Guide to the application for ethics review

Compliance & Data Office
Research Support Office

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Karolinska Institutet

Karolinska Institutet

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Introduction

The purpose of this guide is to be an extra support for when you are filling in the application for ethics review. The idea is that you should have the guide in front of you at the same time as the ethics application is filled out. The guide has a KI-perspective and is intended to supplement the information already available in the Swedish Ethics Review Authority's application portal Ethix, by clarifying certain sections and give suggestions on how you can reason about certain parts. The guide also explains some common concepts, gives examples of different types of research as well as general information about ethics review and ethics application.

All sub-questions in the ethics application will not be brought up in this guide, but only the sections where extra guidance and clarification is usually needed. Be aware that depending on what your research is about, different follow-up questions will come up in Ethix. You may therefore not always see all the examples in your application that are covered in this guide.

For questions or comments, send an email to: compliance@ki.se.

General information about the ethics application and the ethics review

The application for ethics review, with the associated approval from the Swedish Ethics Review Authority, is required for you to conduct research on living or deceased humans, on biological samples from humans or research involving the handling of sensitive personal data. It is the Ethical Review Act *"Act (2003:460) on ethical review of research involving humans"* that regulates what types of research that requires ethics review. At the Swedish Ethics Review Authority's website, it says:

> *" The Act applies to research conducted in Sweden if the research:*
> - *involves physical intervention, on living and deceased persons alike.*
> - *is carried out with a method that aims to affect the research participant physically or mentally or involves an obvious risk of harm to them in body or mind.*
> - *are performed on biological samples from a living or deceased human being and can be traced back to that person.*
> - *involves processing of sensitive personal data or of personal data relating to criminal offences."*

An ethical approval must be in place before recruitment of participants, or any other part of the research, may begin. It is not possible to apply for ethical approval in retrospect.

At the Swedish Ethics Review Authority's webpage are answers on commonly asked questions about ethical review (unfortunately only in Swedish at the moment), and a "Questions and answers"-page, in Swedish, is also available when logged in to Ethix.

Fee for the ethics application

The fee for the ethics application must be paid before the processing can begin. When the responsible researcher and the authorized representative of the research principal have signed the application in Ethix, the application is automatically sent to the Ethics Review Authority. First thereafter you will receive information on how the payment is to be made. The fee for a new application is either 5 000 SEK or 16 000 SEK. For an amendment application, the fee is 2 000 SEK.

The fee is 5 000 SEK for:

- Research in which only one research principal participates.
- Research where more than one research principal participates, but the research participants have immediate connection with only one of the research principals.
- Research that only regards the processing of existing personal data (regardless of the whether the research project will be conducted by one or more research principals).

The fee is 16 000 SEK for:

- Research that applies to clinical pharmaceutical trials.
- Research where more than one research principal participates. This also applies to research projects where processing/analyzes of data is conducted at one research principal but where research participants are included in the activities of several research principals.

If you are unsure whether your research project requires ethical review

If you are unsure whether your research requires ethical review or not, it is always best to submit an ethical application and receive the answer that ethical review is not necessary, then realize too late that an ethical approval was needed. To conduct research without ethical approval, which should have been ethically reviewed, is punishable and the consequences for conducting such research can be extensive (from that results cannot be published, and PhD students being stopped from their dissertation, to, in worst case, imprisonment). Applying for ethical approval afterwards is not possible.

Concepts and examples of different types of research

Pseudonymized personal data vs. anonymized personal data

In research, the concepts *pseudonymized personal data* and/or *anonymized personal data* are often used. It is very important that you as a researcher know the difference between these concepts as in some cases can make the difference as to whether ethical review is required or not.

Pseudonymized personal data, sometimes called "coded personal data", means that direct identifiers, such as e.g., social security numbers and name relating to a research participant, have been removed and replaced with a code, where the code then can be connected to the name/social security number via a code key. Thus, there is a possibility that the direct identity of the research participant can be traced. It doesn't matter where the code key is, or how few people who have access to the code key. The personal data is considered traceable even if the code key is another country or only one person has access to it and even if you as a researcher don't have, or even has the legal right to have, access to it. If there is a code key saved somewhere, the personal data is pseudonymized (traceable) and ethical review is required.

Anonymized personal data means that social security numbers and name or other identifiers have been completely removed (not replaced with a code) and an eventual code key has been destroyed. Then it is no longer possible to trace the data to the identity of an individual research participant. Some research that is conducted on anonymized data does not need ethical review, for example research on anonymized (and commercial) biological samples (like blood or stem cells) or anonymized genomic data. However, be careful that the data you are using is truly anonymized, and not just pseudonymized.

Re-identification can exist when you have an anonymized collection of data/samples, and by adding together different variables (like age, disease, profession, an individual person can be identified. This may apply if, for example, you receive a data set that has been anonymized (the code has been deleted) but the same dataset, with code and associated code key, exists somewhere else. To reduce the risk of re-identification, variables can be re-coded so that, for example, age and income are stated in a larger interval and a geographical place is stated in larger areas. Which variables (indirect identifiers) need to be re-coded depends on what type of data/samples has been collected in a research project.

Using existing data or biological samples previously collected

If in your research project you are going to process/analyze data or biological samples that has already been collected, ethical review is required if the data or the biological samples can be traced back to the research participant/donor. If

the data/biological samples are traceable and pseudonymized, ethical review is required. If the data/biological samples are anonymized, no ethical review is required. See the section Pseudonymized personal data vs. anonymized personal data.

Keep in mind, that even if ethical review is not required, different types of agreements may be required. For example, if samples from a biobank will be used, a Material Transfer Agreement (MTA) or Data Transfer Agreement (DTA) may be required. Here you can read more about agreements at KI Biobank.

Use of stem cells

If you will conduct research on stem cells, ethical review is required if you are going to produce the stem cells yourself or if they are pseudonymized. However, if you are using anonymized commercial stem cells that are already produced, no ethical review is required. Se the section Pseudonymized personal data vs. anonymized personal data for more detailed information.

It is important to mention, however, that even if you use anonymized commercial stem cells, you are not allowed to do whatever you want with them. You can conduct research and do experiments on commercial anonymized stem cells without ethical review, but you may not, for example, put the stem cells back into a person again or artificially create a fetus.

Using samples from a biobank

If you will use samples from a biobank, you are required to have an ethical approval before you send in your biobank application (if you conduct a clinical pharmaceutical trial that includes samples from a biobank, other procedures apply, see section Clinical pharmaceutical trials). It is also important that you include all the necessary information in the ethics application that is required so that you then will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. What needs to be included in the ethics application is:

- The research principal must be the same in the ethics application as in the biobank application.
- Research principals for the study's participating locations/sites must be specified.
- All participating researchers, with organizational affiliation, must be specified (if several research principals).
- Which sample types are to be collected.
- What sample quantities and how often samples should be collected.
- Total amount of samples collected.
- Which analyzes are planned.
- To which country/countries samples are to be sent for analyzes (this also applies to sharing personal data).

- What will happen to samples after study is completed (also applies for sharing personal data).
- Whether samples will be saved for future research.
- How samples are coded and how and where the code key is stored and who has access to it.
- How personal data will be managed and stored.
- Start and completion date for the study.
- If the sample collection is to be disclosed to another principal's biobank.
- Responsible biobank (name and registration number with IVO).
- If exemptions to the scope of the act shall be invoked.

The points in the list above are described in each section of this guide where relevant. More information is available on Biobank Sweden's webpage.

Receive data/biological samples from another country

If the collection of data/biological samples is conducted in another country than Sweden, the collection itself must not be ethically reviewed in Sweden. However, the Ethics Review Authority must review the part of the research that is to be conducted in Sweden, for example analyzes carried out on the data received from the foreign data collection. Ethical review is then required regardless of whether you receive biological samples that is sent to Sweden from abroad, or if you only receive personal data. See more information in the section Using existing data or biological samples previously collected.

Clinical pharmaceutical trials

On January 31, 2022, the EU Clinical Trials Regulations 536/2014 (CTR) became applicable and replaced the previous EU Directive 2001/20/EC. The procedure for applying for ethical review differs depending on whether you follow the old directive or the new regulation. Until January 31, 2025, there is a transition period to smoothly switch from the old directives to the new regulation.

EU directive (the old regulations)

An ethical application must be submitted to the Swedish Ethics Review Authority through Ethix and an application for clinical pharmaceutical trial must be submitted to the Swedish Medical Products Agency. If relevant, you also need to submit an application to a Regional Biobank Centrum. Please note that application according to this directive will not be possible after January 30, 2023.

EU Clinical Trials Regulations (the new regulations)

Responsible principal shall submit a clinical trial application through the web portal CTIS (Clinical Trials Information System), which includes ethical review. CTIS is a new EU-common web portal and database for clinical trials within EU. *A clinical trial that complies with the new EU-regulation CTR must therefore* ***not*** *submit an ethical application through Ethix*. When a clinical trial application is submitted to CTIS, both the Swedish Ethics Review Authority and the Swedish

Medical Products Agency get access to the application, which is processed jointly in CTIS. Important to note is that in CTIS it is not possible to specify other/participating research principals. Therefore, it is even more important that the roles, tasks, responsibilities etc. of all involved research principals are clearly described in the CTIS application.

If relevant, a biobank application must be submitted separately to the Regional Biobank Centrum on the same day as the CTIS application is submitted to CTIS. The biobank application will however not be reviewed until the clinical trial has been approved. On Biobank Sweden's webpage, the is more information about clinical trials on biobank samples.

Transitional period

- Between January 31, 2022 – January 30, 2023, you can choose whether your clinical trial should follow the old regulations (EU directive) the new CTR. If you know that your clinical trial will continue after January 31, 2025, it is recommended to follow the new regulations and submit a clinical trial application through CTIS.
- From January 31, 2023, all new clinical trials must follow the new regulation CTR and submit a clinical trial application (that includes the ethical application) through CTIS.
- Until January 31, 2025, clinical trials that have already been submitted in accordance with the old EU directives can continue to be carried out according to the old regulations.
- From January 31, 2025, all clinical trials that *are still ongoing, **must** be transferred* to CTIS and start to follow the new regulations CTR.

On the Staff Portal you can read more about when KI is research principal and will submit a clinical trial application in CTIS according to the new regulation CTR.

Ethical principles for human research outside Sweden

KI has ethical principles for human research outside Sweden. The purpose of these guidelines is to ensure that research conducted abroad matches the ethical standards that apply to research conducted in Sweden. In the event of doubt as to whether a research project to be conducted outside Sweden is in compliance with these guidelines, researchers are asked to contact the KI ethics resource team.

Ethical guidelines for international collaboration

KI has ethical guidelines for international collaboration that must be followed when KI is involved in research projects that are conducted in other countries than Sweden. The guidelines for international collaboration referrer and relate to several internal and external policy documents, rules, guidelines and other

information concerning ethical issues. They include discrimination, harassment and victimization, ethical review and documentation and risk assessment. The basic principle is that research should not be located in a country with lower levels of research ethics than Sweden just to be able to conduct more/other interventions, but the research should be located in the country where the research question can best be answered and that the research project could also be approved in Sweden.

Create an initial application

The application for ethical review is made through the portal Ethix, and it is also there that you receive the decision. You log in to Ethix with your Bank-id or two-step authentication. You create an application by logging in, select "Ansökningar" in the menu at the top and then select "grundansökan".

Note! If you are conducting a clinical pharmaceutical trial, you should not use Ethix. Read more in the section Clinical pharmaceutical trials.

The application must be written and submitted in Swedish. There are support templates in English to use if needed, but please note that the application must still be submitted in the Swedish version. On the Ethics Review Authority's webpage you can find the English support templates.

1. General information (Huvudsakliga uppgifter)

1.2 Entity responsible for the research (forskningshuvudman).

When choosing the responsible research principal for the ethical application, several aspects need to be considered. If several institutions/hospitals/universities are involved in the study, it can sometimes be unclear who should be listed as the responsible research principal and who are the other research principal(s). "Responsible principal" refers here to the entity who has the coordinated responsibility to submit the ethical application on behalf of all participating research principals, and to be the coordinator who notifies the other participating research principals on the decision of the ethical review. The other research principals must be listed under 1.4.1 Other entities responsible for the research taking part in the project.

It is up to the researchers how many research principals a research project should have. However, if any part of the *research* is conducted at an institution/hospital/university that is related to the project, then that entity *can* be seen as a research principal. Every principal is responsible for the part of the research that is conducted within its own entity.

An example when only KI should be the sole research principal is if personal data is disclosed from a hospital to KI from a patient record concerning a research

participant with the purpose of being used in a research study at KI. In this case the hospital *shall not* be listed as a research principal and shall not be counted as participating in the research.

An example when both KI and a hospital can be research principals in the same project is if the hospital conducts a treatment/intervention on patients/research participants and in connection with that collects personal data on the research participants. The personal data is disclosed to KI for storage, analyzes and writing of results. Who should be the responsible or the participating research principal depends on the approach of the study, read more below.

Below are some questions that may be good to answer when there is uncertainty about who should be the responsible research principal (a benchmark is that the institution/hospital/university that is the answer on the majority of the questions should also be the responsible research principal):

- Where will the research participants be recruited?
- Where will the data be collected?
- Where will the data be stored?
- Where will the data be analyzed?
- Who will manage the finances of the study?
- Who will manage contracts and agreements?
- Who will be responsible for registration and reporting of the study in the clinical trial registry?
- Is there an appointed principal responsible for the study?

Sometimes, the study's approach can point towards who should be the responsible research principal. If it is, for example, a study that involves an invasive procedure[1] on patients, it *may* be appropriate that the hospital who performs the procedures is the responsible research principal on the ethical application. An example is if the collection of personal data/biological samples are conducted on the Karolinska University Hospital with an invasive procedure, but the personal data/biological samples will be stored, processed, and analyzed at Karolinska Institutet, both KI and the hospital can be listed as research principals, where the hospital is the responsible and KI is the participating.

Projects where KI collaborates with health care providers in Region Stockholm: KI, together with Region Stockholm, has drafted "Guidance – appointing a responsible research principal for the ethical application for research where Karolinska Institutet collaborates with health care providers in Region Stockholm". The guidance provides advisory examples and basis for

[1] Invasive procedure here means: a physical procedure on a living or deceased person or is conducted with a method that aims to affect a person physically or psychologically or involves an obvious risk of harming the research participant physically or psychologically, where there is more than an insignificant risk to the research participant.

suggestions when appointing the responsible research principal for the ethics application.

If you will use samples from a biobank, you must be careful to include all the necessary information in the ethics application that is required so that you later will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. Information that must be included under "*1.2 Entity responsible for the research (forskningshuvudman)*" is:

- The research principal must be the same in the ethics application as in the biobank application.

1.3 Authorized representative of the entity responsible for the research.

It is always the Head of Department that must be stated when KI is the responsible research principal and submit the ethical application. When another entity is the responsible research principal, it can be for example head of unit or head of operations.

1.4 Does the project have more than one entity taking part in the project?

Answer yes if the study has several research principals responsible for different parts of the project and add them to the list. For more information, see section 1.4.1 below.

1.4.1 Other entities responsible for the research taking part in the project:

For information on how to reason about who should be listed as responsible research principal and who/which should be listed as other research principal(s), see section 1.2 Entity responsible for the research (forskningshuvudman).

For projects that are fully or partially conducted in a country other than Sweden, the foreign party must only be listed as other research principal if they are part of/participates in the part of the research that is conducted in Sweden (that is, the part of the research that you will apply for ethics review). Example: KI collaborates with University X located in another country. University X has applied for ethics review in its country and received approval to collect biological samples from people in that country. Personal data belonging to the biological samples are sent to KI for processing and analyzes. The personal data is pseudonymized, i.e., a code key is stored abroad at University X. Only KI analyzes the personal data. If only KI is involved and conducts the analyzes, and only the analyzes are conducted in Sweden, University X does *not* need to be listed as other research principal.

If you will use samples from a biobank, you must be careful to include all the necessary information in the ethics application that is required so that you later will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. Information that must be included under "*1.4.1 Other entities responsible for the research taking part in the project*" is:

- Research principals for the study's participating locations/sites must be specified.
- All participating researchers, with organizational affiliation, must be specified (if several research principals).

More information is available on Biobank Sweden's webpage.

2. Type of research – initial questions

2.5 Does the project involve new collection of samples?

Biological samples also include smaller components, for example blood plasma, antibodies, or other components from blood. Ethical review is always required if you yourself is responsible for the entire process of collection, for example if you collect blood samples for the purpose of producing antibodies.

For projects that are fully or partially conducted in a country other than Sweden, remember that the Ethics Review Authority only review the part of the research that will be conducted in Sweden. If the collection of biological samples is conducted abroad and KI's part of the project is, for example, only to process/analyze the data or the samples from abroad, then this does not count as having newly collected biological samples.

2.6 Does the project plan to use biological samples from humans from one or more existing sample collection?

According to the Ethical Review Act 4 § 3 and 4 § 5, ethical review is required if the research involves studies on biological samples that has been taken from a living or deceased person and can be traced back to this person. That is, the biological samples are traceable. If you are using an already existing sample collection, you need to know if the biological samples you receive is pseudonymized (coded) or anonymized (de-identified). See section Pseudonymized personal data vs. anonymized personal data.

If you will use samples from a biobank, see section Using samples from a biobank.

If you will use anonymized commercial stem cells, see section Use of stem cells.

4. Method

4.1 Explain the methodology including procedures, technique, or treatment.

Here, you must describe everything that is part of the project that has to do with the method.

If the project has several research principals, describe carefully which research principal is responsible for what and conducts which part(s) of the project as well as where those parts will be conducted.

If it's a clinical study or clinical trial, write which research principal (if several) who is responsible for the registration of the study/trial and report results after study completion in an international clinical trial registry, for example ClinicalTrials.gov for clinical studies or CTIS for clinical trials. (For more information on the new regulation regarding clinical trials, see section Clinical pharmaceutical trials.

For projects that are fully or partially conducted in a country other than Sweden, remember that the Ethics Review Authority only reviews the part of the research that are conducted in Sweden. These are the parts you should focus on describing in detail in the methods section. If your collection of personal data/biological samples has been collected in another country (where ethical approval has been obtained in that country) and is to be sent to Sweden and KI for processing and analyzes, you can write that your collection of personal data/biological samples has already been collected abroad where ethical approval is available (which it should be! However, it does not need to be attached to your ethical application). The important thing is to be clear about which parts are performed where and by whom.

If you will use samples from a biobank, you must be careful to include all the necessary information in the ethics application that is required so that you later will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. Information that must be included under "*Method 4.1*" is:

- Which sample types are to be collected.
- What sample quantities and how often samples should be collected (a brief description is enough).
- Total amount of samples collected (a brief description is enough).
- Which analyzes are planned (a brief description is enough).
- To which country/countries samples are to be sent for analyzes (this also applies to sharing personal data).
- If the sample collection is to be disclosed to another principal's biobank.
- Responsible biobank (name and registration number with IVO).

Note! The number of samples, the number of pieces and/or the volume to be collected as well as the analyzes to be conducted will need to be described in more detail later in the application, under section 14. Description of biological samples.

More information is available on Biobank Sweden's webpage.

5. Timetable

5.2 Expected end date of the project:

End date is the date on which you estimate that your collection of personal data/biological samples and/or intervention and/or analyzes of register data/biological samples and compilation of results is expected to be complete. Avoid specifying a date for when the personal data/biological samples will be deleted/destroyed, as this cannot be promised with certainty. (Archiving/long-term storage are not included under this headline. KI is subject to the archive act and if the study is to be preserved, the associated data must also be preserved.)

For projects that are fully or partially conducted in a country other than Sweden, the end date is the date for the part of the research that are conducted in Sweden, which is the part of the research that is reviewed by the Swedish Ethics Review Authority.

If you will use samples from a biobank, you must be careful to include all the necessary information in the ethics application that is required so that you later will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. Information that must be included under "*Timetable 5.1 and 5.2*" is:

- Start and completion date for the study.

More information is available on Biobank Sweden's webpage.

5.3 Timetable for the different parts of the project:

This is where you specify the timetable for when all parts of the project is estimated to be carried out, like recruitment of research participants, collection of personal data/biological samples, interventions, processing and analyzes of personal data/biological samples, compilation of results, publication in a journal and, if relevant, reporting of results in a clinical trial register. The management and long-term storage of the personal data/biological samples are not included here.

6. Data collection

6.1 Explain how data will be collected and describe the nature of the data.

Here you explain how the collection of personal data/biological samples is to be conducted. If several research principals are included, indicate which research principal is responsible for which part. Examples of different collections:

- Survey data will be collected via paper surveys/data management tools/eCRFs (e.g., KI REDCap).
- Blood samples/other types of biological samples from patients are collected at hospital XX. Patient data/clinical data from medical records. Audio recordings/videos are recorded with format XX etc.
- The personal data collection/samples/interviews will be collected/conducted by a nurse/doctor/research assistant etc.

- Register data will be obtained from Statistics Sweden according to the register keeper's routines for register extracts.

For projects where the collection of personal data/biological samples are conducted fully or partially in a country other than Sweden, you can write that the collection has already been/will be conducted abroad. But if you have information about how the collection was/will be done, you can briefly describe it.

6.4 How will the data that is collected be managed and stored?

General advice: Describe where eventual survey data/samples/audio files etc. will be stored. Personal data must be stored in KI-approved systems that is security classified for storage of sensitive personal data. (Here you can read more about storing and sharing files at KI and here you can read more about how to plan your research data management. Keep in mind that the entire research process must be documented in the electronic notebook ELN.)

Remember to be specific enough with details. You don't need to specify exactly how long samples/data are to be stored, but it is sufficient to refer to "*in accordance with current legislation and KI's internal rules*".

If the personal data/biological samples you've collected is to be transferred to other countries, do not limit unnecessarily to which countries the data/samples will be transferred, but be specific enough with the details. For example, it is enough to write something like "*Pseudonymized personal data may be shared with recipients within and outside the EU/EEA area and will then be done in accordance with the legislation in force at that time*". With this wording, you can also ensure that the Ethics Review Authority can allow future sharing of personal data/biological samples with collaboration partners, even if this was not part of the plan at the start of the study. Remember, however, that the information about consent to the research participants must agree with the information in the ethical application. And, importantly, that all the necessary agreements in the case of disclosure of personal data/biological samples are in place when the time comes. You don't need to specify exactly which agreements are to be written, but a more general wording such as "*Relevant agreements are drawn up in accordance with current legislation*" is sufficient.

When transferring personal data *outside* the EU/EEA area, special strict rules apply. Here you can read more about what applies to the transfer of personal data to third country. It may also be good to contact the data protection officer at dataskyddsombud@ki.se when a transfer outside the EU/EEA will take place and where KI is the research principal.

If you will use samples from a biobank, you must be careful to include all the necessary information in the ethics application that is required so that you later

will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. Information that must be included under "*Data collection 6.4*" is:

- What will happen to samples after study is completed (also applies for sharing personal data).
- Whether samples will be saved for future research.
- How samples are coded and how and where the code key is stored and who has access to it.
- How personal data will be managed and stored.
- If exemptions to the scope of the act shall be invoked.

Exemptions to the scope of the act means that the Biobank Act does not apply to samples that are intended for research and that are analyzed within six months of the time of sampling and are destroyed immediately after the analysis. Both conditions (analyzed withing six months and destroyed immediately after) must be met for the exemption rule to apply.

More information about the exemption rule and the point in the list are available on Biobank Sweden's webpage.

7. Ethical considerations

7.1 What risks might the research participants run by taking part in the research project?

Be careful to identify any potential risks that may exist, even if the risks feel small/near non-existent. If there is no risk at all, describe why there is no risk.

For projects where the personal data/biological samples are already collected, or the collection is fully conducted in a country other than Sweden, the Swedish Ethics Review Authority must assess the risks that exist with KI receiving and processing/analyzing the personal data/samples. A risk could be, for example, that even if the personal data is pseudonymized, there is a risk that the identity of the research participants can be identified. There may also be risks related to IT security, such as how and where you store personal data (at KI, personal data must always be stored in KI-approved systems, see section 6.4 How will the data that is collected be managed and stored?). Mention these risks and describe how and where any code key for pseudonymized personal data/samples are stored and also how that location is secure.

7.2 – 7.4 Benefits and risks with the research project

In case personal data/biological samples already have been collected or if the collection is conducted in another country, see question 7.1 above.

8. Research participants

8.1 – 8.5 Selection, number, selection criteria and the relationship between researchers and research participants.

For projects where the personal data/biological samples are already collected in Sweden, or the collection is fully conducted in a country other than Sweden, write that you *only* receive the data for processing/analyzes.

If you still know how the selection of research participants was done, how many that already has been/planning to be recruited, inclusion- and exclusion criteria and the relationship between researchers and research participants, describe that as well.

If you don't know, you can refer to that it is already described in the existing (Swedish) ethical approval for the project where the collection is coming from, or in the ethical approval issued in the country where the collection of personal data/biological samples is to be conducted (which must exist!).

8.6 What insurance cover is available for the research participants involved in the project?

It's important that the correct insurance for research participants is in place before you start your research. There are different types of insurance that apply depending on the type of study and where the stud is conducted (i.e., which research principal is responsible for that part of the research). Each research principal (if several) is responsible for having the correct insurances in place for the part of the research for which they are responsible. Some examples of insurances that apply to KI are:

- **Personal injury protection** covers the research participant's stay on KI's area as well as direct travel between the home and KI.
- **Patient injury insurance** covers when samples/procedures are conducted on the research participant. Note that different guidelines apply to who can conduct the procedure depending on where it is conducted and who is the research principal.
- **Pharmaceutical insurance** applies to clinical pharmaceutical trials.

Here you can read more about the different insurances that apply to KI, and here you can read more about patient insurance when your research project is a collaboration between KI and health care providers in Region Stockholm.

For projects where the personal data/biological samples are already collected in Sweden, or the collection is fully conducted in a country other than Sweden, this is not relevant.

9. Information and consent

9.1 Will the research participants be given information about the research project and be asked whether they want to be involved?

The Swedish Ethics Review Authority has summarized what information the research participant are entitled to receive (only available in Swedish).

Support templates: Support templates (only available in Swedish) are available for information for research participants, consent form to participate in the project and for consent to future research. The last one can be used in case collected samples are to be saved and potentially will be used in future research that is not yet planned. However, consent cannot be obtained for research that has not yet been specified or approved but is rather of providing information that collected data may be used in future research, which will then be reviewed by the Ethics Review Authority and that the research participant may then be contacted again.

Keep in mind that the information the research participants receive must agree with the information contained in the ethical application. For example, it must be stated in the information if personal data may be shared with recipients both within and outside the EU/EEA are and if personal data/samples will be saved to enable future research (for more information on this, see section 6.4 How will the data that is collected be managed and stored?).

The support templates can be found in Ethix under "Ansökan" and then "Stödmallar". The information for research participants and the consent forms must be attached to the application in the section Information for research participants and consent form, where more detailed information about the support templates is available.

For projects where the personal data/biological samples are already collected, or the collection is fully conducted in a country other than Sweden, write that the personal data/samples are already collected or will be collected abroad. Keep in mind, however, that the data that has already been collected must have previously been collected to be used specially for research.

If you know how the information to the research participants and consent went about, describe it briefly but make it clear that this has already taken place, or will take place abroad.

If you don't know, you can refer to that it is already described in the existing (Swedish) ethical approval for the project where the collection is coming from, or in the ethical approval issued in the country where the collection of personal data/biological samples is to be conducted (which must exist!).

9.3 Will research participants, who are not able to consent to their own participation for reasons of a medical condition, mental disorder, weakened state of health or similar condition, be included in the research project?

9.3.1 [If yes to 9.3] Give reasons for this group of research participants being included in the project.

For projects where the personal data/biological samples are already collected in Sweden, or the collection is fully conducted in a country other than Sweden, write that the personal data/samples are already collected or will be collected abroad.

If you know the reasons to why this group of research participants shall be included in the project, describe it briefly but make it clear that that they have already been included, or will be included abroad.

If you don't know, you can refer to that it is already described in the existing (Swedish) ethical approval for the project where the collection is coming from, or in the ethical approval issued in the country where the collection of personal data/biological samples is to be conducted (which must exist!).

9.3.2 [If yes to 9.3] Describe how next of kin, trustees or legal guardians are to be consulted.

Next of kin, trustees or legal guardians can never represent a research participant (with the exception of minors) and consent to participation in a research study on his/her behalf. But in the case research involves research participants who are not able to consent to their own participation, consultation must take place with the next of kin, who must be given the opportunity to oppose participation.

For projects where the personal data/biological samples are already collected in Sweden, or the collection is fully conducted in a country other than Sweden, write that the personal data/samples are already collected or will be collected abroad. Make it clear that they have already been included or will be included abroad. If you know how the consultation with the next of kin went about, describe it briefly.

If you don't know, you can refer to that it is already described in the existing (Swedish) ethical approval for the project where the collection is coming from, or in the ethical approval issued in the country where the collection of personal data/biological samples is to be conducted (which must exist!).

12. Reporting the outcome

12.1 How is access to data guaranteed for the entity responsible for the research and other researchers involved?

For projects with several research principals, where for example a health care provider is responsible for collecting personal data/biological samples and KI is responsible for processing and analyzes of the personal data/samples, KI considers that the personal data/samples should be *disclosed* (utlämnas) to KI. A decision on disclosure means that KI becomes (legally) responsible for the data/samples and thus gets to decide what to do with the personal data. When samples are disclosed to KI, KI can send them to third parties after signing a Material Transfer Agreement. When personal data is disclosed to KI, KI can share the personal data with third parties after signing a suitable data agreement (DPA, Data Transfer Agreement or Data Controller Agreement).

DPA (Data Processing Agreement) should be avoided between health care provider and KI, if KI is part if the research project where, for example, we are independently responsible for the storage and analysis of the personal data/samples. In that case, KI must be seen as, and stated in the ethical application, as a research principal (responsible or other participating research principal depending on the study's approach, se section 1.2 Entity responsible for the research (forskningshuvudman).).

12.2 Who will be responsible for data processing and the written report of the results?

Here it is important to state the correct organization(s)/institution(s), rather than names of individual researchers.

Also address whether collaborations within and outside the EU/EEA may be relevant.

12.3 How and when will the results be published?

If the project is a clinical study, in addition to indicating when the results are planned to be, for example, published in scientific "peer review" journals and presented at conferences, also plan to report the results to the clinical trial registry where the study was registered, for example ClinicalTrials.gov. KI strongly recommends that all clinical studies report results within 12 months after study completion. For clinical pharmaceutical trials, results must be reported to EudraCT or CTIS the latest 12 months after study completion.

12.4 In what way will the research participants' right to privacy be guaranteed when the material is published?

Examples here are that results will be reported at group level, excerpts from interviews have been de-identified, characteristics of specific individuals cannot be distinguished, images are without identification possibilities, etc.

14. Description of biological samples

14.1 Will new biological samples from humans be collected for the project?

14.1.4 [If yes to 14.1] For how long is the project to have access to the biological samples?

Estimate how long the project will need access to the biological samples but try not to limit yourself too much.

14.1.7 [If yes to 14.1] For how long is the biological samples to be accessible after the project has been completed?

Estimate for how long the biological samples will be accessible after the project has been completed but try not to limit yourself too much and avoid specifying a date for when the samples should be destroyed.

14.2 Does the project plan to use biological samples from humans from one or more existing collections of samples?

14.2.2 [If yes to 14.2] How much biological sample is planned to be used?

If you will use samples from a biobank, you must be careful to include all the necessary information in the ethics application that is required so that you later will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. Information that must be included under "*Description of biological samples 14.2.2*" is:

- What sample quantities and how often samples should be collected.
- Total amount of samples collected.

More information is available on Biobank Sweden's webpage.

14.2.7 [If yes to 14.2] What analyses will be carried out on the biological samples?

If you will use samples from a biobank, you must be careful to include all the necessary information in the ethics application that is required so that you later will be able to sign a biobank agreement and get access to samples covered by the Biobank Act. Information that must be included under "*Description of biological samples 14.2.7*" is:

- Which analyzes are planned.

More information is available on Biobank Sweden's webpage.

14.2.10 [If yes to 14.2] For how long is the biological samples to be accessible to the project?

Estimate how long the project will need access to the biological samples but try not to limit yourself too much.

14.2.12 [If yes to 14.2] How long is the biological samples to be accessible after the project has been completed?

Estimate for how long the biological samples will be accessible after the project has been completed but try not to limit yourself too much and avoid specifying a date for when the samples should be destroyed. See more information in the section 6.4 How will the data that is collected be managed and stored?.

Annexes

Advertising material for the recruitment of research participants

If you need tips and help regarding advertising for the recruitment of research participants, KI's Communications and Public Relations Office can provide you with support regarding how you can recruit research participants for your research project.

Information for research participants and consent form

According to 6 § of the Ethical Review Act, the research participants must be informed about (information according to the GDPR must also be provided!):

- The overall plan for the research.
- The aim of the research.
- The methods that will be used.
- The consequences and risks that the research may entail.
- Who is the research principal.
- That participation in the research is voluntary.
- The research participant's right to cancel their participation at any time.

The Ethics Review Authority has summarized what information the research participants are entitled to receive (only available in Swedish). Keep in mind that the information to the research participants must be the same as the information in the ethical application when it comes to processing, storage and sharing of personal data/samples. For example, it must be stated in the information in case personal data/samples may be shared both within and outside the EU/EEA area as well as if personal data/samples will be saved to enable possible future research (see section 6.4 How will the data that is collected be managed and stored? for more information about it). The information must be kept as concise and easy to understand as possible so that the research participants can easily understand it (and be adapted to the recipient – for example minors, elderly, impaired function, different languages, etc.).

Support templates for the information for research participants

The Ethics Review Authority has support templates that you can use. The support templates (only available in Swedish) can be found in Ethix under "Ansökan" and then "Stödmallar".

The support templates available are:

- **Information for research participants.** The Ethics Review Authority recommends using this template. However, it is not fully complete regarding information according to GDPR.
- **Consent form to participate in the project.** It is not fully complete regarding information according to GDPR. This template is either not fully

complete regarding clinical pharmaceutical trials, as it lacks monitor access to medical records and doctor's signature.

- **Consent to future research.** This template can be used in case collected samples will be saved and possibly be used in future research not planned yet. However, consent cannot be obtained for research that has not yet been specified or approved but is rather of providing information that collected data may be used in future research, which will then be reviewed by the Ethics Review Authority and that the research participant may then be contacted again.

Biobank Sweden has created a guide vägledning gällande utformande av forskningspersonsinformation (only available in Swedish) that can be used for research projects that will collect samples to be saved in a biobank.

Signature and certification

Responsible researcher and the authorized representative of the research principal (as specified in section 1.3 Authorized representative of the entity responsible for the research.) must sign the application with Bank-id. The authorized representative receives an email to the stated email address when it is time to sign.

When responsible researcher and the authorized representative of the research principal have signed the application in Ethix, the application is automatically submitted to the Ethics Review Authority. The responsible researcher then receives information on how the fee is to be paid. The fee for the ethical application must be paid before the review can begin. Read more about fees in the section Fee for the ethics application. Responsible research principal must then notify participating research principals (if several) of any amendments and decisions.

When a decision comes from the Ethics Review Authority, the decision, together with the complete ethical application (including information for research participants, consent form and other annexes), must be registered (diarieföras) at KI. It is usually the responsible researcher who is responsible for the registration of research documents.