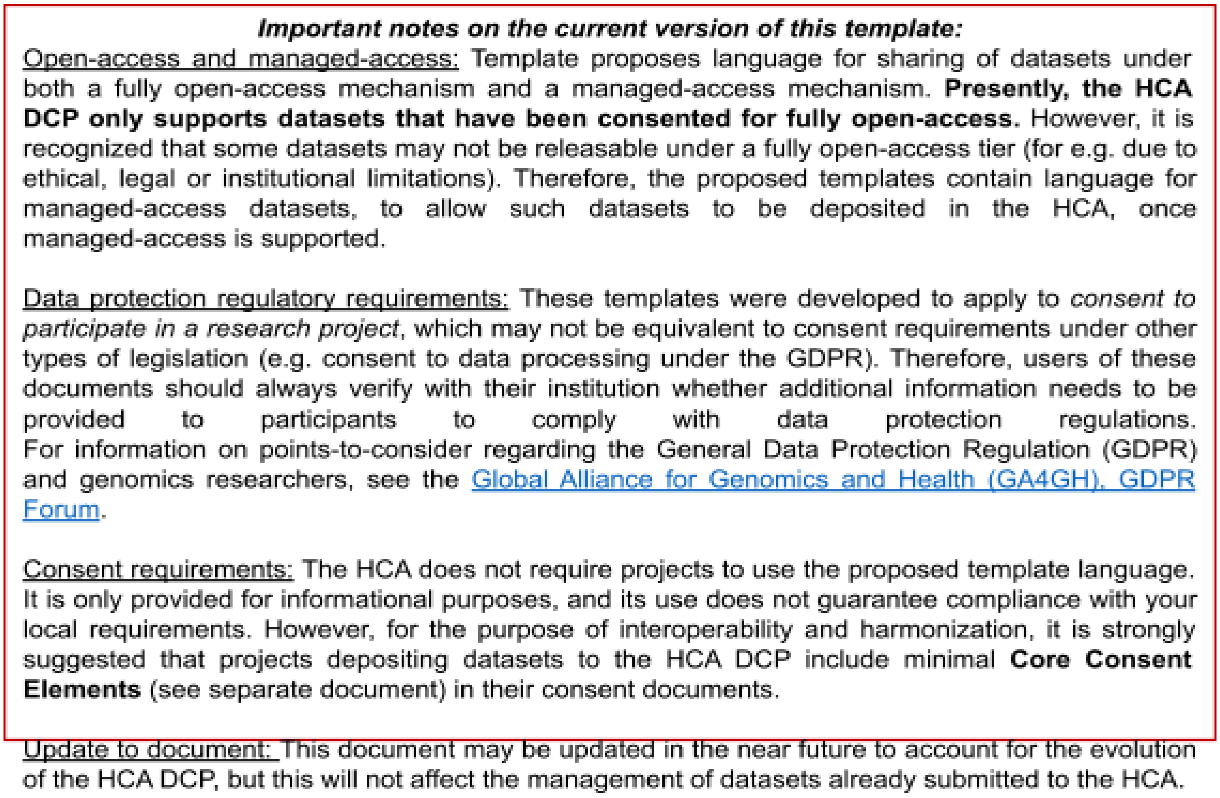
Human Cell Atlas

B4. Template Consent Form - Use of Embryos for Research[1]

(Embryos created for fertility purposes but in excess of clinical need)



Important notes on the current version of this template:

Open-access and managed-access: Template proposes language for sharing of datasets under both a fully open-access mechanism and a managed-access mechanism. **Presently, the HCA DCP only supports datasets that have been consented for fully open-access.** However, it is recognized that some datasets may not be releasable under a fully open-access tier (for e.g. due to ethical, legal or institutional limitations). Therefore, the proposed templates contain language for managed-access datasets, to allow such datasets to be deposited in the HCA, once managed-access is supported.

Data protection regulatory requirements: These templates were developed to apply to *consent to participate in a research project*, which may not be equivalent to consent requirements under other types of legislation (e.g. consent to data processing under the GDPR). Therefore, users of these documents should always verify with their institution whether additional information needs to be provided to participants to comply with data protection regulations. For information on points-to-consider regarding the General Data Protection Regulation (GDPR) and genomics researchers, see the Global Alliance for Genomics and Health (GA4GH), GDPR Forum.

Consent requirements: The HCA does not require projects to use the proposed template language. It is only provided for informational purposes, and its use does not guarantee compliance with your local requirements. However, for the purpose of interoperability and harmonization, it is strongly suggested that projects depositing datasets to the HCA DCP include minimal **Core Consent Elements** (see separate document) in their consent documents.

Update to document: This document may be updated in the near future to account for the evolution of the HCA DCP, but this will not affect the management of datasets already submitted to the HCA.

This document is part of the HCA ethics toolkit. It includes consent clauses for projects contributing data derived from embryonic cells to the HCA. The language in this document provides an example, and can be modified to reflect local consent requirements. In particular, **research use of embryos may be subject to country-specific restrictions or limitations that are not reflected in this template. It is important that researchers verify any applicable legal requirement before using this template.**

In some jurisdictions, it may not be legal, or it may be ethically sensitive to donate or use embryos for research purposes. Researchers would always comply with local laws and requirements and policies, and it may not be possible to use this template in all countries.

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Furthermore, in some jurisdictions, there may be pre-existing networks to coordinate embryonic/fetal tissue collection. They may also provide samples for research use (e.g. U.K. Human Developmental Biology Resource). In such cases, researchers may not need to collect their tissues using this HCA-specific template consent form. Rather, researchers should consider whether consents and ethics approvals obtained to create these existing resources are suitable for use of tissues in the HCA (see: *HCA Ethics Tool: Consent filter*).

Who is this document useful for?

- This document provides template language to researchers/research studies intending to collect embryonic tissue samples in order to generate gene expression data and submit these datasets to the HCA DCP.

How do I use this document?

- The clauses below provide examples of language illustrating core elements to enable contribution of data to the HCA. These can be modified and adjusted to comply with your institutional requirements and existing templates.
- Text in *grey italics* indicates explanation notes for the drafter.
- Sections highlighted are meant to indicate text that should be customized based on drafter's project-specific context.
- These clauses are designed for collection of samples by projects contributing to the HCA and sharing of data with HCA of **embryonic tissue (embryos created for fertility purposes and in excess of clinical need).**

Who do I contact if I have questions?

- For any questions about this document, you can contact the HCA Ethics Helpdesk at: ethics-help@humancellatlas.org

Informed Consent to Donation of Leftover Embryos

(Embryos created for fertility purposes and in excess of clinical need)

Description of [Study]

[*If applicable, please insert wording specific to the local project.*]
You are being invited to donate embryos for a research project led by [name of principal investigator] at [name of institution].

The project is collecting embryos to help scientists from around the world understand how genes work. Genes carry the information that is passed from parent to child and can affect such things as eye color or how likely you are to get certain diseases. The goal of [Study] is to [insert project specific goal].

Donated embryos will be studied by [Study] [*or: if transferring samples to other institution for processing and analysis, please detail how this will be done*] to increases scientific knowledge about the genes in different types of cells.

Description of the Human Cell Atlas

[In addition to participating in [Study]], we invite you to provide information learned from your donated embryo to the Human Cell Atlas (HCA), which is led by an international group of researchers.

The HCA is building **a reference map of all the cells in the human body, through the creation of an online database made up of gene expression data (also called "transcriptomic data")**. Genes are the basic 'instruction book' for the cells that make up our bodies. Genes are made out of DNA, and all of the DNA in each cell is called the genome. Different genes are turned on in different types of cells. In order for them to be turned on, another type of molecule called RNA copies certain parts of the DNA. RNA acts as a 'messenger' to send the genetic information that is turned 'on' in different kinds of cells. The HCA will use different types of genetic sequencing technologies to study RNA.

The HCA will study the RNA of cells to look at the patterns of genes that are 'on' or 'off'. This is called "gene expression". More specifically, to build the portion of the HCA called the developmental cell atlas, it will study how cells in the developing embryo are divided and become specialized cells (for example, kidney, liver, lung cells, etc.). The HCA database will be available to scientists around the world and will be useful for a broad range of research, including to understand human health and disease.

The HCA is an open science project. Open science aims to make data and research findings as openly available as possible to researchers all over the world. In doing so, its goal is to help scientists to work together more easily, and to speed up discoveries.

Nature of participation:

People from various parts of the world are invited to take part in the HCA, through studies like [Study]. Different types of cells will be provided by different people.

For this part of the project, [Study] will collect cells from embryos. Your embryo donation is completely voluntary. You have the right to agree or to refuse to donate your embryos for this project. The quality of your current or future medical care at [Institution] will not change in any way whether you agree or refuse to donate any embryos for this research project.

Embryos can be donated for this research project only if the sperm and egg donors and, if applicable, the people for whom the embryos were created each give their permission by signing their own copies of this form.

Neither of these other individuals who must provide permission for embryo donation will be told about your decision. If you are undergoing fertility treatment, your treating physician will not know what you have decided, unless you choose to provide this information.

[Cooling-off periods: Some jurisdiction may require "cooling-off" periods for the donation of embryonic tissue for research purposes. Depending on the country, there may be the following elements to consider:

- *Some countries require that a certain period of time lapses between the presentation of the study/consent discussion and the acceptance of consent by the participant;*
- *Some countries require that a certain period of time lapse between the consent provided by the participant and the use of the tissue for research;*
- *Finally, some countries require that consent to donation be renewed after a certain period of time*

If any of these requirements apply, please include the appropriate language in the consent form.]

Sample and data collection:
If you choose to take part in [Study], [Study] will collect your embryos that are no longer required for reproductive purposes. *[Insert any additional information about source of embryos, for example PGD embryos, frozen embryos, poor quality embryos, or fresh and good quality embryos.*]

We will use the embryonic tissue sample to generate gene expression data (information about the genes that are turned "on" or "off" in different cells of the embryo).

We will also collect other types of data about the sample (this is called "metadata"). This can include information about where the embryo was collected, the developmental stage of the embryo, [include other types of metadata that may be required].

This information (which includes RNA sequencing data, gene expression data and metadata about the embryo) will be sent to the HCA and stored on the HCA online database, as described in this consent form.

None of the embryos that are donated to this research project will be used to produce a baby or a pregnancy. And no embryos used in research will be allowed to develop for more than a total of 14 days after conception [*Adjust based on local practices, e.g. if using frozen embryos*]

After it is processed, the embryo sample will be [indicate what will be done with the tissue sample after processing and analysis, e.g. used in another project, biobanked locally, biobank in another institution, destroyed, etc.]

Data storage in the HCA

The information about the embryo will be stored in the HCA data coordination platform (DCP) that is coordinated by several institutions and can be used by researchers around the world. The HCA database is hosted on commercial cloud servers. The cloud refers to software and services that run on the Internet, instead of on a specific computer. These cloud servers might be located outside your country.

Data will be stored indefinitely on the HCA DCP, or until it is withdrawn or no longer useful for research.

[*If identifiers of participants are collected by the Study and a subset of data (e.g. metadata) related to the participants is sent to the HCA, include this sentence*] The HCA will receive and store 'coded' data. This means that before [Institution] sends your information to the HCA, the parts of the information that directly identify you, like your name, will be replaced with a 'code' or 'ID number.' The code is used so that [Institution/Study] does not share information that directly identifies you (like your name or your contact information) with the HCA.

Broad consent for future, unknown research use of data on an international scale

If you choose to allow [Study] to share information from the embryo with the HCA, you agree to allow this information to be used for a broad range of future, unknown research uses. These research uses may be conducted across the world, and may involve a wide range of research topics. These projects can also take place in universities, hospitals, nonprofit groups, for-profit companies, or government laboratories.

Data sharing

[Option 1: Public data sharing (open access) - *Use this language if your project intends to share all contributed datasets, including raw RNAseq data and all metadata under a fully open access tier. Before doing so, please ensure that depositing raw RNAseq data files and metadata is allowed under your institutional policies and all applicable laws including the local regulatory framework*]:

By giving your consent, you agree that all of the coded information from your embryo collected for this project, including all of the RNA sequencing data, gene expression information and metadata from the embryo, can be stored on the part of the DCP that anyone can access without restriction. The information in this open part of the HCA is available to anyone with internet access, and will be shared freely with anyone who wishes to use it. The HCA will not control the kinds of projects that may use the embryo's information in its open access part.

[Option 2: Managed/controlled access

*Important note: Currently, the **HCA DCP does not accept any data that requires managed/controlled access**. Only data meeting open access tier consent language, can currently be submitted. However, some projects collecting data to build next phases of the HCA may not be able to deposit certain datasets in public (open) databases and thus need to obtain consent for managed/controlled access (for example, due to ethical or legal constraints). While these datasets will have to be deposited in other repositories at the present time, they could eventually be included in next phases of development of the HCA DCP.*

*Use this consent language **only** if your project is required to share raw RNAseq data and metadata under a controlled/managed access tier. This applies if there are regulatory, institutional or other restrictions on sharing raw RNAseq and metadata under a fully open access model. Gene count expression matrices and limited metadata will always be shared publicly, through open access.]*

Some parts of the coded information, like genetic information and metadata from the embryo, will be stored on the secured part of the DCP and made subject to access controls. Information in this controlled part of the HCA can only be accessed and used by researchers who have been granted formal approval to access data by the HCA and who have signed agreements to protect the confidentiality of the information. Information in the controlled-access part of the HCA DCP includes things like detailed RNA sequencing data and detailed metadata (for example, geographical region, etc.) The access agreements also require researchers to respect the laws and ethical guidelines for scientific research.

Other parts of the coded information from the embryonic sample, including certain types of gene expression data and metadata, will be stored on the part of the DCP that anyone can access. This information presents minimal risks of reidentification. It includes things like ‘lists’ of the genes that were activated in the embryo’s cells, and general, minimal risk metadata about the embryonic tissue sample (for example, general characteristics such as developmental stage). It has a low risk of being reconnected to the donated embryo or the individuals who donated their biological material to produce the embryo.

Finally, the HCA will also use all of the coded information from the embryonic sample to create reference maps of different cells in the human body. In some cases, this could be done by combining the donated embryo’s information with the information of other embryos. The combined information of many embryos that makes up these reference maps is also minimal risk, and may be made public (openly accessible) to anyone without restriction.

Withdrawal of data from the HCA

You may withdraw your consent for whatever reason at any time before your embryo has left the fertility clinic.

However, if you withdraw your consent after the embryo has left the fertility clinic, then the embryo will no longer be suitable for reproductive purposes and will have to be destroyed.

Even if you choose to take part in [Study], you can decide you don't want to be in the study anymore and remove the information about your embryo from [Study] and from the HCA database at any time by contacting [insert name] at [insert contact information]. [*Note: Some countries require that consent to withdrawal for research with embryos be provided in writing. Please specify this, if applicable in your country.*] Once we know that you don't want to be in the study anymore, the information about your embryo will be removed from the HCA. However, some information that has been used to create the reference map in the open access part of the HCA may remain in the HCA database even after you leave the study as we are not always able to find individual data in this reference map.

Finally, information in the HCA that has been used by or sent to other researchers around the world cannot be withdrawn if it has already been used or published.

Benefits

You will not benefit personally from sharing information from your embryo with the HCA. Your participation is expected to help researchers in many areas of scientific research, such as health and genetics. In particular, this information will help develop a reference map of human cells, and how genes are expressed in the development of different types of cells.

[*If data is placed in public (open access) database*: Because information derived from your embryo will be made available in a fully public, open access database, this means that it will be rapidly and freely available to a wide range of researchers around the world. This has the potential to speed up and improve the way research is done by scientists working together.]

Risks

[*Include if donation involves all leftover embryos* If you donate all of these embryos for this research project, none of them will be available for future fertility uses. This means that if you later decide that you want to have a child through in vitro fertilization, you will have to undergo a completely new in vitro fertilization cycle.

Donating embryos for this project may involve some risk to your privacy. If your sperm or eggs were used to create the donated embryos, then the resulting embryo and its cells will be a partial genetic match to you. To protect your privacy, the data from the embryo sent by [Study] to the HCA will be coded, which means it will not be associated with any information that directly identifies you (direct identifiers) (for example, your name, address, contact information).

Nonetheless, it is very difficult to make genetic information completely anonymous. There is a risk that people that have this information could try to connect it to your identity by combining it with other personal information about you, through a process called re-identification. Also, in the future, new technologies could be developed that make it easier to connect genetic information to your identity. The risks related to re-identification are difficult to predict, at this time.

Though it is unlikely that your genetic information that is sent to HCA will be connected to your identity, it is not impossible. In some cases, genetic and gene expression data can reveal sensitive information about a person. For example, this could include the risk of getting certain diseases and other medical conditions, or reveal certain lifestyle information (for example, if a person is a heavy drinker or smoker). Because genetic information is shared amongst people who are biologically related, it is possible that information about related family members could also be revealed.

Also, there is always a risk that information from genetic studies might be used to make certain statements or conclusions about groups or communities. In some cases, this can lead to discrimination against individuals, families, groups or communities. You might not always agree with the results of research that has used the information from the embryo, that is in the HCA.

[*If data is placed in public (open access) database*: HCA will share genetic information for unknown future uses. Because the HCA will involve public, open access to information from the donated embryo, there is very little control over how researchers use the information. For this reason, it is difficult to know all the risks related to sharing information with the HCA. There may be other risks that have not been thought of at this time.]

Privacy

[*If applicable and if participant information is collected by Study*]: To protect your privacy, information that directly identifies you (direct identifiers), including [list any direct identifiers that are collected] will only be kept by [Study] and be stored in a secure and encrypted database that is held at [Institution of Study]. This information will not be sent to the HCA database.

[*If data is placed in the public (open access) database*: To protect your privacy, only coded information will be available in the public, open access area of the HCA. Coded means that direct identifiers (like your name, contact information) are removed by [Study] and replaced with a code. Your personal information, such as your name, address and contact information will not be stored in the HCA.

[*If data is placed in controlled-access database:* To protect your privacy, only coded information will be available in the controlled-access area of the HCA. Coded means that direct identifiers (like your name, contact information) are removed by [Study] and replaced with a code. Your personal information, such as your name, address and contact information will not be stored in the HCA.]

You will not be identified as an embryo donor if results from the information are shared at scientific conferences or appear in scientific publications.

Commercialization

You will not receive any cash or payment in goods or services for the embryos you give to this project.

You will not be reimbursed for the cost of embryo storage for the time period before the embryos are donated for this research project.

Some of the research done with the information stored in the HCA may one day lead to new software, tests, drugs, or other commercial products. If this happens, you will not receive any of the profits from these new products.

Research Results

You will not be told which research projects have used the information from your embryo in the HCA database. However, there will be general information on the HCA website (www.humancellatlas.org) to learn generally about the kinds of research projects that are being performed using information from the HCA database, and their results.

Who can I contact if I have questions or concerns?

If you have any questions or concerns, please contact [name of person] free of charge at [insert telephone number] or by mail/email at [insert mailing address and/or email address]. If you wish to make a complaint about any part of this study at any time, please contact [name of person] free of charge at [insert telephone number] or by mail/email at [insert mailing address and/or email address].

[*Note: Include consent sheet for every individual legally required to consent to the donation (for example, egg donor, sperm donor, if applicable, individuals for whom the embryo was created), in your jurisdiction. Please verify your country's legal requirements regarding consent*]

CONSENT TO PARTICIPATE

Consent and Signature

Please read the information below, and sign if you agree.

I have been provided all the information I need to make a decision. I have been able to ask questions if I did not understand the information.

I agree:

- That [Study] can collect embryos created for fertility purposes that are no longer needed for reproductive purposes;
- that [Study] can deposit the information, including the gene expression data and metadata, derived from these embryos in the HCA online, [public (open access)/managed access] scientific databases;
- that this information be studied by researchers from around the world;
- that I will not receive any profits if commercially valuable product(s) result from these studies;
- that data that has already been used by researchers accessing the HCA cannot be withdrawn.

I know that participating is my choice. I understand that I may withdraw at any time without having to give a reason.

Your Signature _______________________________________ Date ______________

Researcher Signature __________________________________ Date ______________

Copy given to participant: _____Yes