

Introductory note for deliverable D5.3 from Working Group 5 of COST Action 21151, “Generation of Human Induced Pluripotent STEM Cells from Haplo-selected Cord Blood Samples” (HAPLO-iPS)

D5.3 comprises two sets of documents related to informed consent for donors to HLA-haplotyped biobanks of iPSCs. Each set consists of a General Information Document and an Informed Consent Form. One set is for adult donors and the other is for infant donors.

The HAPLO-iPS COST Action has a primary focus on the use of umbilical cord blood banks as starting material for generating HLA-haplotyped GMP-compliant iPSCs for clinical applications in regenerative medicine. This means that the starting biological material is derived from infant donors. However, some HAPLO-iPS members are establishing HLA-haplotyped iPSC biobanks using starting material from adult donors.

The rationale behind developing a separate set of documents for these two donor categories is that donation of biological material from infants involves a situation in which consent is provided not by the donor, but by the donor’s parent(s) or guardian(s). This presents an extra ethical issue impacting on the rights of the infant donor, in particular the donor’s right to withdraw consent, which for an infant donor necessarily is delayed until they reach adulthood. The right to withdraw consent as a general right is well-established through international guidelines defined in the *Declaration of Helsinki* and the Council of Europe’s Additional Protocol ([2005](#): Art 13, s.3) to the *Oviedo Convention* (1997).

For this reason, both sets of documents are based on the principle of dynamic consent, which provides both donor and biobank the opportunity for re-contact after a donation is made. Re-contact is especially important for protecting the rights of donors in the realm of biological material donated for iPSC generation, since iPSCs can be maintained indefinitely and may be subject to future applications that are difficult to predict. Should such future applications cross into areas that a donor finds unacceptable, re-contact through dynamic consent allows the donor to assess developments and impose restrictions on use compatible with their personal ethical standards. In the special case of infant donors, dynamic consent ensures that the rights of the donor to modify or even withdraw consent are maintained until they reach adulthood and can make decisions for themselves about how their biological material is used. Comparison of the two sets of documents highlights the particular ethical and practical issues that arise when donations of biological material are made by infants rather than adults.

Dynamic consent as an ethical instrument, and the pros and cons of using it in the case of iPSC biobanking, are discussed in recent review articles^{1,2}.

The rationale behind separating into a General Information Document and an Informed Consent Form is based on practical experience gained over many years by the Norwegian Bone Marrow Donor Registry (NBMDR), which is associated with efforts in Norway to establish an HLA-haplotyped iPSC biobank where dynamic consent is used (the Norwegian iPSC Biobank for Clinical Applications, or NIBCA). The NBMDR has learned that providing prospective bone marrow donors with too much information in one document often leads to information overload and lower recruitment rates. Separating into a General Information Document that can be perused in advance and at leisure and the Informed Consent Form (containing more concise information) that the donor needs to sign after careful consideration, creates a situation that is easier to handle for the donor.

These documents are intended to be used as guidelines for those interested in establishing HLA-haplotyped iPSC biobanks. They are therefore designed as templates that can be utilized by any institution or entity. Modifications are to be expected depending on country- or use-specific legal constraints. Should they be used, with or without modifications, HAPLO-iPS would appreciate being cited as a source.

References

1. Isasi R, Bentzen HB, Fabbri M, Fuhr A, Glover JC, Mah N, Mascalzoni D, Mueller S, Seltmann S, Kurtz A (2024) Dynamic governance: A new era for consent for stem cell research. *Stem Cell Reports*. 19(9):1233-1241. doi: 10.1016/j.stemcr.2024.07.006.
2. Lewis J, Holm S (2026) Reconceptualizing the right to withdraw in stem cell research: Striking a balance between donor autonomy and scientific utility. *Research Ethics* 22(4):748–767. doi: 10.1177/17470161261424047.

INFORMATION DOCUMENT

BIOBANK OF INDUCED PLURIPOTENT STEM CELLS (iPSCs)

BACKGROUND, PURPOSE AND INTENTION

The purpose is to establish a biobank of immature stem cells for treatment of patients. Such stem cells, called induced pluripotent stem cells (iPSCs), can be created in the laboratory from blood, skin or other types of cells obtained from donors. iPSCs can then be used to make any type of cell in the body through a process called differentiation. Differentiated cells can potentially be used in the treatment of patients with serious injuries and diseases in which cells either do not function as they should, have been lost, or where supplying new cells could improve tissue or organ function. By transferring (transplanting) the cells we generate from iPSCs to an organ or tissue in a patient, it can be possible to slow down or stop a disease, or to replace cells that have been lost. Such treatments represent a key aim in the fields of regenerative medicine and tissue engineering.

To reduce the risk of the transplanted cells being rejected, people who have tissue types (HLA types) that are compatible with a large proportion of the population are needed as donors. We are contacting you because your HLA type is particularly suitable for this purpose, and we hope that you will be willing to donate.

A skin biopsy and/or blood sample will be taken from you, and from these we will obtain cells that will be frozen and stored in the biobank. These cells will be converted into iPSCs, which will also be frozen and stored in the biobank. iPSCs can be used as a starting point to generate different types of mature cell types that can be used for clinical research and treatment. An iPSC biobank will be a very important resource in Europe and world-wide. iPSCs in the biobank can be used to produce cells for patients both in your home country and internationally, much faster than if we were to use a patient's own cells, which is also not always possible.

PARTICIPATION IS VOLUNTARY

Donating your biological material to this biobank of iPSCs (hereafter referred to as "the Biobank") is completely voluntary. You have the right to agree or to refuse to provide your biological materials for this project. The quality of your current or future medical care, or your participation as a donor in any other context, such as donating blood or bone marrow, will not change in any way whether you agree or refuse to provide cells for the Biobank.

WHO OWNS AND RUNS THE BIOBANK?

The Biobank is owned by (...name of institution...). The (...name of institution...) has a Tissue Establishment certification for biobanking issued by (...name of regulatory agency...). The Biobank consists of 1) a recruiting and contact office, which will be responsible for all contact with you including the scheduling of donations, the collection, processing and storage of personal data, and any subsequent contact, and 2) a laboratory facility responsible for storage and characterization of your donated tissue and cells and the production, storage and characterization of the iPSCs derived from your cells. The (...facility that carries out the biobanking and production...) has the necessary expertise and a certificate of Good Manufacturing Practice (GMP) issued by (...name of regulatory agency...). This ensures high-quality production of iPSCs from the donated cells, and the characterization and analysis of iPSCs to ensure that they can be used safely for GMP-compliant production of differentiated cells for treating patients. The (...name of institution...) will be responsible for ensuring the storage of pseudonymized information obtained through characterization and analysis of the donated cells and iPSCs. Pseudonymized information means there is no direct link to your name, personal identification numbers, or any other information that can be used to directly identify you (see Section on Archiving and Use of Personal Data, below).

SKIN BIOPSY AND BLOOD SAMPLE – WHAT HAPPENS TO YOU?

A sample of whole blood (of about 20 milliliters, obtained by venipuncture) and possibly a skin sample (obtained by skin biopsy) will be taken from you. From this material, we will grow a specific type of blood cell (mononuclear

cells) or skin cell (fibroblasts) which will be frozen and stored in the Biobank. These cells will be converted into iPSCs, which will also be frozen and stored in the Biobank.

The blood sample will also be tested for specific indicators of infectious diseases and serious diseases of internal organs, such as hepatitis, HIV and syphilis, and subjected to other control analyses. Testing for infectious diseases is necessary before we can process cells further and so that we can ensure that cells generated from your iPSCs can be safely used in patients.

The skin biopsy and/or blood sample will be taken on the same day, by experienced doctors at the contracted clinical site with certification for Tissue Establishment at (...name of institution...). The appointment will be arranged by the recruiting and contact office at (...name of institution...). Transportation costs and other expenses will be covered by the (...name of institution...). A second blood sample will be needed at a later date in connection with testing for infectious diseases (see section on Testing for Infectious Diseases and Quality Control Analyses, below).

The skin biopsy and venipuncture are not dangerous. Blood drawn by venipuncture is done in the same way as used for blood donations. The skin biopsy is performed on an area of skin that is first sterilized and locally anesthetized to avoid pain during the procedure. A special tool is used that cuts out a round piece of skin. The tool reaches down to the deepest skin layer, so there may be some bleeding. The wound is then closed with either a special bandage or with a few stitches, and will leave a small, white scar. After the anesthetic wears off, there may be slight to moderate discomfort, quite similar to what you experience when a minor cut in the skin is healing. Ordinary painkillers will help with the discomfort that may arise. If the wound is closed with stitches, these will have to be removed a couple of weeks later, which can be done by your GP.

The skin biopsy and blood sample will be delivered to the (...facility that carries out the biobanking and production...) where further procedures are carried out.

WHAT HAPPENS TO THE CELLS DERIVED FROM YOU?

Both the skin fibroblasts and blood cells and the iPSCs produced from these will be stored frozen in the Biobank. If we run out of iPSCs, we will be able to produce new ones from the original cells donated by you. In this way we will not need to request new biopsies later. The iPSCs will be used as a starting point to generate different types of mature cells that can be used for basic, applied, or clinical research aimed at developing cell-based treatments, and in carrying out such treatments on patients.

The research and treatments may take place both in (...indicate country...) and abroad, but always in accordance with relevant legislation, regulations, agreements and approval.

If you are interested in the regulations that govern the use of the iPSCs and cells derived from them, the Biobank can provide links to specific documents.

Cells produced from iPSCs may be used for clinical research and treatment of diseases or injuries in all the body's organs and tissues. However, they will not be used to produce gametes (sperm and egg cells) that can be used to create new individuals (cloning).

Cells produced for specific research projects and patient treatments will only be used for these purposes. Any residual material will either be returned to the Biobank or destroyed.

You will not be able to decide which institutions or researchers can use the iPSCs, the cells derived from iPSCs, and the pseudonymized information obtained from these cells.

TESTING FOR INFECTIOUS DISEASES AND QUALITY CONTROL ANALYSES

In connection with taking the skin biopsy and/or blood samples, we will have a short conversation with you to inform you about the procedures, and you will be asked to fill in a questionnaire about health and lifestyle (roughly the same as the form one fills out when donating blood or bone marrow). We will then take the blood sample to test whether you have any infectious diseases and to confirm your blood and tissue typing. Testing for

infectious diseases is done to check that you are healthy and that there is no risk of transmission of any infection from you to patients who may receive cells derived from your donated cells in the future. Moreover, GMP-compatible production of cell-based products does not permit the use of potentially infected materials in clean rooms due to the risk of cross-contamination between cells from different donors.

The blood sample will be stored together with your donated cells for any future analyses. The donated cells will be kept in quarantine for six months. After six months, another blood sample (of smaller volume than the first) will be taken from you to test for the presence of infection. This is necessary because if you acquire an infectious disease shortly before the first blood sample is taken, it may not be detected in that sample. Taking a second blood sample later allows us to be certain that you were not infected at the time of the first sample. If the second blood sample is negative for infectious diseases, your cells will be further processed. You will of course be informed if we detect an infection, so that you can receive relevant treatment for this.

If cells originating from you are later to be used in a patient, we will carry out new control analyses of iPSCs and cells produced from them, partly to check that they are of good quality, and partly to make sure that no changes in the cells that can be dangerous to the patient have occurred during cell storage or cultivation. A limited mapping of genetic markers in the donated cells and iPSCs will also be carried out to ensure unique identification of the cells during any future use (a strict requirement in research and clinical applications). In special cases, it may also be relevant to determine whether cells derived from you have any gene mutations that would make it inappropriate to use them in a patient. Should we discover anything through genetic analysis that is relevant for medical follow-up, the (...name of institution...) will be able to contact you to provide you with information and possibly genetic counseling. Please note that you must give separate consent whether you do or do NOT want to be contacted in such an event.

ARCHIVING AND USE OF PERSONAL DATA

The recruiting and contact office at (...name of institution...), which is separate from the facility at the Biobank that will process, store and characterize cells obtained from you and the iPSCs derived from these, will create a unique code for each donor who submits a skin biopsy and/or blood sample, so that cells derived from you will be identified only by this code and not by your name or any other form of personal identification such as your personal identification number (this is the process of pseudonymization). This code, together with gender, age, ABO blood type and HLA type will then be transferred to the Biobank. It is important that the Biobank has information about gender, age, and blood and HLA type, as these features determine which patients can be treated with the cells.

The pseudonymized information will be stored and handled in accordance with applicable law. Pseudonymized information will be processed by certified data controllers of the Biobank and by health service providers who use cells derived from you for clinical purposes, in accordance with Regulation 2016/679 of the European Parliament and of the EU Council on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). The specific conditions governing your consent to the processing of this information are indicated in the Informed Consent Form.

Your identity will therefore not be known to any other person or institution, including the laboratory that stores and processes your cells at the Biobank and any entity that uses cells derived from you, except for the recruiting and contact office at (...name of institution...). Cells originating from you, data from analyses of the cells, and the aforementioned pseudonymized information will be designated only by the unique code created by the recruitment and contact office.

Pseudonymized information can be shared with those who use your cells for basic, applied or clinical research and treatments, both in your country and abroad. The (...name of institution...), which is the owner of the Biobank, is responsible for the transfer of this information in accordance with national law and EU Directive 2016/679 (see above).

The unique code will also be used if it is deemed necessary to contact you regarding future medical applications, or in connection with future analyses that reveal information about you that is relevant for medical follow-up.

The Biobank will then relay this information to the recruiting and contact office that generated the code, which can then link the code to your name and contact you.

All pseudonymized information obtained from you and your cells will remain with the Biobank to ensure that it is not compromised for as long as the Biobank exists. If the Biobank is terminated, your cells and archived pseudonymized information will be destroyed. However, termination of the Biobank or destruction of cells originating from you will not involve the deletion of data from clinical research or treatments that have already been published, nor the deletion of information where continued use is required by law, as may be the case for some treatments or research projects for safety reasons. Specifically, if cells have already been transferred to a patient, archived pseudonymized information cannot be deleted due to legal requirements for traceability for (...XX years, specify according to country...) thereafter.

Commented [JG1]: This is 30 years in the EU.

Aside from the Biobank, only persons authorized by appropriate national regulatory authorities and ethics committees will have access to your pseudonymized information, if necessary. These include 1) those authorized to produce cells and to implement the research projects, clinical trials and treatments using the cells, and 2) foreign medical regulatory authorities where treatments using cells derived from you are approved. These persons will be bound by confidentiality agreements to not disclose this information to anyone else.

To summarize, all information needed for producing and using cells for medical purposes will remain in pseudonymized form. Personally identifiable information will never leave the recruiting and contact office at (...name of institution...) where it is stored securely and separate from the laboratory facility at the Biobank that stores, characterizes and distributes the cells.

The information that is collected, processed and included as part of the pseudonymized information may include potentially sensitive information about you, such as your race, ethnicity, and physical health. By your signature on the Informed Consent Form, you acknowledge that you consent to the use of your pseudonymized information as described above. However, you have the right to withdraw this consent. Specifically, you have the right to access and inspect all records relating to you, and to correct or delete information about you and the cells derived from you. In the event of disagreement or uncertainty regarding the processing of your information, you have the right to register an inquiry or a complaint with the supervisory authority responsible for data protection in your country. If you wish to exercise any of these rights, please contact the office at (...name of institution...) that collected the information in connection with your recruitment to the project.

APPROVAL OF FUTURE CLINICAL RESEARCH AND TREATMENTS

All future research and treatment of patients based on iPSCs from the Biobank must be approved in advance by the national regulatory authorities and appropriate committee for medical and healthcare research ethics (...indicate country...) and possibly corresponding foreign ethics committees if other countries are involved. Should clinical research or treatment involve the use of cells in foreign countries, this will first be evaluated and approved by the Biobank based on professional guidelines and carried out according to appropriate restrictions that apply to such research and treatments.

Results from research and patient treatment involving cells derived from you may be published in national and international scientific journals. This is important to ensure that knowledge gained relevant for the clinical use of the cells is appropriately disseminated and can be verified and established as standard treatment.

Examples of diseases and injuries for which cells originating from you may be used in clinical research or treatment include Parkinson's disease, Alzheimer's disease, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), stroke, spinal cord injuries, diabetes, liver diseases, heart failure, articular cartilage degeneration, bone fragility, retinal degeneration, lung diseases, cancer in various organs, and others.

Biomedical research can lead to new medical breakthroughs and treatment options that are difficult to predict in advance. Such new scientific knowledge and technological advances can enable the use of your cells in ways that we currently cannot envision and therefore have no opportunity to inform you about. You are therefore asked to consent that the Biobank can contact you in the future if there are grounds for extending the consent you are now providing.

POTENTIAL COMMERCIALIZATION

Future use of cells that lead to new treatment options may involve patentable innovations and opportunities for commercialization. In addition, some phases of preclinical research and the implementation of clinical trials is expensive and often requires financial support from pharmaceutical, biotechnological or other medical industry companies. This will likely also require some form of commercialization. The Biobank cannot outline all potential plans for or details of future commercialization, as these will only be defined once treatment development and implementation occur. It is important to understand that your consent for the use of cells derived from you does not involve a financial contract, and potential future commercialization will not include drawing up a financial contract with you later. In other words, your consent means that you also waive the right to claim personal monetary gain from any subsequent commercialization. This is indicated specifically in the Informed Consent Form.

INFORMATION REGARDING FUTURE USE OF YOUR CELLS

You will not automatically be informed when cells originating from you are used in a future research project or patient treatment. If you are interested in following the Biobank's activities, including what the cells derived from you have been used for, you may contact the owner of the Biobank at any time (see under "Contact" in the Informed Consent Form) for more information. Because only the recruiting and contact office at (...name of institution...) that separately stores your name and personal identification number will know your identity, all inquiries need to be addressed to that office, which will then convey your inquiry to the laboratory facility at the Biobank using the unique code.

The owner of the Biobank (...name of institution...) will be able to give you information of a general nature without being able to say whether cells originating from you have been or will be used in a specific research project or a specific treatment. The owner of the Biobank (...name of institution...) may, however, be able to answer more detailed questions after consultation with the Biobank itself. Obtaining more detailed information about the use of cells derived from you will again involve use of the unique code to protect your identity.

The Biobank may create a website about its activity, on which information about research and treatments based on iPSCs in the Biobank may be presented. This will never include information that can be used to identify you or the other donors from whom the iPSCs originate.

CONSENT TO DONATE BIOLOGICAL MATERIAL TO:

BIOBANK OF INDUCED PLURIPOTENT STEM CELLS (iPSCs)

IN BRIEF ABOUT BACKGROUND, PURPOSE AND INTENTION

As described in more detail in the Information Document (attached), the purpose of this biobank of induced pluripotent stem cells (iPSCs), hereinafter called the Biobank, is to collect immature stem cells from donors that can be used for the production of various mature cell types for use in patient treatment and for applied and clinical research that lead to development of new treatments. With such a biobank in place, it will be possible in the future to make cells needed to treat patients with serious illnesses and injuries much more quickly than if the patients' own cells were used.

To generate the iPSCs in this biobank, we need a skin sample (skin biopsy) and/or blood samples from you. Skin cells or blood cells will be used to make the iPSCs. The blood samples will also be used for control analyses to ensure that iPSCs from you can be safely used to treat patients.

WHAT YOU ARE CONSENTING TO

Before we can use skin and blood samples from you, you need to agree to their use as described here and in more detail in the Information Document.

We ask you to consent that specific information about you (gender, age, ABO blood type, HLA type) can be used in pseudonymized form by the Biobank and transferred by the Biobank to other research institutions or treatment centers that will use your cells. "Pseudonymized" means that common information that can be used to directly identify you, such as name and personal identification number, is stored only by the recruiting office of the Biobank and cannot be accessed by anyone else, including the laboratory of the Biobank that processes and stores the skin and blood samples and creates, stores, characterizes and distributes the iPSCs made from them (see the Information Document for details). All information obtained from analyses of the skin and blood samples, the iPSCs and other types of cells derived from the iPSCs, including genetic data, will be pseudonymized. In practical terms, this means that this information will be archived separately and labeled by a code that only the recruiting office of the Biobank can use to link to your identity. We ask you to consent to archiving of this additional, pseudonymized information by the laboratory of the Biobank. This information is necessary to ensure that the cells can be used safely in patients. We ask you to agree that this information can be shared with other research institutions and treatment centers that will use the cells for basic, applied and clinical research as well as treatment of patients. Such use may occur both in your country as well as in other countries, if the latter is necessary for the development or utilization of such treatments.

You also need to consent to the publication in national and international scientific journals of results from research projects and patient treatments involving your cells.

POSSIBLE FUTURE EXPANSION OF CONSENT

Biomedical research can lead to new medical breakthroughs and treatment options that are difficult to predict in advance. We therefore ask you to permit the Biobank to contact you in the future if reasons arise to extend the consent you are now giving.

FUTURE COMMERCIALIZATION

Substantial financial backing is required to implement clinical trials using cells derived from iPSCs. This will often involve commercial partners, for example within the pharmaceutical industry. It is important to understand that your consent to the Biobank to use iPSCs and cells derived from the iPSCs includes a waiver by you of any financial interest or monetary gain from future commercial use.

IN THE EVENT WE DISCOVER INFORMATION THAT IS RELEVANT TO YOUR HEALTH

The skin and blood samples and the cells that originate from them will need to be analyzed to ensure that cells derived from the iPSCs can be used safely in patients. This may involve genetic and other analyses that may reveal information about you that is relevant for medical follow-up. You must indicate separately below whether or not you want the Biobank to contact you should such information arise.. Should this include genetic issues (for example mutations or predispositions), you will be offered appropriate genetic counselling.

RIGHT TO WITHDRAW CONSENT, RIGHT TO ACCESS AND INQUIRY, RIGHT TO COMPLAIN, DESTRUCTION OF MATERIAL

You can at any time have access to the pseudonymized information about you and about the iPSCs and other cells that are generated from them that the Biobank has archived. You have the right to inquire into how this information is stored and handled, including assessments of data security risks. You also have the right to have any errors in the information corrected.

You have the right to register complaints to the appropriate national and institutional data protection authority about the handling and processing of the information we obtain about you and about the iPSCs and other cells that are generated from them.

You can withdraw your consent at any time and demand that biological material from you be destroyed, without giving a reason. The right to withdraw consent at any time will not, however, affect research or treatments already initiated before consent is withdrawn. If cells from you are already included in a research project or treatment, or are processed and included in another biological product with or without commercialization, the possibility for destruction may be restricted in accordance with legislation that regulates and protects the objectives of the research, treatment or commercialization.

PARTICIPATION IS VOLUNTARY

Donating biological material to the Biobank is voluntary and requires your consent. If you choose not to give consent, or if you later wish to withdraw your consent, there will be no negative effects on your rights or access to your health care system, or your rights to donate cells or tissue later for other purposes.

CONTACT INFORMATION

If you have questions about the Biobank or later wish to withdraw your consent, you can contact the Biobank :

Web page: E-mail:..... Telephone:

If you have questions regarding the practices and regulations governing handling of personal information and information privacy (GDPR), you can contact the relevant Data Protection Officer:

Name: E-mail: Telephone:

CONSENT TO DONATE A SKIN BIOPSY AND/OR BLOOD SAMPLE TO THE BIOBANK OF iPSCs AND TO PERMIT PSEUDONYMIZED INFORMATION TO BE HANDLED AND ARCHIVED AS DESCRIBED ABOVE

After having read the Information Document, and having had the opportunity to ask questions, and after reading through this consent form, I am sufficiently informed about what it entails to give a skin biopsy and blood sample and thereby contribute to establishing this biobank of iPSCs. My decision regarding participation in the establishment of the Biobank is as follows :

☐ Yes ☐ No	I hereby agree that biological material (skin and blood sample) from me can be stored in the Biobank in accordance with what is described above and in the Information Document. I agree that cells originating from me can be used for applied and clinical research and treatment of patients in my own country and abroad in accordance with what is described. I agree that scientific results from applied and clinical research and treatment involving cells originating from me can be published in national and international scientific journals. I agree that pseudonymized information about me and obtained from cells originating from me can be processed and archived as described. I understand that the development and implementation of clinical research, clinical trials, and clinical treatments can involve commercialization, and that by signing this consent form I waive all future financial interest in the iPSCs derived from my biological material, cells derived from the iPSCs, scientific knowledge obtained from them, and any clinical treatment or product that is generated as a result. I also understand that I have the right to withdraw my consent at any time without stating a reason, as described here and in the Information Document.
☐ Yes ☐ No	I agree that I may be re-contacted by the Biobank at a later date if the Biobank needs additional biological material.
☐ Yes ☐ No	I agree that I may be re-contacted by the Biobank at a later date if the Biobank needs additional information.
☐ Yes ☐ No	I agree that the Biobank may contact me in at a later date should it become necessary to extend the scope of the consent already given.
☐ Yes ☐ No	I agree that the Biobank may contact me at a later date if analyses reveal health information, including genetic information, about me that may be relevant for medical follow-up.

Date:

Place:

Signature:

Name (printed in
capital letters):

Personal identification number:

Email address:

Telephone number:

I confirm that I conducted the donor consultation and have obtained the donor's consent.

Name of the person obtaining consent

INFORMATION DOCUMENT

BIOBANK OF INDUCED PLURIPOTENT STEM CELLS (iPSCs)

BACKGROUND, PURPOSE AND INTENTION

The purpose is to establish a biobank of immature stem cells that are generated in the laboratory from donor cells. Such stem cells, which are called induced pluripotent stem cells (iPSCs), can be created in the laboratory from cells obtained from the umbilical cord shortly after birth. iPSCs can be used to make any type of cell in the body, and these can then be used in the treatment of patients with serious injuries and diseases in which cells either do not function as they should, have been lost, or where supplying new cells could improve tissue or organ function.. By transferring (transplanting) the cells we generate from iPSCs to an organ or tissue in a patient, it can be possible to slow down or stop a disease, or to replace cells that have been lost. Such treatments represent a key aim in the fields of regenerative medicine and tissue engineering.

To reduce the risk of the transplanted cells being rejected, we need to make iPSCs from donors who have tissue types (HLA types) that are compatible with a large proportion of the population. We are contacting you because cells from the umbilical cord are particularly suitable for this purpose and because your child's HLA type may be compatible with a large proportion of the population (this will be determined by the HLA-typing that we will perform on your child's cells). We hope therefore that you will be willing to approve donation of such cells when your child is born.

A blood sample will be taken from the umbilical cord of your child shortly after birth, and from this we will obtain cells that will be frozen and stored in the biobank. These cells will be converted into iPSCs, which will also be frozen and stored in the biobank. iPSCs can be used as a starting point to generate different types of mature cell types that can be used for clinical research and treatment. An iPSC biobank will be a very important resource in Europe and world-wide. iPSCs in the biobank can be used to produce cells for patients both in your home country and internationally, much faster than if we were to use a patient's own cells, which is also not always possible.

PARTICIPATION IS VOLUNTARY

Donating your child's biological material to this biobank of iPSCs (hereafter referred to as "the Biobank") is completely voluntary. You have the right to agree or to refuse to provide your child's biological materials for this project. The quality of your current or future medical care, or your participation as a donor in any other context, such as donating blood or bone marrow, will not change in any way whether you agree or refuse to provide cells for the Biobank.

WHO OWNS AND ADMINISTERS THE BIOBANK?

The Biobank is owned by (...name of institution...). The (...name of institution...) has a Tissue Establishment certification for biobanking issued by (...name of regulatory agency...). The Biobank consists of 1) a recruiting and contact office, which will be responsible for all contact with you including the scheduling of donations, the collection, processing and storage of personal data, and any subsequent contact, and 2) a laboratory facility responsible for storage and characterization of your child's donated cells and the production, storage and characterization of the iPSCs derived from those cells. The (...facility that carries out the biobanking and production...) has the necessary expertise and a certificate of Good Manufacturing Practice (GMP) issued by (...name of regulatory agency...). This ensures high-quality production of iPSCs from the donated cells, and the characterization and analysis of iPSCs to ensure that they can be used safely for GMP-compliant production of differentiated cells for treating patients. The (...name of institution...) will be responsible for ensuring the storage of pseudonymized information obtained through characterization and analysis of the donated cells and iPSCs. Pseudonymized information means there is no direct link to your or your child's name, personal identification numbers, or any other information that can be used to directly identify you or your child (see Section on Archiving and Use of Personal Data, below).

Commented [JG1]: Text used in HaploPS Adult Donor Information Document:

The Biobank consists of 1) a recruiting and contact office, which will be responsible for all contact with you including the scheduling of donations, the collection, processing and storage of personal data, and any subsequent contact, and 2) a laboratory facility responsible for storage and characterization of your donated tissue and cells and the production, storage and characterization of the iPSCs derived from your cells.

Example of text used by the Norwegian iPSC Biobank for Clinical Application (NIBCA) for adult donors: The Biobank is a collaboration between the Norwegian Bone Marrow Donor Registry, the Norwegian Center for Stem Cell Research and the Ex Vivo Cell Laboratory, all at the Department of Immunology and Transfusion Medicine. The Bone Marrow Donor Registry will be responsible for recruiting donors and for the collection, processing and storage of personal data, for collecting the biological material needed to produce iPSCs, and any future contact. The Ex Vivo Cell Laboratory will be responsible for the storage of the donated biological material and the production and storage of the iPSCs in the Biobank. The Norwegian Center for Stem Cell Research contributes expertise on the production and characterization of iPSCs to ensure that they can be used safely to generate different types of cells for treatment of patients. Both the Norwegian Center for Stem Cell Research and the Ex Vivo Cell Laboratory will carry out analyses of the donated biological material and the iPSCs.

COLLECTION OF UMBILICAL CORD CELLS

Collection of cells from the umbilical cord will be taken shortly after the birth of your child, by experienced doctors at <insert name of hospital or birth clinic>.

The collection of cells from the umbilical cord does not affect your newborn child in any way. It is performed <insert details about procedure>. The umbilical cord cells will be delivered to the <insert name of laboratory producing and storing the iPSCs> at the Biobank where further procedures are carried out.

WHAT HAPPENS TO THE CELLS THAT DERIVE FROM YOUR CHILD'S UMBILICAL CORD?

Both the umbilical cord cells and the iPSCs produced from these will be kept frozen indefinitely in the Biobank. If we run out of iPSCs, we will be able to produce new ones from the stored umbilical cord cells. The iPSCs are used as the starting point to generate different types of mature cells that can be used for basic, applied, or clinical research aimed at developing cell-based treatments, and in carrying out such treatments on patients.

The research and treatments may take place both in (...indicate country...) and abroad, but always in accordance with relevant legislation, regulations, agreements and approval.

If you are interested in the regulations that govern the use of the iPSCs and cells derived from them, the Biobank can provide links to specific documents.

Cells produced from iPSCs may be used for clinical research and treatment of diseases or injuries in all the body's organs and tissues. However, they will not be used to produce gametes (sperm and egg cells) that can be used to create new individuals (cloning).

Cells produced for specific research projects and patient treatments will only be used for these purposes. Any residual material will either be returned to the Biobank or destroyed.

You will not be able to decide which institutions or researchers can use the iPSCs, the cells derived from iPSCs, and the pseudonymized information obtained from these cells.

TESTING FOR INFECTIOUS DISEASES AND QUALITY CONTROL ANALYSES

Prior to the birth of your child, we will have a short conversation with you to provide you with information about the procedure, and we will then take a blood sample from you to test whether you have any infectious diseases. Testing for infectious diseases is done to check that there is no risk of transmission of any infection from you to the cells in your child's umbilical cord. You will of course be informed if we detect an infection, so that you can receive relevant treatment for this by your healthcare system.

If cells originating from the iPSCs that we make are later to be given to a patient, we will carry out control analyses of the iPSCs and cells produced from them, partly to check that they are of good quality, and partly to make sure that no changes in the cells that can be dangerous to the patient have occurred during cell storage and cultivation. A limited mapping of genetic markers in the umbilical cord cells and iPSCs will also be carried out to ensure unique identification during any future use (a strict requirement in clinical applications). This mapping is only used to ensure that later developed cell products to be used in a patient derive from a single donor and are not contaminated by cells from another donor. In special cases, it may also be relevant to determine whether cells have any gene mutations that would make it inappropriate to use them in treatments. Should we discover anything through genetic analysis that is relevant for medical follow-up, the <insert name of host institution> will be able to contact you to offer you information and possibly genetic counseling. Please note that in the Informed Consent Form you must indicate whether you do or do NOT want to be contacted in such an event.

ARCHIVING AND USE OF PERSONAL DATA

Only the <insert name of host institution> knows your identity and the identity of your child. The <insert name of host institution> will be the recruiting and contact office at <insert name of host institution>, which is separate

from the facility at the Biobank that will process, store and characterize cells obtained from you and the iPSCs derived from these, will create a unique code for each donor of umbilical cord blood, so that cells derived from your child will be identified only by this code and not by your or your child's name or any other form of personal identification such as personal identification number (this is the process of pseudonymization). This code, together with gender, age, ABO blood type and HLA type of your child will then be transferred to the <insert name of laboratory producing and storing the iPSCs>. It is important that the <insert name of laboratory producing and storing the iPSCs> has information about gender, age, and blood and HLA type, as these features determine which patients can be treated with the cells.

The pseudonymized information will be stored and handled in accordance with applicable law. Pseudonymized information will be processed by certified data controllers of the Biobank and by health service providers who use cells derived from you for clinical purposes, in accordance with Regulation 2016/679 of the European Parliament and of the EU Council on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). The specific conditions governing your consent to the processing of this information are indicated in the Informed Consent Form.

Your identity and the identity of your child will therefore not be known to the <insert name of laboratory producing and storing the iPSCs> or anyone who carries out future clinical research or treatment with cells originating from your child's umbilical cord. Those cells, data from analyses of the cells and the iPSCs made from them, and the aforementioned pseudonymized information will be designated only by the unique code.

Pseudonymized information can be shared with those who use the iPSCs for clinical research and treatments, both in <insert name of country> and abroad. <insert name of host institution>, which is the owner of the Biobank, is responsible for the transfer of this information in accordance with legislation in <insert name of country> and EU data protection regulations (GDPR; EU 2016/679).

The unique code will also be used if it is deemed necessary to contact you regarding future medical applications, or in connection with future analyses that reveal information that is relevant for medical follow-up. The <insert name of laboratory producing the iPSCs> will then be able to send the code to the <insert name of host institution>, which can link the code to your name and then contact you. Note that re-contact is also relevant when your child becomes an adult and attains legal competence, as described in the section related to re-contact below.

Pseudonymized information will be archived at the <insert name of laboratory producing the iPSCs> for as long as the Biobank exists (but see next paragraph below). If the Biobank is terminated, information archived at the <insert name of laboratory producing the iPSCs> will be deleted. The only information archived thereafter will be the donor information archived at the <insert name of host institution>.

Termination of the Biobank or destruction of cells originating from your child's umbilical cord will not, however, involve the deletion of data from research or treatments that have already been published, nor the deletion of information where continued use is required by law for patient safety reasons, as may be the case for some treatments or research projects. Specifically, if cells have already been transferred to a patient, archived pseudonymized information cannot be deleted for <XX years, specify according to country> due to legal requirements for traceability.

Commented [JG2]: This is 30 years in the EU.

APPROVAL OF FUTURE CLINICAL RESEARCH AND TREATMENTS

All future clinical research and treatment of patients based on iPSCs from the Biobank must be approved in advance by the national regulatory authorities and appropriate committee for medical and healthcare research ethics in <insert name of country>, and possibly corresponding foreign ethics committees if other countries are involved. Should clinical research or treatment involve the use of cells in other countries, this will first be evaluated and approved by the Biobank based on professional guidelines and carried out according to appropriate restrictions that apply to such research and treatments.

Results from clinical research and patient treatment involving cells originating from your child's umbilical cord may be published in national and international scientific journals. This is important to ensure that knowledge

gained about the clinical use of the cells is appropriately disseminated and can be verified and established as standard treatment.

Examples of diseases and injuries for which cells originating from your child's umbilical cord may be used in clinical research or treatment include Parkinson's disease, Alzheimer's disease, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), stroke, spinal cord injuries, diabetes, liver diseases, heart failure, articular cartilage degeneration, bone fragility, retinal degeneration, lung diseases, cancer in various organs, and others.

Biomedical research can lead to new medical breakthroughs and treatment options that are difficult to predict in advance. Such new scientific knowledge and technological advances can enable the use of iPSCs made from your child's cells in ways that we currently cannot envision and therefore have no opportunity to inform you about. You are therefore asked to consent that the Biobank can contact you in the future if there are grounds for extending the consent you are now providing.

RE-CONTACT AND TRANSFER OF CONSENT WHEN YOUR CHILD REACHES ADULTHOOD

When your child reaches adulthood and legal competence, existing international ethics **codes** indicate that the consent that you gave on your child's behalf must be transferred to your child, to protect your child's rights as a donor. For this reason, it is necessary for the Biobank to re-contact you and/or your child at that time. The **<insert name of host institution>** will therefore register date of birth and appropriate contact information when the blood sample is taken from your child's umbilical cord. Note that if re-contact is not possible, this may invalidate use of the cells beyond the date when your child reaches adulthood and legal competence.

Commented [JG3]: Reference can be made to the Declaration of Helsinki and the Council of Europe's Additional Protocol (2005: Art 13, s.3) to the Oviedo Convention (1997).

POTENTIAL COMMERCIALIZATION

Future use of cells that lead to new treatment options may involve patentable innovations and opportunities for commercialization. In addition, some phases of preclinical research and the implementation of clinical trials is expensive and often requires financial support from pharmaceutical, biotechnological or other medical industry companies. This will likely also require some form of commercialization. The Biobank cannot outline all potential plans for or details of future commercialization, as these will only be defined once treatment development and implementation occur. It is important to understand that your consent for the use of cells originating from your child's umbilical cord does not involve a financial contract, and potential future commercialization will not include drawing up a financial contract with you later. In other words, your consent means that you also waive the right to claim personal monetary gain from any subsequent commercialization. This is indicated specifically in the Informed Consent Form.

However, this waiver from you does not legally extend to your child. When your child reaches adulthood and attains legal competence, the right to consent will be transferred to your child, who will then assume the right to approve, modify or reject the consent that you have agreed to when you sign the Informed Consent **Form**.

Commented [JG4]: Note that exactly how this transfer of consent will affect use of iPSCs and cells derived from them is still not well established. HaploIPs is in communication with the EU Committee on Substances of Human Origin (SoHo) to assess this issue as the new SoHo regulations become defined.

INFORMATION REGARDING FUTURE USE OF CELLS FROM YOUR CHILD'S UMBILICAL CORD

You and your child will not automatically be informed when cells originating from your child's umbilical cord are used in a future research project or patient treatment. If you or your child are interested in following the Biobank's activities, including what the cells originating from your child's umbilical cord have been used for, you may contact the **<insert name of host institution>** at any time for more information (see under "Contact" in the consent form). Because only the **<insert name of host institution>** will know your and your child's identities, all inquiries must go to the **<insert name of host institution>**.

The **<insert name of host institution>** will be able to give you information of a general nature without being able to say whether cells originating from your child have been or will be used in a specific clinical research project or a specific treatment. The **<insert name of host institution>** may, however, be able to answer more detailed questions after consultation with the **<insert name of laboratory producing the iPSCs>**.

The Biobank may create a website about its activity, on which information about clinical research and treatments based on iPSCs in the Biobank may be presented. This will never include information about the donors from which the iPSCs originate.

CONSENT TO DONATE BIOLOGICAL MATERIAL TO:

BIOBANK OF INDUCED PLURIPOTENT STEM CELLS (iPSCs)

IN BRIEF ABOUT BACKGROUND, PURPOSE AND INTENTION

As described in more detail in the Information Document (attached), the purpose of this biobank of induced pluripotent stem cells (iPSCs), hereinafter called the Biobank, is to collect immature stem cells from donors that can be used for the production of various mature cell types for use in patient treatment and for applied and clinical research that lead to development of new treatments. With such a biobank in place, it will be possible in the future to make cells needed to treat patients with serious illnesses and injuries much more quickly than if the patients' own cells were used.

To generate the iPSCs in this biobank, we need a sample of blood from the umbilical cord of your newborn infant. The blood cells will be used to make the iPSCs. The blood sample will also be used for control analyses to ensure that the iPSCs can be safely used to treat patients.

WHAT YOU ARE CONSENTING TO

Before we can use the umbilical cord blood sample, you need to agree to its use as described here and in more detail in the Information Document.

We ask you to consent that specific information about your child (gender, age, ABO blood type, HLA haplotype) can be used in pseudonymized form by the Biobank and transferred by the Biobank to other research institutions or treatment centers that will use your child's cells. "Pseudonymized" means that common information that can be used to directly identify you or your child, such as name and personal identification number, is stored only by the recruiting office of the Biobank and cannot be accessed by anyone else, including the laboratory of the Biobank that processes and stores the blood sample and creates, stores, characterizes and distributes the iPSCs made from the blood cells (see the Information Document for details). All information obtained from analyses of the blood cells, the iPSCs and other types of cells derived from the iPSCs, including genetic data, will be pseudonymized. In practical terms, this means that this information will be archived separately and labeled by a code that only the recruiting office of the Biobank can use to link to you or your child's identity. We ask you to consent to archiving of this additional, pseudonymized information by the laboratory of the Biobank. This information is necessary to ensure that the cells can be used safely in patients. We ask you to agree that this information can be shared with other research institutions and treatment centers that will use the cells for basic, applied and clinical research as well as treatment of patients. Such use may occur both in your country as well as in other countries, if the latter is necessary for the development or utilization of such treatments.

You also need to consent to the publication in national and international scientific journals of results from research projects and patient treatments involving the iPSCs and cells derived from them.

POSSIBLE FUTURE EXPANSION OR LIMITATION OF CONSENT

Biomedical research can lead to new medical breakthroughs and treatment options that are difficult to predict in advance. We therefore ask you to permit the Biobank to contact you in the future if reasons arise to expand the consent you are now giving. We also ask you to permit us to contact your child once they reach adulthood and attain legal competence, so that they can be informed of the existing consent regarding the cells derived from them. At this time, they will assume the right to approve, modify or withdraw the consent you have given as stipulated on the signature page and explained in the Information Document.

FUTURE COMMERCIALIZATION

Substantial financial backing is required to implement clinical trials using cells derived from iPSCs. This will often involve commercial partners, for example within the pharmaceutical industry. It is important to understand that your consent to the Biobank to use iPSCs and cells derived from the iPSCs includes a waiver by you of any financial interest or monetary gain from future commercial use. However, because the iPSCs in the

Biobank are derived from your child, who is not yet legally competent, your waiver of financial interest and monetary gain does not extend to your child. When your child assumes responsibility for consent, the regulations governing basic and clinical research and commercial use that exist at that time will then apply and it will be your child's right to decide whether to accept a waiver of financial interest for future commercial use. As indicated in the Information Document, any use already established in the interim may be protected by law from a withdrawal of consent by your child.

IN THE EVENT WE DISCOVER INFORMATION THAT IS RELEVANT TO YOUR OR YOUR CHILD'S HEALTH

The blood sample and the iPSCs that are generated from it will need to be analyzed to ensure that cells derived from the iPSCs can be used safely in patients. This may involve genetic and other analyses that may reveal information about your child and thereby potentially also about you that is relevant for medical follow-up. You must indicate separately below whether or not you want the Biobank to contact you should such information arise. Should the information include genetic issues (for example mutations or predispositions), you will be offered appropriate genetic counselling.

RIGHT TO WITHDRAW CONSENT, RIGHT TO ACCESS AND INQUIRY, RIGHT TO COMPLAIN, DESTRUCTION OF MATERIAL

You can at any time have access to the pseudonymized information about your child and about the iPSCs and other cells that are generated from them that the Biobank has archived. You have the right to inquire into how this information is stored and handled, including assessments of data security risks. You also have the right to have any errors in the information corrected.

You have the right to register complaints to the appropriate national and institutional data protection authority about the handling and processing of the information we obtain about your child and about the iPSCs and other cells that are generated from them.

You can withdraw your consent at any time and demand that biological material derived from your child be destroyed, without giving a reason. The right to withdraw consent at any time will not, however, affect research or treatments already initiated before consent is withdrawn. If iPSCs generated from the blood sample or cells derived from the iPSCs are already included in a research project or treatment, or are processed and included in another biological product with or without commercialization, the possibility for destruction may be restricted in accordance with legislation that regulates and protects the objectives of the research, treatment or commercialization. This is also the case when your child reaches adulthood and attains legal competence, and then assumes the right to modify or withdraw consent.

PARTICIPATION IS VOLUNTARY

Donating biological material to the Biobank is voluntary and requires your consent. If you choose not to give consent, or if you later wish to withdraw your consent, there will be no negative effects on your or your child's rights or access to your health care system, or your or your child's rights to donate cells or tissue later for other purposes.

CONTACT INFORMATION

If you have questions about the Biobank or later wish to withdraw your consent, you can contact the Biobank :

Web page: E-mail: Telephone:

If you have questions regarding the practices and regulations governing handling of personal information and information privacy (GDPR), you can contact the relevant Data Protection Officer:

Name: E-mail: Telephone:

Field Code Changed

CONSENT TO DONATE AN UMBILICAL CORD BLOOD SAMPLE TO THE BIOBANK OF iPSCs AND TO PERMIT PSEUDONYMIZED INFORMATION TO BE HANDLED AND ARCHIVED AS DESCRIBED ABOVE AND IN THE INFORMATION DOCUMENT

After having read the Information Document, and having had the opportunity to ask questions, and after reading through this consent form, I am/we are sufficiently informed about what it entails to donate a blood sample from my child's umbilical cord and thereby contribute to establishing this biobank of iPSCs. My/our decision regarding participation in the establishment of the Biobank is as follows :

☐ Yes ☐ No	I/we hereby agree that biological material (umbilical cord blood) from my/our child can be stored in the Biobank in accordance with what is described above and in the Information Document. I/we agree that iPSCs generated from this blood sample and cells derived from the iPSCs can be used for applied and clinical research and treatment of patients in my/our own country and abroad in accordance with what is described. I/we agree that scientific results from applied and clinical research and treatment involving these cells can be published in national and international scientific journals. I/we agree that pseudonymized information about my/our child and obtained from cells derived from my/our child can be processed and archived as described. I/we understand that the development and implementation of clinical research, clinical trials, and clinical treatments can involve commercialization, and that by signing this consent form I/we waive all future financial interest in the iPSCs derived from my/our child's biological material, cells derived from the iPSCs, scientific knowledge obtained from them, and any clinical treatment or product that is generated as a result. I/we also understand that I/we have the right to withdraw consent at any time without stating a reason, as described here and in the Information Document. I/we understand that the Biobank will need to contact my/our child once my/our child has attained legal competence, and that at that time my/our child will assume the right to approve, modify or withdraw the consent given here.
☐ Yes ☐ No	I/we agree that I/we may be re-contacted by the Biobank at a later date if the Biobank needs additional biological material.
☐ Yes ☐ No	I/we agree that I/we may be re-contacted by the Biobank at a later date if the Biobank needs additional information.
☐ Yes ☐ No	I/we agree that I/we may be re-contacted by the Biobank at a later date should it become necessary to extend the scope of the consent already given.
☐ Yes ☐ No	I/we agree that I/we may be re-contacted by the Biobank at a later date if analyses reveal health information, including genetic information, about my/our child and also about me/us that may be relevant for medical follow-up.

Date:

Place:

Signature(s):

Commented [A1]: Note that including which specific legal statutes pertain can be dealt with here in this way and don't necessarily have to be dealt with in detail in the Informed Consent Form and Information Document. In particular, the Information Document states explicitly that links to relevant legal documents can be provided on request. There are two issues at play here: 1) legal frameworks are not static, so specific statements in these documents may become outdated, and 2) by experience (according to Norwegian Bone Marrow Donor Registry, which has 30 years experience in recruiting donors) adding too much detailed information, and in particular "legalese", is a turn off for potential donors, who may avoid the entire process as a result.

Name(s), printed in
capital letters:

Personal identification number(s):

Email address(es):

Telephone number(s):

I confirm that I conducted the donor consultation and have obtained the donor's/donors' consent.

Name of the person obtaining consent