M3. Instruction for completion of application N1a: *"Access to newly collected biobank samples and associated personal data in multicentre studies"*

This is an instruction to the template that shall be used by the researcher who shall initiate a multicentre study with newly collected samples where the sample collection shall be released (document N1a). The application shall be sent to a **Regional Biobank Centre (RBC).** Addresses to RBCs can be found at www.biobanksverige.se.

To which RBC shall the application be sent?	
For research studies with ethical approval from the Swedish Ethical Review Authority (approval after January 1, 2019).	The application shall be sent to the RBC in the healthcare region where the Research Principle/Principle Investigator is active.
For research studies with ethical approval from a Regional Ethics Review Board (approval before January 1, 2019).	The application shall be sent to the RBC in the healthcare region where the ethical application was approved.
Template includes:	
Application for access to newly collected biobank samples and associated personal data in multicentre studies	Specific terms for the multicentre principle; the samples shall be **newly collected** and shall be **released** to a recipient biobank. Complete application with both "*appendix A*" (in document N1a) and "*appendix B*" (document N1b) enclosed is required for approval.
Appendix A	Enclose appendix with Sweden's regions (in document N1a).
Appendix B	Enclose appendix with Principal Investigators involved in the study (document N1b). Information about Principal Investigators is needed because, according to the multicentre agreement, they are required to contact the e-biobank in their respective region regarding traceability of samples. The Biobank Act entitles a sample donor to withdraw a previously granted consent at any time, the healthcare provider and the e-biobank custodian are therefore obliged to ensure that samples can be traced back in a secure way.

Definitions 1

Release of samples
Responsibility for and the right to use the samples in question are transferred from the Healthcare Principal to the Research Principal**.** The samples are moved to a location outside the Healthcare Principal's operations and form a *secondary sample collection* at the Research Principal. A secondary sample collection may not be released further. The Healthcare Principal continues to be responsible for saving documentation regarding samples and to whom samples are released to make tracing possible.

E-biobank

In the multicentre principle, sample collections are released through an e-biobank at the Healthcare Principal. The RBC Directors have authorisation from the e-biobank custodians to make decisions regarding registry and release of sample collections into and from their respective e-biobank.

Private Healthcare provider

Please note that the multicentre principle can not be applied if there are only private healthcare providers in the study. For the multicentre principle to be applicable the Principal Investigator needs to be in a Swedish region, municipality or university, and at least one region needs to be included in the study. If an investigator from a private healthcare provider wants samples released from a region's e-biobank, a written authorisation between the private healthcare provider and the e-biobank is needed. The authorisation means that the sample collection is included as a primary sample collection in the region's e-biobank. Proposals on how to set up authorisations can be found at www.biobanksverige.se (document N4).

Multi-centre study concerns/relates to	
New application or a request for alteration of a previous application	Mark the box if the application relates to a **clinical trial**, **other study** *and* if it is an **alteration of a former application**. *There are two types of alterations:* 1. If it is an alteration of study content (for alteration of sample types, sites, principal investigator, investigators or sampling period see below), the entire application doesn't have to be filled in. Only information needed to identify the previous application has to be included, that is to say: • **RBC's ID** of the former application (can be found, when available, at the top of the previously approved biobank application) • **Name of the Study** • **Working title of the study** • **Study-ID** • **Swedish Ethical Review Authority reference number (dnr)** (before January 1 2019 Ethics Review Board) • and **the details that have changed since the previous application.** 2. If the alteration regards new samples, new principal investigator, new sampling period, addition of sites or investigators, fill in document N2:*"Request for alteration of multicentre study application, Appendix A + B"* An enclosed letter to and a decision from the Swedish Ethical Review Authority is required for both types of alterations. If any changes regard patient information, please enclose the version of patient information in question.

1. Details of research study	
Study title	Descriptive title without using classified information. Must accord with the title indicated in the ethical vetting application and in the information to study/research participant
Study working title	If the project has a working title it shall be mentioned here. Must accord with the title indicated in the ethical vetting application and in the information to study/research participant

Study-ID	For Clinical Trials, the Study-ID shall be stated. If study-ID's for other types of research studies are available, they should be filled in here as well. Must accord with the title indicated in the ethical vetting application and in the information to study/research participant
EudraCT-no	To be specified at drug trials. In order to identify clinical trials in Europe each clinical trial have a unique number (EudraCT number). For more information on the EudraCT number go to the Swedish Medical Products Agency's website (Läkemedelsverket) www.lakemedelsverket.se/english/
Decision from Ethical Review Authority (before January 1 2019 Ethics Review Board)	To use samples in a research study, approval from the Ethical Review Authority (before January 1 2019, Ethics Review Board) is required by law. Please note: An ethical approval is valid until further notice as long as the research has been initiated within two years of the approval coming into force and that a request for alteration of the ethical application is needed if the study has been altered in a way that the security of the research participants is affected or if the alteration in general can affect the risk/benefit assessment that has been done in connection with the previous review of the application (e.g. if a larger number of research participants is included, if a larger volume of samples is wanted or if a new method or new analysis will be conducted on already collected material). Specify in the biobank application: • the reference number from approved ethical vetting application. Enclose to the biobank application: • A copy of the signed ethical application and all alteration to said application, if any. • Study/research participant information. • Decision from the Ethical Review Authority (before January 1 2019, Ethics Review Board) including alteration, if any. Please note: During the process of reviewing the biobank application a comparison to see if the biobank application coincides with the approved ethical agreement, and in some cases also the research participant information, is taking place. To avoid delays it is important that the biobank gets the last version that is approved by the Ethical Review Authority (before January 1 2019, Ethics Review Board) or the last version that has been sent to the Ethical Review Authority for approval. If the complete ethical vetting application is not enclosed, at least decision and copies of following sections from the Ethnical review application must be submitted; *After January 1, 2019:* 1, 2, 3, 4.1, 4.2, 5, 6.2, 8.2, 9, 13.1, 14. If applicable, enclose appendix 4 and/or appendix 5. *Before January 1, 2019:* 1:1-1:6, 2:4, 2:5, 2:6, 4:1-4:2, 8, 9.

2. Healthcare Principal – Involved Biobank	
Specify the Biobank Principal/Principals	The Principal in the entity, where samples are collected, is the Healthcare Principal. The Healthcare Principals (regions) in question shall be selected with a cross in "*Appendix A"* (in document N1a). The samples are registered in the Healthcare Principal's e-biobank and then released to a recipient biobank as indicated in paragraph 6.

	If an investigator from a private healthcare provider wants samples released through a region's e-biobank, a written authorisation between the private healthcare provider and the e-biobank is needed. (see definitions 1).

3. Information about Applicant/ Research Principal	
Specify the Principal for the research study	Please note that the Research Principal specified here, must be the same as stated in the ethical application. A Research Principal can never be a person. Only a region, a Healthcare provider, a Pharmaceutical company or a Research Institution.
Principal Investigator/Researcher (Sample collection controller)	Specify the Principal Investigator for the study, according to the ethical application (the person who signed the application).
Other contacts	Specify contact details for other collaborators, for example one responsible for the local implementation of the study in case of several principals (e.g. an investigator, a coordinator or a research nurse).
Other responsible researchers	In "*Appendix B: Principal investigators included in the study"* (document N1b) the other responsible investigators shall be listed. Firstly, name and contact details of the Principal Investigator (alternatively the national coordinator). Then the other responsible researchers and collaborating investigators (e.g. research nurse, research coordinators etc.).

4. Describe sample collection	
Study period	Specify the dates when the study is scheduled to start and expected to finish.
Sampling period	If applicable, specify the date of the planned sampling (from first sample to the last). When the sampling period is over, it should be reported. Submit the notification of completion ("*Report on completed sampling in multi-centre studies*", document N3a) *with* "*Appendix 1; Final report*" ("*Appendix 1: Report on completed sampling*", document N3b), to the RBC which approved the release of biobank samples for the study.
Sample collection shall	Please select how the sample collection should be handled during and after the study(trial). Specify if the samples should be destroyed or saved. It is possible to select more than one option if parts of the sample collection are handled differently. If samples will be stored indefinitely after the study is completed, write "until further notice" instead of specifying numbers of years.

Samples in study	Describe content and volume of the sample collection and which samples are to be released. Information about which samples to be released is needed in order to report to IVO (the Swedish Health and Social Care Inspectorate) Describe type of tissue, blood, urine, cells. Specify the **total number of individuals in the study**. Specify **sample type** and **number of samples** (do not specify the method of analysis). The information filled in here must correspond to that indicated in the ethical application and the patient information. See **Example 1** below

Example 1: 4 blood samples and 2 urine samples per patient in the study.

Describe content and proportion e.g. type of tissue, cells/cell lines, blood, serum, plasma, cerebrospinal fluid (CSF), prepared DNA, urine, prepared DNA, urine etc:	No. of individuals	No. of samples
Blood	150	150 x 4=600 sample
Urine	150	150 x 2=600 sample

5. Handling of sample and personal data	
Access to personal data	State here if you want access to personal data in addition to code/pseudonym. If the answer is Yes – specify the information. See Definitions 2 below regarding personal data. Please note: The Biobank agreement only regulates access to personal data that is directly related to the sample. The agreement does not regulate access to any other personal data from the patient's medical records such as information about diagnosis, test results or received treatment. A decision of release of data from the patient's medical record for research purposes is taken according to local routine for confidentiality assessment.

Definitions: 2

Personal Data is any information relating to an identified or identifiable natural person. An identifiable natural person is a person that directly or indirectly can be identified, in particular by reference to an identifier such as a name, an identification number, location data, sample code/sample ID (if it can be traced to an individual), or one or more factors that is specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.

Information that relates to a name or an identification number is always personal data. Even information that does not point to an individual directly can be personal data if it in any way is possible to make the connection to a specific individual. An example can be when a lot of/or detailed information together can make it possible to make the connection to a person. Coded or encrypted information is also personal data as long as someone can make them readable and as a consequence identify individuals, i.e. as long as the code key still exists. All records with personal data shall be reported to the Personal Data Controller at the Principal.

Handling of sample and personal data before sample transport	Please note, since this agreement treats newly collected samples that immediately will be released it is the receiving Biobank Custodian that is responsible for the sample immediately after sampling.

Handling during study period	Describe how samples and personal data is handled during the study. Account specifically for international collaborations and sample handling overseas.
Handling after terminated study	Specify how samples and personal data is handled after termination of study, how long and where the samples will be stored.
Coding/pseudonymization	Specify how samples and personal data is coded, where the code keys are stored and who has access to the code keys.

6. Recipient biobank

State here information about the recipient biobank. The recipient biobank is responsible for the samples after release. Recipient biobank is found at the Research Principle (according to the ethics application) or at another Principal with which the Research Principal has an agreement. Specify the registration number from the Health and Social Care Inspectorate (IVO) and contact information to contact person and Biobank Custodian.

7. Main agreement (in case of clinical trials)

Mark the box if this agreement constitutes a supplemental agreement to the “Main Agreement” met between the region and the Company with regards to clinical trials.

8. Terms & Conditions

Transportation of samples	Specify who is responsible for the transportation of the samples and the costs.
Special terms	Specify if any special conditions exist.

9. Billing address (if applicable).

Regional Biobank Centre (Regionalt Biobankscentrum) take an administrative fee of 5000 SEK (w/o VAT) for handling the application and 500 SEK (w/o VAT) for alterations of the application. Specify the billing address here.

10. Conditions for release

1. Approval of the Ethical Review Authority (before January 1 2019 Ethical Review Board).
2. Samples may not be used for research other than specified in the ethical review application.
3. If samples, included in the sample collection are required for the care of the donor/patient, the samples shall primarily be used to meet care needs.
4. If samples included in the sample collection can advantageously be used in other research, which the Ethical Review Authority (before January 1 2019 Ethical Review Board) has considered and approved, may the Principal for the secondary sample collection issue approval for such procedure.
5. The Biobank Custodian at the recipient biobank is responsible, after release, for the samples' quality being secured and that the patient’s identity is protected.
6. Upon release of samples and personal data, there are requirements of how the samples’ and personal data’s identity designation (“Sample ID” and “Personal data ID”, respectively) shall be formulated. The code key linking "Sample ID" and "Personal data ID" with the patient's identity shall be stored with the region.
7. Released samples may not be released to third party.
8. Terms of consent on research studies with associated part-studies. If a research participant withdraws his/her consent from the principal study, the Responsible Investigator shall ensure that

the research participant is asked about withdrawal of consent of other associated studies that the research participant may be part of, as well.

9. Other:

11. Specific conditions for release

1. The responsible investigators shall **contact their region's Biobank Custodian immediately** to agree on the traceability of samples. If private healthcare providers are included, a power of attorney is necessary.
2. The Principal Investigator/Researcher must inform the Deciding RBC if the conditions for the study are materially changed (e.g. if new sites are added, if a number of research participants or samples are to be included, or if new a method or analysis is to be conducted on already collected samples).
3. The Principal Investigator must inform the Deciding RBC on when the sample collection is completed and on the final extent of the number of individuals per region. (Document N3a *"Report on completed sampling in multicenter studies"* and document N3b *"Appendix 1: Report on completed sampling"*, all documents can be found at www.biobanksverige.se)
4. The Sample Collection Controller is responsible for the documentation of consent and collected samples, documents withdrawals of consent, and takes care of tracking samples and other measures resulting from withdrawal of consent.

12. Signatures

Principal Investigator/Researcher (Sample Collection Controller)	The Principal Investigator/Researcher that applies for access to samples, **according to the ethics application** (the same person as specified in paragraph 3) The Principal Investigator must sign before the application is sent to the deciding RBC.
Authorised representative at recipient Biobank	Authorised representative at the recipient biobank shall sign before the application is sent to the deciding RBC office.
Healthcare Principal **RBC Director**	Signed by deciding RBC (see page 1) with authorisation from affected e-biobank custodian. Decision can also be taken by a representative appointed by the RBC director. Mark the box if the application is approved or not. • If the application is approved, specific conditions can be specified. Conditions for release, article 9. "Other" • If the application is not approved, the reasons should be motivated to the applicant in an appendix.