Pediatric consent tools

Human Cell Atlas

Reference Notes on Template Consent Form - Pediatric participants - Leftover Clinical Tissue

Important notes on the current version of this template:

- Open-access and managed-access: Template proposed 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. Only data meeting open-access tier consent language can currently be submitted.** However, it is recognized that some datasets may not be able to be released under a fully open-access tier (for e.g. due to ethical, legal or institutional limitations). Some projects collecting data to build next phases of the HCA may not be able to deposit certain datasets in open-access tier and need to obtain consent for managed/controlled access. In some jurisdictions, this may include datasets from pediatric participants. 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. 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 your local laws or in Europe, 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, including standards applicable to data from children.

  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, 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 aims to provide clauses for research use of residual (leftover) tissue sampled in a clinical context. These clauses can be used either *prospectively,* before tissues are sampled for clinical purposes (e.g., biopsy, resection) or *retrospectively,* for example, in cases where re-consent is necessary to use these tissues for research purposes, for example, in the HCA (see Consent filter for legacy samples/data). It includes core elements for consent to contributing to the HCA, as well as language specific to collecting tissue samples from pediatric participants. The language in this document is intended to provide an example, and can be modified to reflect local consent requirements.

Who is this document useful for?

- This document is intended to provide template language for researchers/research studies intending to collect tissue samples from pediatric participants in order to generate gene expression data and submit these datasets to the HCA DCP.

How do I use this document?

- **This document should be used to develop consent forms for parents (or legally authorized representatives) who are consenting on behalf of children below the age of majority or maturity in their jurisdiction.**
    - **In most jurisdictions, the legal age of majority constitutes the age where minors are considered capable of providing consent to research. However, in certain jurisdictions, minors may consent to research at a legislatively-fixed age of maturity to consent to medical care prior to the legal age of majority.**
    - **Other jurisdictions adopt the mature minor rule, which relies on physician evaluation of the minor's capacity to provide consent to research. The mature minor rule allows minors to make certain decisions (e.g., medical care, consent to participate in research) prior to reaching the legal age of majority in their jurisdiction.**
- This form can be used along with an Assent form when applicable (see separate template).
- The clauses below provide examples of language illustrating core elements to enable the 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 the drafter's project-specific context.
- Blue highlights indicate pediatric-specific clauses
- These clauses are designed for the collection of samples by projects contributing to the HCA and the sharing of data with the HCA of **pediatric research participants (healthy and diseased).**
- *Throughout the form, if applicable, please insert wording specific to the local project.*

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

Template Consent Form –Leftover clinical samples - Pediatric participant (parental consent/legally authorized representative consent,)

If you are a parent or legally authorized representative of a child, you are being asked to provide informed consent on behalf of the child you represent. Throughout this form, "you" means the child you represent.

Description of [Study]

[*If using this consent form to prospectively obtain permission for research use, for the HCA*]: You are being invited to this project because you will be undergoing a surgical procedure at [Institution], and we would like to ask your permission to use tissue leftover from the procedures for research purposes, in a study called [Study].

[*If using this consent form to retrospectively obtain permission for research use (re-consent), for the HCA*]: You are being invited to this project because you have undergone a surgical procedure at [Institution] in the past, and some of your tissue from that procedure has been stored. We are asking for your permission to use tissue leftover from that procedure for research purposes, in a study called [Study].

The project is collecting tissue samples (e.g. blood, saliva) from donors, including children, 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 tissues will be studied by [Study] [*or: if transferring samples to other institutions for processing and analysis; please detail how this will be done*] to increase scientific knowledge about the genes in each of their cell types.

Description of the Human Cell Atlas

In addition to participating in [Study], we invite you to share information (data) about your samples 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"). In particular, the HCA includes a pediatric cell atlas. The Pediatric Cell Atlas focuses not only on understanding the characteristics of normal cells from children's/minors' tissues, but how these cells and tissues change over the course of childhood and adolescence. The way cells develop during childhood and adolescence is different than in adulthood. 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". Researchers using the HCA will be able to look at why different types of cells do different things (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 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, including by children and minors.

[*If inclusion criteria apply to Study, or to a specific type of tissue atlas, please include a clause, e.g.:*]
Example: In order to take part, you must:
[inclusion criteria]

For this project, we will ask you to provide:
[insert type of tissue collected]

Sample and information collection:
If you choose to take part in [Study] and agree to share your information with the HCA, we will ask the pathology department at [Institution] to give us part of the tissue leftover from your clinical procedure [insert more information on the type of tissue sampled] for research purposes. We will use your tissue sample to generate gene expression data and RNA sequencing data (information about the genes that are “on” or “off” in that particular kind of tissue) and to increase knowledge about genes.

We will also collect other types of information about you and about your tissue (this is called “metadata”). This can include information about your sex, age, ethnicity, diseases you may have and the location in your body where the sample was collected. On its own, this metadata does not contain identifying information that could be used to identify who you are. However, there is a small chance that one day this information could be combined with other information in order to reveal personal or private information about you.

[*Optional alternative clause for metadata, consider using this clause if Study is collecting and sharing richer types of donor metadata with the HCA*]: [Study] will be collecting some detailed information about you and about your health and lifestyle and about your tissue (this is called “metadata”). This could include, for example, information about your: [*adjust list as necessary, depending on the type of data Study is collecting*] body measurements (for example, weight and height); ethnicity; sex, age, diseases you may have, medical history (including for example, medications, treatments, alcohol consumption, smoking history, nutrition information, etc.), and [*include any other donor information that is collected and submitted as metadata*]. On its own, this metadata does not contain identifying information that could be used to identify who you are. However, there is a small chance that one day this information could be combined with other information in order to reveal personal or private information about you. Because it contains some information about your health status and lifestyle, it could reveal some sensitive information about you.

[*Optional Clause, to add if Study requires access to medical charts/records to obtain metadata*]: You (parent) authorize [Study] to see your (child's) medical records in order to collect information needed for this research. This includes [list types of data fields that need to be collected].

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

Your tissue sample will be [indicate what will happen after processing and analysis, e.g. biobanked locally, biobank in another institution, biobanked internationally, destroyed, etc.]

Data storage in the HCA

Your information will be stored on 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.

The HCA will receive and store 'coded' data. This means that before [Institution/Study] 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.' This 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.

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

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

If you donate your tissue sample and allow [Institution/Study] to share your information 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. You will not be told which research projects have used your information stored in the HCA DCP.

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 your coded information collected for this [Study], including all of your RNA sequencing data, your gene expression information and detailed metadata, 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 publicly available to anyone with internet access, and will be shared freely with anyone who wishes to use it, for any purpose. The HCA will not control

the kinds of individuals or projects that may use your information in its public (open access) part.

The HCA will also use your coded information to create reference maps of different cells in the human body. In some cases, this could be done by combining your information with the information of other people. This combined information will also be made public (openly accessible) to anyone without restriction.

[***Option 2: Managed/controlled access***

Important note: Currently, the ***HCA DCP does not accept any data that requires managed/controlled access****. See the first bullet point in the Reference Notes for further explanation.*

Use this consent language ***only*** *if your project is required to share individual-level raw RNAseq data and metadata from pediatric participants 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 your coded information, like genetic information and metadata, 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, health information, geographical region, etc.) The access agreements also require researchers to respect the laws and ethical guidelines for scientific research.

Other parts of your coded information, including certain types of gene expression data and metadata, will be stored on the part of the DCP that anyone can access publicly, without restriction (open access). This information is considered minimal risk. It includes things like 'lists' of the genes that were activated in your cells, and general, minimal risk metadata about you and your sample (for example, general characteristics such as biological sex and age). It has a low risk of being reconnected to you.

Finally, the HCA will also use all of your coded information to create reference maps of different cells in the human body. In some cases, this could be done by combining your information with the information of other people. The combined information of many people making up these reference maps is also minimal risk, and may be made public (openly accessible) to anyone without restriction.

Withdrawal of your information from the HCA

Your participation in [Study] is voluntary. You are free to withdraw at any time, without giving any reason. Your medical care and legal rights will not be affected in any way.

Even if you choose to take part in [Study] now, you can still change your mind at any time. If you decide you don't want to be in [Study] anymore, we will try to destroy your remaining tissue samples, and to stop using your information for the [Study]. Once we know that you don't want to be in the study, your information will be removed from long-term storage in the HCA database. However, some information that has been used to create the reference map in the

open access part of the HCA will remain in the HCA database even after you leave the study as we are not always able to find individuals in this reference map.

To withdraw, contact [insert name] at [insert contact information]. Upon withdrawal, your tissue samples and information will be [destroyed/no longer be used]. However, data in the HCA that has been used by or sent to other researchers around the world cannot be removed if it has already been used or published.

Recontact

At majority [*OR* [X] years old], [Study] will contact you to ask if you still want to be in this study. You will be given the option to participate or not. [*OR*] At that time, [Study] will notify you that they will continue to use your tissue samples and information unless you object.

[*in the case of recontact at majority, please add:*] Upon recontact at majority, the final decision will be made by you.

[*Note to drafters*: Please note that HCA will not recontact research participants at majority. If Study re-contacts participants at the age of majority, it is the responsibility of the data contributor to inform the HCA of any withdrawal requests received. For studies that perform recontact at the age of majority, it is recommended that Study informs research participants that non-response will be interpreted as continued consent to research participation, provided that this is possible according to local law, ethical guidelines, and institutional policies.]

Benefits

Personal. You will not benefit personally from taking part in the [Study]. Participating in the study may help researchers in many areas of scientific research, such as health and genetics. In particular, your information will help develop a reference map of human cells for pediatric populations, and help understand how genes are expressed in these cells, during childhood and adolescence.

[*If data is placed in an open access database*]: Because your information 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.

Financial. Neither you nor your family members will receive any financial benefit if [Study] leads to new treatments, devices, drugs, medical tests, softwares or other commercial products.

Risks
[If applicable, add any specific physical risks related to the collection of the tissue sample.]

Privacy. The HCA will receive and store ‘coded’ data. This means that before [Study] 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.’ On its own, coded data does not contain information that could be used to identify you. However, there is a small chance that one day this coded data could be combined with other information to reveal your identity or personal information (re-identification). It is very difficult to make genetic information completely

anonymous and as technology advances, the risks of re-identification cannot be predicted at this time.

Stress and Relatives. In some cases, genetic information can reveal information about you, such as the risk of getting certain diseases or other medical conditions. This information can cause anxiety and stress for both you and your family. Since genetic information is shared among people who are biologically related to you, it is possible that the detection of such a condition could affect the health care needs of your biological relatives.

Genetic Discrimination. 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. It can also lead to stigmatization for insurability or for employment for both you and your family.

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

Privacy Protection

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

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

[*If data is placed in a controlled-access database*]: To protect your privacy, only coded information will be available in the controlled-access area of HCA. Coded means that direct identifiers (for example, your name, address, 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 if results from your information are shared at scientific conferences or appear in scientific publications.

Research results

HCA will not return any individual results to [Study]. However, general information is available on the HCA website (www.humancellatlas.org) to learn about the kinds of research projects that are being performed using information from the HCA database, as well as their results.

[*If Study is returning individual-level results, consider including appropriate language. HCA will **not** enable the return of any individual-level findings to the Study*]: [Study] that you are participating in and that collected your tissues / information [may/will] return actionable results.

[*If Study is returning individual-level results, consider adding the following for pediatric specific language*]:

- *Systematic return of medically actionable findings:*
  - A doctor will review your results. The doctor will tell [you/physician/researcher] about anything for which there is prevention or treatment available, during childhood.
- *Possible return of medically actionable findings:*
  - If the laboratory identifies a gene change in a gene known to cause a medically actionable disease with onset in adulthood, it [will *OR* may] be reported to [parents/legally authorized representatives/physician/researcher] if reporting could prevent serious harm to the health of a relative [or], if the release of this information is desired by you.
  - You can decide if you want us to tell you (or not) if we find a DNA change that is known to cause an adult-onset condition for which prevention or treatment is available. This information may be important to your health as an adult, or the health of other family members.
- *Right not to know:*
  - [Study] may learn that you are a carrier for/at high risk of developing a genetic disorder other than the one(s) targeted by this study. Some people would like to know this information, others may find it stressful. A genetic counsellor can explain what these results mean for you and your family before you decide if you want to be informed or not.

Who can I contact if I have questions or concerns?

Question. 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].

Complaint. 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].

CONSENT TO PARTICIPATE

Consent and Signature

If you are a parent or legally authorized representative of a child, you are being asked to provide informed consent on behalf of your child you represent. Throughout this form, "you" means the child you represent.

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

[Study] was explained to me. I have been given all the information I need to make a decision. I have also been able to ask questions if I did not understand the information.

I agree:

- that [Study] can use tissue that [is/was] leftover from your clinical procedure from the pathology department at [Institution for research purposes];
- that [Study] can contribute my information, including gene expression data and metadata, to the online, [public (open-access)/managed access] HCA database;
- that my information may be used by anyone from around the world;

- that I will not be identified in scientific publications and at conferences;
- that I will not receive any profits if commercially valuable product(s) result from these studies;
- that my information that has already been used for research cannot be withdrawn.

I know that being in this study is my choice. I understand that I may stop being in the study at any time without having to give a reason.

Name of Participant (minor/child): _____

_____ _____ _____
Signature of Parent/Legally authorized representative PRINTED NAME Date

_____ _____ _____
Researcher signature PRINTED NAME & ROLE Date