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 is processed by the **Regional Biobank Centre (RBC)** in the region where the ethical review was conducted. Addresses to RBCs can be found at www.biobanksverige.se.

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 County Council's and 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 virtual biobank in their respective County Council/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 biobank custodian are therefore obliged to ensure that samples can be traced back securely.

Definitions 1

Release of samples

Responsibility for and right of use to the samples in question is transferred from the healthcare principal to the research principal by a release**.** Recipients of released samples are either biobanks belonging to a research principal or another designated biobank with whom the research principal has an agreement. Samples can only be released to a biobank registered in Sweden. The samples are then 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's biobank custodian continues to be responsible for saving documentation regarding samples and to whom samples are released to make tracing possible.

Virtual biobank

In the multicentre principle, sample collections are released through an electronic biobank at the healthcare principal. The RBC Director has authorisation from the virtual biobank custodians to make decisions regarding registry and release of sample collections into and from their respective virtual biobank.

Private Healthcare provider

If an investigator from a private healthcare provider, wants samples released from a County Councils virtual biobank, a written authorisation between the private healthcare provider and the virtual biobank is needed. The authorisation means that the sample collection is included as a primary sample collection in the County Council/region virtual biobank. Proposals on how to set up authorisations can be found at

www.biobanksverige.se. Please note that the multicentre principle can't be applied if only private healthcare providers are in the study. At least one County Council/region must take part in the study when using the multicentre principle.

Multi-centre study concerns/relates to	
New application or supplementation of a previous application	Mark the box if the application relates to a **clinical trial**, **other study** *and* if it is a **completion of a former application**. *There are two types of completion:* 1. If it is a completion of study content (for completion of sample types, sites or investigators see below), the entire application doesn't have to be filled in. Only information needed to identify the previous application has to be filled i.e.: • **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 Ethics Review Board reference number (dnr)** • and **the details that have changed from since the previous application.** 2. For completion of new samples, addition of sites or investigators, fill in document N2: *"Supplementation to multicentre study application, Appendix A + B*" An enclosed letter to and a decision from the Swedish Ethics Review Board is required for both types of completion. 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 application for ethical vetting and patient/researcher information
Study working title	If the project has a working title it shall be mentioned here. Must accord with the title indicated in the application for ethical vetting and patient/researcher information
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 application for ethical vetting and patient/researcher information
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 MPA website (Läkemedelsverket)

Decision from Ethics Review Board	To use samples in a research study, approval from Ethics Review Board is required. • Specify the reference number from approved ethical vetting application. • Appendix: With the application, a copy of the ethical (vetting) application, patient/researcher data information and decision from Ethics Review Board must be submitted. It is important that the Biobank receive the latest version of the ethical vetting application, approved or submitted to the Ethical Review Board for approval. If the complete ethical vetting application is not enclosed, at least decision and copies of the headings in the Ethnical review application must be submitted; 1:1-1:6 Information on Research Principal, 2:4 Give an overview of procedures for examination, data collection and nature of data, 2:5 Indicate whether biological material will be stored in a biobank, 2:6 Documentation, data protection and filing/archiving, 4:1-4:2 Information and consent, 8 Signature and 9 appendix 1.

2. Healthcare Principal – Involved Biobank	
Specify the principal/principals at the biobank	The principal in the entity, where samples are collected, is the Healthcare principal. Concerned Healthcare Principals (County Councils/regions) shall be selected with a cross in "*Appendix A"* (in document N1a). The samples are recorded in HealthCare Principal's virtual biobank and then released to a recipient biobank as indicated in paragraph 6. If an investigator from a private healthcare provider wants samples released County Councils/regions virtual biobank, a written authorisation between the private healthcare provider and the virtual biobank is needed. (see definitions 1).

3. Information about Applicant/ Research Principal	
Specify the Principal for the research project	Please note that the Research Principal specified here, must be the same as stated in the application to the Ethics Review Board. A Research Principal can never be a person. Only a County Council/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 application to the Ethics Review Board.
Other contacts	Specify contact details for other collaborators, e.g. investigator, coordinator or 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	
Sampling period	If applicable, specify the date of the planned sampling (from first sample to the last). When the sampling period is finalised, 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.
Study period	Specify the dates when the study is scheduled to start and expected to finish.
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 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 ethics 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.

Definitions: 2

"**Personal data** is information that can be linked, directly or indirectly to a physically living person. This means that information linked to name or social security number are always personal data. Indirect information which don't link directly to a person, can also be personal data, if it can be used to trace a specific individual. Detailed information that indirectly points out where a person lives, such as property designation or geographical coordinates, are examples of personal data. Another example is when many and/or detailed information in combination makes it possible to link information to a

person(individual). Also, coded or encrypted information are personal data as long as someone can use it to identify individuals, that is as long the code – or encryption key is still valid. It is not necessary that the researcher have direct access to the key for the information to be considered as personal data. Even if the key is stored at another authority and this authority have a non-disclosure agreement, the personal data are with the researcher."

Source: Personal Data in research, which rules applies? Brochure can be found at www.datainspektionen.se

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. Describe especially 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/pseudonymisation	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. 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.

8. 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 supplementation of the application. Specify the billing address here.

9. Conditions for release

1. Approval of a regional 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 sample 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 a regional Ethical Review Board has considered and approved, may the principal for the secondary sample collection issue approval for such procedure.
5. The biobank custodian upon 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 County Council/region.

7. Released samples may not be released to third part.
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 also is asked about withdrawal of consent of other associated studies that the Research Participant may be part of.
9. Other:

10. Specific conditions for release

1. The principal investigators shall **contact their County Council/region biobank custodian immediately** to hand over personal ID numbers for sample tracking and signing of a power of attorney in the event that private health care providers are included.
2. The Principal investigator must inform the Deciding RBC if the conditions for the study are materially changed.
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 county council/region.
4. The Sample collection controller is responsible for the documentation of consent and collected samples, documents the withdrawal of consent, and takes care of tracking samples and other measures resulting from withdrawal of consent.

11. 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 a representative of the Healthcare principal. It is the RBC director at the RBC office, in the region where the ethics application is processed, that has authorisation from the County Council's/region's biobank custodians to approve release of sample according to this agreement. 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.