ethical Review Act.
- The biobank custodian handles applications for access to samples for research. For a biobank custodian to approve an application, certain conditions are set: an approval in accordance with the Ethical Review Act and consent from the donors that the samples be used for the specific purpose.
- Samples can be made available for research or clinical trials by remaining in the biobank and being analyzed on site, by being sent for analysis or investigation, or by being released from the healthcare principal’s biobank to the principal in whose project the research will be conducted.
- The Biobank in Medical Care Act also applies to samples sent for analysis abroad. If samples are to be sent for analysis abroad, the biobank custodian of the biobank sending the samples, together with the recipient abroad, must establish the terms that the samples are to be returned or destroyed when they are no longer needed for the purpose for which they were sent.
• Sample collections released from healthcare (secondary sample collection) may not be released again. However, such samples may be sent for a specific measure, such as investigation or analysis.

• Samples that are being sent should normally be coded. If a donor’s personal data is to be sent at the same time as a coded sample from the donor, they must be sent in such a way that the personal data cannot be linked to the sample (pseudonymized).

• Samples from a biobank may not be released or transferred for profit.

• Transfer of a biobank, or parts of a biobank, or closure of a biobank must be approved by the IVO.

Information and consent

Provisions regarding consent from the donor and providing information to the donor (or person who can consent on the donor’s behalf) in the Swedish Biobanks in Medical Care Act state that:

• The donor (or person who will decide on the donor’s behalf) must be informed that a sample may be saved and for what purpose, and consent to this.

• Consent must be documented in the patient’s medical record.

• The donor has the right to withdraw consent at any time. This also applies to samples taken and stored before the Swedish Biobanks in Medical Care Act came into force. If the withdrawal applies to all types of use, the samples shall be destroyed or anonymized immediately (i.e., as soon as possible). This requires that each individual sample, that the Biobank Act applies to, can be traced and found.

• Samples may not be used for purposes other than those covered by prior information and consent without the donor being informed and consenting to the new purpose. But an Ethics Review Board may grant exceptions to this rule. If samples are to be used for a new purpose related to research or clinical trials, the information and consent regarding the new purpose must meet the requirements established in the prior research ethics trial. If a donor has previously submitted a withdrawal of consent stating that samples may not be used for the purpose of research, the samples may only be used for research if the donor changes the statement and agrees to the project.

• If samples for research purposes are to be sent for analysis abroad, the donor must be informed and consent to this. If coded samples are to be sent to a country within the EU/EEA (or other countries with adequate protection, see www.datainspektionen.se), it may be enough to provide information that samples may be sent abroad for analysis. However, if samples are to be sent to third countries, it is required that the information clearly states that samples may be sent for analysis to countries outside the EU/EEA.

• In research cases, the principal investigator for the project must ensure that the information and consent requirements are met, unless another agreement is made with the biobank where the samples are stored.

More information about the Swedish Biobanks
in Medical Care Act and research participant information can be found at www.biobanksverige.se and www.epn.se.

**Biobank responsibility of samples in studies**

All samples covered by the Swedish Biobanks in Medical Care Act must be established in a sample collection in a biobank with a biobank custodian who has been appointed by the principal of the biobank. Universities and county councils/regions have agreements resulting in universities often storing their sample collection in the county councils/regions biobanks. The healthcare principal biobank custodians therefore have formal responsibility for the sample collections. In sponsor-initiated studies, it is more common for samples to be released from the healthcare principal’s biobank to the company’s biobank in Sweden or to a biobank in Sweden with which the company has an agreement. In cases where the company does not have a biobank in Sweden, the principal, by agreement, may continue to be responsible for the samples. This means the healthcare principal will be given continued responsibility for the samples during the research project, including traceability of samples when consent is changed. Thus, county councils/regions establish a Material Transfer Agreement (MTA) with the receiving laboratory that regulates how the samples will be handled during and after the study (see 6. Biobank application).

**Proposal of a new Swedish “Biobanks in Medical Care Act”**

On behalf of the government, an investigator has made a proposal for more expedient regulation of biobanks in Sweden. Among other things, the directive of the investigation included reviewing how the use of biological materials in biobanks, in combination with various registry data such as population-based registers, can be made available with the aim of internationally strengthening Sweden’s competitiveness in high quality medical research while maintaining protection of personal integrity. The proposal was submitted in January 2018. A new Swedish Biobanks in Medical Care Act can come into force in 2019 at the earliest.

**Other legislations**

**Processing of personal data**

The Swedish Biobanks in Medical Care Act regulates how samples may be used, whereas usage and release of personal data is regulated by the Public Access to Information and Secrecy Act (OSL) as well as regulations in the Personal Data Act and the Patient Data Act. The Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation/GDPR) entered into force on May 25, 2018. The GDPR aims to strengthen individuals’ rights by regulating protection of the fundamental rights and freedoms of physical persons with regards to the processing of personal data, as well as to harmonize data privacy laws across the EU to enable the free movement of personal data within the EU. The law provides detailed rules on processing personal data. The GDPR regulates processing of personal data in a personal data
controller’s operation, unless special rules exist in the Patient Data Act (2008:355). The Patient Data Act regulates automated processing of personal data (patient records) in the healthcare sector. Personal data processed in a research study is governed by the provisions in the GDPR.

Samples and personal data in research
Research concerning sensitive personal data, which involves a physical intervention on a research participant or relates to biological material that has been taken from a living or deceased person and can be traced to that person, in accordance with the Act concerning the Ethical Review of Research Involving Humans (2003:460) (Ethical Review Act), may only be conducted if approved by an Ethics Review Board. The purpose of the Ethical Review Act is to protect individuals and human integrity when research is conducted. The ethical vetting also involves a review of whether processing of personal data in the project is in accordance with the provisions of article 9 in the GDPR. Article 9 of the GDPR means that specific categories of personal data (sensitive personal data), such as genetic or biometric data or health data, may be used for research purposes only if a special protective measure is taken, e.g., ethical vetting.

How may clinical data be released?
Release of clinical data from a biobank, i.e., data from a patient’s medical record (such as information about examinations results from analyses or diagnosis), require approval from an Ethics Review Board as well as consent from the patient. If the patient’s consent cannot be obtained, e.g., if the patient is deceased, decision-making incapable or if an exception from the consent rule has been given by an Ethics Review Board for another reason, access to a medical record may be given after assessment of harm from the healthcare provider. An assessment of harm means that the person responsible for release of data from a patient’s medical record assesses whether or not the release is of harm for the patient or the patient’s genetic relatives.

It is stated in the Public Access to Information and Secrecy Act (2009:400) who is responsible for the assessment of harm. The Act states that if an employee of an authority, in accordance with the procedure or due to specific decisions, is responsible for the care of a record (such as a medical record), it is primarily that person who determines if the record can be disclosed. In case of doubt, the employee must let the authority investigate if it can be done without unnecessary delay. Within healthcare, it is primarily the person responsible for the patient’s medical record who is responsible for assessing the risk of harm. This is usually the head of operations at the healthcare unit/clinic where the information is available.

Regarding clinical trials of pharmaceutical drugs and medical technological products
In clinical trials (clinical pharmaceutical trials or clinical trials of medical technological products when the product is to be tested on humans), an approval from the Swedish Medical Products Agency is required. For more information, see www.lakemedelsverket.se.

New EU Regulation on clinical pharmaceutical trials – came into effect on 16 April 2014 (expected to be implemented in the autumn 2019)
On 16 April 2014 the Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use and repealing Directive 2001/20/EC (EU regulation on clinical pharmaceutical trials) was adopted. The purpose of the EU regulation is to simplify the authorisation procedure within the EU and make the application process faster. In Sweden, the government has assigned the Swedish Medical Products Agency and the Regional Ethics Review Boards the task to create structures and forms of cooperation to ensure that decisions on access can be made in accordance with the regulation. To ensure that the process of cooperation is well-functioning when the regulation is to be applied, a joint pilot project has been initiated, which means that
applications included in the pilot project are handled nationally in a process that replaces the regular handling of the Swedish Medical Products Agency, the Ethical Review Boards and the Regional Biobank Centres (RBC).

New EU Regulation on medical technological products – went into effect on 26 May 2017 (with gradual implementation)

There is also new legislation for medical technological and in vitro diagnostics (IVD) products. Two new EU regulations have been adopted to gradually replace the current three directives. The purpose of the regulations is to establish a powerful, open, predictable and sustainable rule and regulation for medical technological and IVD products that guarantees a high level of health and safety and supports innovation. For more information, see www.lakemedelsverket.se.

7. Biobank applications

To facilitate the management of requirements of the Swedish Biobanks in Medical Care Act, Sweden’s biobanks have, through Biobank Sweden, joint principles and application forms for access to biobank samples for research and clinical trials, as well as functions for regulatory service in formatting and signing of biobank agreements (see heading 10. Advice and practical support). Principles and application forms are administered, updated and established by working committee 1 on behalf of Biobank Sweden (for regulatory biobank service) and can be found at www.biobanksverige.se. See heading 12. Agreements and instructions. Research can be conducted both on newly collected samples for a specific study (according to study protocol or SIB) and on existing samples either taken in a healthcare context and stored for diagnostics, care and treatment or taken for research purposes). For newly collected samples, sampling can start as soon as the biobank application has been approved. Samples can be made available either by releasing the samples to the research principal’s biobank in Sweden or by letting the samples remain in the healthcare principal’s biobank. Access to samples is regulated in the biobank agreement. Irrespective of if samples remain in the principal’s biobank or are released to the research principal’s biobank, samples can be sent for analysis to a recipient biobank in Sweden or abroad.

Release of samples: Upon release of samples, the responsibility and right to use them is transferred from the healthcare principal to the research principal or company. In accordance with the Swedish Biobanks in Medical Care Act, IVO must be notified of any release of samples. Released samples are referred to as secondary sample collections. Secondary sample collection samples may not be released further but can be sent on for analysis. Release of samples requires that the recipient has a biobank registered at IVO. More information can be found at www.ivo.se.

Send for analysis: For certain purposes, samples may be sent for analysis, from both primary and secondary sample collections to a recipient in Sweden or abroad without it being considered a release of samples. The samples are sent to the recipient for a specific purpose, and are not placed at the disposal of the recipient.

What is required in order to use newly collected or existing samples in research?

• Decision of a biobank custodian (authorized representative of the principal’s biobank) based on a submitted biobank application together with applicable appendices.
• An approved ethical vetting application in accordance with the Ethical Review Act. The approved ethical vetting application, the decision
and any completions to the biobank application should also be submitted. This makes it possible for the biobank custodian to review whether the application corresponds with the approval from the ethical vetting. If the biobank application concerns existing samples, an assessment will also be made regarding availability of sufficient material to grant access (for further information, see paragraph “Special assessment for access to existing samples”).

• Normally, explicit consent of the patient or donor is needed, but the Ethics Review Board can grant exceptions to the established requirements for consent. If consent is required, it is important to append the research participant information approved by the Ethics Review Board, as well as the consent form.

Please note, guidance on biobank agreements can be given by the county councils’/regions’ biobank coordinators or RBC before the decision by the regional Ethics Review Board (see heading 10. Advice and practical support). However, the formal decision by the biobank custodian (or authorized representative of the biobank) is taken when the ethical application is approved.

### Which application form should I use?

Guidance regarding what application form to use can be found in Biobank Sweden’s document “K2. Form selector”. An interactive form selector can be found at www.biobanksverige.se. See heading 12. “Agreements and instructions”.

Guidance on how researchers and companies should act, what documents to use and what appendices should be provided can be found in document “C2c. Checklist for researchers” and “C2d. Checklist – start research project based on biobank samples”. Documents can be found at www.biobanksverige.se

Instructions for completion of biobank applications can be found in document “K4. Instruction for completion of form L1” and “M3. Instruction to MC N1a”. Documents can be found at www.biobanksverige.se.

### Where can I learn more?

E-learning regarding the Swedish Biobanks in Medical Care Act: the Swedish Academy of Pharmaceutical Sciences, the National Biobank Council (now Biobank Sweden), ASCRO and LIF have developed a basic training course in the Biobanks in Medical Care Act and handling of samples in clinical trials. For more information, see www.lakemedelsakademin.se.

### Types of biobank applications for access to samples.

1. Biobank application in accordance with the multicentre principle: use in multicentre studies with newly collected samples for the specific study to be released to the receiving biobank in Sweden. In these cases, one application (form N1a-N1b) can be submitted to the Regional Biobank Centrum (RBC) located in the healthcare region where the ethical vetting was conducted. Setup of sample collections are established in the participating county councils’/regions’ e-biobanks and are released through the biobank application where the RBC director, by proxy of the county council’s/region’s e-biobank custodian, establishes a sample collection for the specific study.

2. Biobank application regarding single centre studies, newly collected samples not to be released or applications regarding existing samples (form L1a with applicable appendices). The biobank custodian (authorized representative of the biobank) where samples will be established or are stored will approve such an application.
Agreement if samples are to be sent for analysis

In cases where responsibility for samples will remain in the healthcare principal’s biobank and the samples will be sent for analysis for research purposes, a Material Transfer Agreement (MTA) must be signed by the receiving biobank/laboratory before the samples are sent. Among other things, the MTA regulates how the receiving laboratory is allowed to handle samples, especially in cases when they are no longer needed for the purpose for which they were sent. To simplify the process, the county councils/regions use a joint form for MTA (form L2a) in cases where county councils/regions are responsible for samples sent abroad for research or clinical trials. The MTA form can be found at www.biobanksverige.se, form L2a (abroad) and L2b (within Sweden).

How does the application process work?

When the biobank application has arrived at a RBC or a county council’s/region’s biobank coordinator (or the biobank in question), the application is processed as described below.

Processing of the biobank agreement at the biobank

Regardless of whether the samples are newly collected or existing, an administrative examination of the biobank application and applicable appendices is conducted when the application arrives at an RBC or reaches the county council/regions biobank coordinator (or the biobank in question). The administrative examination assures that:

1) the biobank application is complete and includes all relevant appendices, as well as it being the most current version,
2) information about samples in the application for ethical vetting is the same as the study participants have been informed of,
3) information about samples in the application for ethical vetting and the study participant information corresponds with the biobank application.

Special assessment for access to existing healthcare samples

A special assessment is made for biobank applications for access to existing samples (taken in a healthcare context and stored for diagnostics, care and treatment, or taken and stored for research purposes).

When applying for existing healthcare samples, in addition to an administrative review, an assessment by the biobank custodian (alternatively, medically responsible individual/expert on their behalf) is made at the biobank regarding the requested material, assuring

1) that a reasonable amount is requested in relation to the demand,
2) that the material is expected to meet the researcher’s needs.

An expert’s assessment that the request is reasonable is particularly important since samples are a finite resource for individuals, healthcare and research. This assessment requires the approved application for ethical vetting as well as applicable biobank
After a biobank application has been reviewed, the biobank custodian makes a decision. The samples are then collected from the potential research participants/patients at the biobank. As the biobank application applies to existing samples, an approval of the biobank application does not guarantee access to all desired tissue material. This is due to the fact that the sample material must be sufficient for the patient's presumed care and may not run out, except in cases where there are strong reasons to believe this course of action will benefit the patient.

- In each case, it is confirmed that the donor has given consent to samples being used for research and that sufficient material is left for the patient's diagnostics, care and treatment.
- It is also ensured that the quality of the remaining sample material does not deteriorate if access is giving to the sample material.
- In exceptional cases, if there is limited material, scientific expertise may need to be consulted to ensure the possibility of future research involving the same material.

Please note, there may also exist samples available for research in existing sample collections/cohorts for research (see below).

Special assessment for access to existing research samples (in existing sample collections/cohorts for research)

When applying for existing research samples, in addition to an administrative review of the biobank, an assessment by the sample collection controller (alternatively by a steering group linked to the sample collection controller, or scientific experts appointed by the research principal) is made to ensure the scientific question is sufficiently important for the material to be used. In addition, it is assessed if a reasonable amount is requested in relation to the demand and if the material is expected to meet the researcher's needs. Instructions for how to apply for access are given by respective research sample collection. Samples collected for research purposes have been collected with the patient's consent and it is important that the biobank assesses that the consent covers the new inquiry. A requirement for access is an approved application for ethical vetting for the research to be conducted, as well as applicable biobank appendices (form L1a, L1b or L1c).

Estimated time for handling and decision of a biobank application

The handling time depends on how complete the application is when submitted, the need for advice and revisions, and the number of other applications simultaneously processed by the RBC, biobank coordinator or biobank. Applications are handled in the order in which they reach the biobank.

The RBC or the county council's/region's biobank coordinator can provide information about estimated handling time.

In cases where a fast inclusion of a patient in an ongoing clinical trial is needed, there is a routine set by the county council's/region's biobank coordinators (BBS) so the application is prioritized, and the inclusion and the biobank application are handled in parallel. The routine requires that an approved application for ethical vetting exists and that an approved biobank application is granted by the county council/region where the study is conducted. For more information, contact the biobank coordinator in the county council/region where the study was approved. Contact information can be found at www.biobanksverige.se.

Quantity, time and degree of access

The quantity of samples that are made accessible and the amount of time samples may be used in the research project are factors directed by the approval of the Swedish Ethics Review Board, consent from the donor and the agreement (biobank application) with the biobank where the samples are stored. These documents regulate quantity, time (duration of the specified project), and degree of access (access during the study period or also after completion). Please note, for extended access to samples, consent to save the sample after completion of the study must exist.

Compensation and charges

- In accordance with the Swedish Biobanks in Medical Care Act, samples or parts of samples stored in a biobank may not be released or transferred for profit. On the other hand, the biobank or the research sample collection controller may have a charge to cover its costs.
- There are several charges to take into account when accessing samples (newly collected or existing), e.g. costs for sampling, handling of samples, starting fee (on setup of healthcare
integrated biobanking, SIB), storage and retrieval of samples, as well as taking out and preparing existing samples, and administrative charges such as establishing agreements, sending samples and records. Contact the biobank coordinator or the biobank for more information about costs.

Access to anonymized material for quality certification

Anonymized samples required for quality certification may come from many types of sources, e.g. existing tissue samples from clinical pathology, existing liquid-based samples from clinical microbiology, tissue samples from transplant donors or specific samples collected for the quality certification. There is legal basis for accessing all types of sources, but in practice it is not easy to know what is required in a specific case. Researchers/companies wanting access to anonymized material for quality certification should keep the following in mind;

• A trial by an Ethics Review Board is required. In many cases, this means that an advisory statement is given if the Ethics Review Boards define that the material is not to be used for research. An approval or advisory statement is required for the operations to be able to address the issue and feel confident that the law is being followed.
• Consent from the donor is required when collecting specific newly collected samples.
• For existing samples, the donor must not have restricted consent.
• Use the biobank application form (L1 with applicable appendices) for access to existing samples or for collecting new samples.
• In cases of new collection of specific samples, a more comprehensive service may be required. Contact the county council’s/region’s biobank coordinator for more information (www.biobanksverige.se).

8. Ownership and publication

Ownership of samples

In legal terms, it is not meaningful to talk about ownership of samples in Swedish biobanks. The foundational principle is that of joint opportunity to utilize Swedish biobanks. Swedish biobanks should be considered an important common health resource. There are biobank custodians with obligations in accordance with current laws. These laws also allow rights, such as for the sample donors to give their consent after receiving relevant information about the sampling.

Publishing and reporting of results

In order to maintain and further develop the Swedish biobank resources, it is valuable that researchers using samples and data from biobanks and registers make their results available. When releasing samples, biobanks or research sample collections often have the requirement to be mentioned in the acknowledgement upon publication in scientific articles. The purpose is to identify published research results where biobank samples have been used. In addition, when using research sample collections, it often means that the researchers responsible for the sample collection have participated in the design of the study and data retrieval to the extent that they should be offered co-authorship when publishing results.

Today, feedback from research studies or clinical trials is very unusual, and better feedback would add value to the biobanks. In addition, authorities that grant funding for infrastructure development for research, require that biobank operations that have received funds are mentioned in the acknowledgement.

The biobank service and infrastructure available for research is a joint cooperative measure and resource. Researchers and companies using biobank samples are expected to contribute to increasing the value of biobanks.
9. What can I do to facilitate the application process?

- Prepare well ahead of time.
- Read the information about access to samples as well as the information provided in this guide (also found at www.biobanksverige.se).
- Use existing instructions and checklists – complete biobank applications result in shorter turnaround time (available at www.biobanksverige.se).
- Contact the biobank coordinator or RBC for advice and guidance as early as possible.
- If samples are to be sent for analysis abroad, append a signed MTA (form L2a) together with the biobank application if a county council/region will be responsible for the submitted research samples.
- Material is a finite and shared resource. Plan the amount of material carefully and do not ask for more material than needed for the study.
- In order to enhance your and/or your organisation's knowledge of using biobank samples in research, take advantage of available resources such as biobank training (e-learning) at the Swedish Academy of Pharmaceutical Sciences. Courses are frequently organized within county councils/regions, healthcare regions and universities (advertised on www.biobanksverige.se).

10. Advice and practical support

Biobank Sweden has service and expanded support regarding access to samples for research or clinical trials. Contact information can be found at www.biobanksverige.se.

**Regulatory biobank questions and biobank agreements**

Each county council/region has introduced functions for guidance and examinations of biobank agreements with the aim of streamlining the process and completing the documents before they are sent to the biobank for a decision. Several places also offer advice on how to complete research participant information documents and the biobank section in applications for ethical vetting, as well as aid in designing and establishing biobank agreements.

For advice on biobank applications/establishment of biobank agreements, Material Transfer Agreements (MTA), biobank section in applications for ethical vetting and research participant information, please contact;

- Within each county council/region: the county council’s/region’s biobank coordinator (BBS).
- Within each healthcare region: Regional Biobank Centre (RBC). Particularly regarding agreements under the multicentre principle (form N1a).
- General questions regarding agreements and regulatory questions regarding the Swedish Biobanks in Medical Care Act can also be sent to info@biobanksverige.se

**Practical sample handling and collecting new samples**

Every county council/region with a university with a medical faculty have introduced functions for guidance and practical support regarding sample collection, handling of samples, access to samples, etc. Guidance at university hospitals and universities is provided by the operative biobank service. If needed, contact;

- Within each county council/region: the county council’s/region’s biobank coordinator (BBS).
- Within each university county council/region and University: Biobank facilities for extended operative biobank service.
- If it is unclear where questions

**Planning of studies including access to existing healthcare samples**

If access to existing samples is needed, it is advisable to include (or consult with) representatives of the clinical profession (e.g. pathologist), preferably in the planning of the study, so the requests are reasonable and can be expected to answer the question at issue. There are established procedures for access to existing healthcare samples in every county council/region. For more information, contact your county council’s/region’s biobank coordinator.
11. Agreements and instructions

Agreements and instructions can be found at www.biobanksverige.se.

Information about access to samples
- C2c. Checklist for researchers
- C2d. Checklist – start a research project based on biobank samples
- K1. Principles on access to samples for research (only available in Swedish)
- K2. Form selector
- K3. Example of information for research participants (only available in Swedish)

Biobank agreement and instructions for – single centre studies, newly collected samples not to be released or applications regarding existing samples.
- K4. Instruction for completion of L1: Access to sample collection
- L1. Access to sample collection and personal data for research
- L1a. Appendix: Information about existing clinical samples in pathology and cytology biobanks
- L1b. Appendix: Information about existing liquid-based samples in biobanks
- L1c. Appendix: Information about existing samples in the PKU biobank (only available in Swedish)

Agreement when samples are to be sent for analysis within Sweden
- L2b. Agreement on samples sent for analysis within Sweden (only available in Swedish)

Agreements when samples are to be sent for analysis abroad
- K5. Information about AGREEMENTS on the transfer of biological material (Material Transfer Agreement, MTA)
- L2a. MTA-AGREEMENT on the transfer of biological materials

Biobank agreement and instructions for – newly collected samples to be released
- M3. Instruction for completion of the multicentre form
- N1a. Access to newly collected biobank samples in multicentre studies
- N1b. Appendix B – principal investigators included in the study
- N2. Supplement to multicentre study application
- N3a. Report on completed sampling in multicentre studies
- N3b. Appendix 1: Report on completed sampling (only total number of individuals/site)
- N4. Signing of power of attorney

Contact information

Email addresses and phone numbers can be found at www.biobanksverige.se.
## 12. Planning

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<td></td>
<td>For advice on biobank questions in an application for ethical vetting, please contact the biobank coordinator (BBS)/RBC (see heading 10). For advice on the biobank application, please contact the biobank coordinator (BBS)/RBC (see heading 10). For technical advice, please contact the operative service (see heading 10). Please keep in mind; The biobank application can be prepared simultaneously with the application for ethical vetting, but a decision cannot be made until the application for ethical vetting is approved. Tips; If newly collected samples with high quality are needed in accordance with SIB (see heading 4), please contact the operative biobank service or the biobank coordinator (BBS) (see heading 10). If existing samples are required, it is useful if a clinical representative is involved in the planning (e.g. pathologist).</td>
<td>Requirements; • Approved application for ethical vetting. • Information for research participants with forms for informed consent signed by patient/donor (unless the Ethics Review Board decides that collection of consent is not required). • Biobank application, including relevant appendices (see headings 7 and 12). Applications can be done either by the multicentre principle or be sent to each biobank separately (see heading 7). Please keep in mind; Incomplete biobank applications will prolong the time before a biobank custodian can make decisions. Tips; RBC offers administrative review of biobank agreements for existing samples from several biobanks. The purpose of this is to facilitate for applicants and involved biobanks. See <a href="http://www.biobanksverige.se">www.biobanksverige.se</a>.</td>
<td>Requirements; • Approved biobank application, completed using the national biobanks application forms (see headings 7 and 12). Please keep in mind; • Samples must be pseudonymised. • If samples are sent within Sweden for analysis from a biobank at a hospital, – establish agreement L2b with the analysing laboratory. • If samples are sent abroad for analysis from a biobank at a hospital – establish L2a with the analysing laboratory. Please note, in cases where samples are not released from the healthcare principal’s biobank, append L2a/L2b to the biobank application if samples are to be sent for analysis. If samples are released, the receiving biobank is responsible for making sure that L2a/L2b or equivalent is established when samples are sent.</td>
<td>If terms and conditions exist in the approved application for access to samples – remember to mention the biobank or the research sample collection in the acknowledgement when publishing the results.</td>
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<td>What type of sample/material is needed for the study? Are newly collected samples needed (see heading 4) or are there samples already collected for the purpose of care or research (see heading 3).</td>
<td>See <a href="http://www.biobanksverige.se">www.biobanksverige.se</a> to find information, instructions etc. E-learning is available via the Swedish Academy of Pharmaceutical Sciences</td>
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**WORKING GROUP FOR ELABORATION OF THIS GUIDE:**
Karolina Antonov (Läkemedelsindustriföreningen), Gunilla Bergström (RBC Sydöstra sjukvårdsregionen), Sonja Eaker (Beredningsgrupp Biobank Sverige), Malin Hollmark (Swedish Medtech), Östen Karlsson, (Läkemedelsindustriföreningen), Hasse Knutsson (Sveriges Kommuner och Landsting), Chatarina Larsson (Uppsala universitet), Pål Resare (Sveriges Kommuner och Landsting).

**EDITORIAL:**
Jessica Seger (RBC Uppsala Örebro), Hemma Hvitfeldt (RBC Västra Götaland).
Appendix 1. Vocabulary

**Biobank:** An organized unit responsible for one or more sample collections taken in healthcare and stored for more than two months after analysis (the exception does not apply to samples taken for research) and can be traced to a certain person.

**E-biobank:** A registry at a healthcare provider containing information about samples taken for research studies that are released to a research principal/equivalent directly after sampling. The e-biobank serves as a virtual primary sample collection, i.e. it only contains administrative data about what study sample collections were collected for, and to what biobank samples were released. There is no information about individual persons or sample results.

**Sample:** Biological material from a living or deceased person or fetus, regardless of the chemical composition of the sample (organs, solid and liquid tissue, cells and cell lines, genes or parts of genes and other forms of biological material).

**Sample collection:** Collection of samples with at least one common characteristic. Biobanks generally contain one or more sample collections.

**Primary sample collection:** Sample collection included in a biobank established in a healthcare provider’s healthcare operations in Sweden.

**Secondary sample collection:** Sample collection released from the biobank responsible for the primary sample collection. Samples from a secondary sample collection may not be released further but can be sent for analysis within Sweden or abroad.

**Anonymized:** Measure causing the origin of a sample to neither directly nor indirectly be traced to the person or fetus a sample derives from.

**Coding:** Measure that replaces directly identifying data with a code so the origin of a sample can only indirectly be traced to the donor from whom the sample derives.

**Pseudonymisation:** Processing of personal data resulting in the data no longer being attributed to a specific individual without using additional information, provided that the additional information is kept separately and is subject to technical and organisational measures that ensure that personal data are not attributed to an identified or identifiable physical person.

**Healthcare integrated biobanking (in Swedish, SIB):** Healthcare integrated collection and handling of liquid-based samples for research with an aliquoting process implemented in the regular healthcare infrastructure.
Appendix 2. Roles and Services

Sweden has a comprehensive national service and collaboration structure in the biobank sector. The association Biobank Sweden is described on page 5. The key features are described below.

Principal of a biobank: Every biobank has a principal. Only a legal entity can be principal of a biobank, e.g. healthcare provider, university, pharmaceutical company.

Biobank custodian: Every biobank has a custodian, who is designated by the principal, and has operative responsibility for the biobank, making sure that the requirements of the Swedish Biobanks in Medical Care Act are enforced. The biobank custodian is responsible for the existence of routines for destruction or anonymisation of samples, testing applications for access to samples for research, deciding on the establishment of sample collections and release of samples, and signing biobank agreements with an applicant (responsible researcher/primary investigator) and, in applicable cases, receiving biobanks. However, in many places in Sweden, it is the biobank coordinator in the county council/region who administratively reviews the application for access to samples before a decision is made.

Biobank coordinator (in Swedish, Biobankssamordnare, BBS): Sweden’s county councils/regions have chosen to delegate responsibility of coordination of the principal’s/principals’ biobanks to a biobank coordinator. Biobank coordinators offer researchers and companies advice on the Swedish Biobanks in Medical Care Act, biobank applications and biobank services. It is primarily the biobank coordinator in the county council/region where a study is to be conducted that should be contacted for questions on biobanking, access to existing healthcare samples, and existence of research samples/cohorts or application forms. They can also provide advice regarding biobank questions on the application for ethical vetting and patient information before submission to the Ethics Review Board.

Operative biobank service for research: Available in all county councils/regions, and includes support for planning of study, collection, handling, storage, retrieval of samples and IT support for a sample collection. At university hospitals/universities, there is Extended operational biobank service, with additional resources for researchers in planning and implementing a study involving biobank samples.

Sample collection controllers for research sample collections/cohorts: All sample collections or cohorts saved for research purposes have a sample collection controller, or some sort of steering group, that decides on access to a sample collection/cohort before a formal decision on access is made by the biobank custodian.

Sample service coordinators: located at the university hospitals/universities with extended biobank service. They provide support in the planning and start-up of research studies that will be collected on several sites in accordance with healthcare integrated biobanking.

Regional Biobank Centre (RBC): There is an RBC in each healthcare region in Sweden (six in total). RBC is a service- and centre of excellence that provides guidance and support to pharmaceutical companies and the public regarding the Swedish Biobanks in Medical Care Act. They work according to the multicentre principle regarding access to newly collected samples that are going to be released. The RBC is also responsible for administering, updating and establishing Biobank Sweden’s joint documents and website.

Contact information can be found at www.biobanksverige.se
Appendix 3. Definitions of entities responsible for a project

Different regulations result in different definitions.

**Principal (legal entity) responsible for the project:**

- Clinical pharmaceutical trial/medical technological products
  - **Sponsor:** An individual, company, institution or organisation that takes responsibility for the initiation, management and setup of financing of a clinical trial.

- Ethical vetting
  - **Entity principally responsible for research (research principal):** A government authority or a physical or legal entity under whose auspices the research is conducted.
  - Please note, when applying for ethical vetting, it must also be stated whether the research is commissioned and in such cases who the principal is, e.g. a company (clinical pharmaceutical trial or trial of other new products), an organisation or an authority.

**Principal/primary investigator:**

- Clinical pharmaceutical trials/medical technological products
  - **Principal investigator:** An investigator who is the responsible leader for a team of investigators who conduct a clinical trial at a clinical trial site. If the clinical trial has multiple trial sites/medical centres or clinics (multicentre), one investigator is appointed to coordinate the work (coordinating investigator).

- Ethical vetting
  - **Researcher with primary responsibility for the complementation of the project (principal contact).** Responsible for ensuring that those locally implementing a project have sufficient competence to conduct the project and are familiar with “Good Clinical Practice” (GCP), in the interest of the research participants’ safety. If several responsible research bodies are involved, or if several researchers within the same responsible research body are cooperating on the same project, one researcher is appointed principal investigator, and is the contact person for the ethical vetting board.

**Researcher/investigator:**

- Clinical pharmaceutical trials/medical technological products
  - **Investigator:** An individual responsible for the conduct of a clinical trial/investigation at a clinical trial site/investigation site.

- Medical technological products
  - **Researcher** locally responsible for conducting the project.

**Research participant:**

- Clinical pharmaceutical trials
  - **Subject:** An individual who participates in a clinical trial, either as recipient of an investigational medicinal product or as a control person.

- Medical technological products
  - **Subject:** An individual who participates in a clinical investigation.

- Ethical vetting
  - **Research participant:** A living person who is the subject of the research.

**REFERENCES:**

- Läkemedelsverket.se
- Lag (2003:460) om etikprövning av forskning som avser människor och Vägledning till ansökningsblankett (www.epn.se)
Appendix 4. Research samples not covered by the Biobanks in Medical Care Act

On 1 January 2019, a new exemption was introduced into Chapter 1, Section 3, Paragraph 4 of the Biobanks in Medical Care Act (2002:297) regarding samples taken for research but not to be stored in a biobank. This change is due to the adaptation of Swedish legislation to the EU Clinical Trials Regulation.

1. What does this exemption mean?

This exemption means that the Biobanks Act does not apply to samples intended for research that are analysed within six months of the sampling date and that are immediately destroyed following their analysis. Both conditions must be met.

The exemption only applies to studies that have received ethical approval after 1 January 2019. This is because both ethical approval and consent must correspond to the handling of samples.

If samples are collected for a biobank or used for any other purpose than that for which they were taken, the Biobanks Act will apply.

Examples of samples covered by the exemption rule

- Samples analysed directly (e.g., ward, clinic, healthcare centre) and that are destroyed immediately following analysis.
- Routine tests in clinical chemistry, for example, blood count, electrolytes, CRP, etc. analysed at a local laboratory and destroyed immediately following the analysis.

Biobank Sweden recommends that any researcher/company unsure whether the samples in a study are covered by the exemption or not should contact the county council/regional biobank coordinator, or a Regional Biobank Centre (RBC) for advice.
2. What is meant by “immediately following the analysis”?  

Biobank Sweden defines immediately following the analysis, as a maximum of 1–2 days after an analysis has been carried out for the purpose for which samples were taken, for example a patient’s blood values allowing study medication to be administered. That is to say, the time required to ensure that the analysis has been performed correctly and does not need to be re-done.

3. Is an application for ethical approval needed?  

Yes. An application for ethical approval is required regardless of whether a sample is covered by the Biobanks in Medical Care Act or not. Research involving a physical intervention on a research subject or involving biological materials created from a living or deceased person that can be traced to an individual must only, in accordance with the Act concerning the Ethical Review of Research Involving Humans (2003:460) (Ethical Review Act), be conducted where ethical approval has been granted.

This means that ethical approval is always required when biological samples will be used for or handled in research.

4. Is an MTA necessary if samples are sent for analysis?  

If a local authority/region is the research principal:
Yes. A Material Transfer Agreement (MTA) is always required if a sample will be sent for analysis, regardless of whether it is covered by the Biobanks in Medical Care Act or not.

If another principal is the research principal:  
Biobank Sweden recommends that an MTA is always established if samples will be sent for analysis, regardless of whether the sample is or is not covered by the Biobanks in Medical Care Act. However, note that it is not always the case that a separate MTA needs to be established. For example, a separate MTA is not necessary if the agreement between sponsor and central laboratory corresponds to the contents of the MTA.

About MTA:  
The Agreement (MTA) is used to regulate how samples may be handled by the recipient; how the recipient may handle samples and sample code and how samples and sample codes must be handled when they are no longer needed for the agreed purposes.

Note: Samples sent must be coded or pseudonymised.
If personal data will also be sent to the recipient, a data processing agreement must be established.
between the personal data controller and recipient (see document K5).

5. **Recommendation in case of doubt**

Should there be any doubt as to whether the sample falls under the exemption rule or not, Biobank Sweden recommends that samples be handled as though they were subject to the Biobanks in Medical Care Act. This means describing their retention in the application for ethical approval and in the information for research subjects and establishing a biobank agreement with the biobank custodian at the healthcare provider where samples will be collected.

The same recommendation applies if samples are to be sent for analysis to a recipient outside of their own principal and there are no procedures or templates to be able to establish an MTA.

6. **What happens if there is an error, i.e. if there is no ethical approval and biobank agreement for retention of samples?**

The research study will always encounter problems if it becomes clear at a later stage that samples in a study are to be covered by the *Biobanks in Medical Care Act*, but are described in the application for ethical approval and in the consent form such that handling is within the scope of the exemption. Should errors arise, there is a risk of the research study having to discard the samples, even if they are still required for the study.

This would mean that **there is no valid ethical approval** for retention, consent, and that samples are not stored in a biobank in accordance with the *Biobanks in Medical Care Act*.

The *Biobanks in Medical Care Act* provides special rights for sample donors and special protection for samples. This implies, for example, that the donor must be asked if samples may be stored in a biobank and informed about the right to withdraw or limit their consent previously given. There must always be a biobank custodian appointed by the principal. The custodian has special responsibility to ensure that samples covered by the law are fully traceable.

The Swedish Ethical Review Authority will assess whether samples may be stored in a biobank for research purposes. Furthermore, only the Swedish Ethical Review Authority (or the Ethics Review Appeals Board) may authorise exemptions from the requirement for information and consent for samples to be retained in a biobank.
What can the applicant do if at a later stage, it turns out that samples in a study in fact falls under the Biobanks in Medical Care Act? For example:

- if samples are destroyed within 6 months, but not immediately following the analysis,
- if samples will be stored for more than six months,
- if samples will be used for other analyses than those described in the application for ethical approval

**Within 6 months of sample collection**

The project has two options:

1. A supplementary application is sent to the Ethical Review Authority. The Ethical Review Authority needs to be informed when the sample collection has taken place. If the application is approved by the Ethical Review Authority, the sample collection will be set up (registered) in a biobank at the healthcare provider where the samples were taken and suitable agreements can be established retrospectively, depending on whether samples will be analysed on site, sent for analysis or released. 
   
   *Note:* The application needs to be sent to the Ethical Review Authority in good time, as the decision must be made by the Authority before the 6-month period from sample collection has passed. As a guideline, the supplementary application should be sent to the Ethical Review Authority at least 2 months before the 6-month period from date of sampling has passed.

2. Samples are discarded (destroyed or anonymised) immediately.

**After 6 months from sample collection**

The research principal has illegal sample handling and samples must be discarded (destroyed or anonymised) immediately.

**Read more**

More information about the changes and background can be found in the Government Bill Adaptations of Swedish law to the EU Clinical Trials Regulation, Govt Bill 2017/18:196. (https://www.regeringen.se/rattsliga-dokument/proposition/2018/03/prop-201718196/) (in Swedish)

**SUMMARY**

- The exemption for research applies to samples analysed within six months of their date of collection and destroyed immediately following the analysis. Both conditions must be met.
- Biobank Sweden defines "immediately following the analysis" as a maximum of 1-2 days after completion of the analysis, i.e., the time it takes to ensure that the analysis has been conducted correctly and does not need to be re-done.
- The exemption only applies to studies that have received ethical approval after 1 January 2019. This is because both ethical approval and consent must correspond to handling the samples.
- The exemption does not apply if the samples are collected for a biobank or used for any other purpose than that for which they were taken.
- Ethical approval is always necessary. Physical sampling and handling of samples is covered by the Ethical Review Act, regardless of whether the samples are covered by the Biobanks in Medical Care Act or not.
- If a sample will be sent for analysis, a Material Transfer Agreement (MTA) is always required, regardless of whether it is covered by the Biobanks in Medical Care Act or not.
- Problems may arise for the research study if it becomes clear at a later stage that samples in a study are to be covered by the Biobanks in Medical Care Act, but are described in the application for ethical approval and consent form such that handling is within the scope of the exemption rule. In some cases, a supplementary application to the Ethical Review Authority may be possible. Note that the Ethical Review Authority must have issued its decision on the supplementary application before the 6-month period from time of sampling has expired.
- Treat samples as though they are subject to the Biobanks in Medical Care Act if there is any doubt as to whether the sample falls under the exemption rule or not. The same applies if samples are to be sent for analysis to a recipient outside of their own principal and there are no routines or templates to establish an MTA.
Would you like to know more about the Biobanks In Medical Care Act?

Would you like to know about existing biobanks? Or learn more about research ethics? The following websites are recommended if you are looking for further information:

www.biobanksverige.se
www.1177.se

Legislative documentation can be found at www.riksdagen.se