Human Cell Atlas – Recruiter Training Materials

These materials are intended to support researchers during the informed consent process of studies contributing data to the Human Cell Atlas (HCA).

Research ethics and legal requirements regarding research participant consent differ considerably around the world, and also depend on the context in which research consent is being obtained (e.g. from vulnerable populations, minors, or incapable adults / clinical trails vs. epidemiological studies). All necessary approvals from research ethics boards (REBs), institutional review boards, and other relevant bodies should be obtained prior to obtaining consent to research.

Sometimes, it is also a recommended best practice to discuss research protocols with relevant institutional personnel before obtaining consent. These can include institution legal counsel and Technology Transfer Offices or equivalent bodies.

The HCA Recruiter Training Materials contain four sections.

The first section is a **Guide to the HCA consent form templates.** This guide describes the different consent form templates made available to researchers by the Human Cell Atlas.

The second section is a series of **General discussion points** for obtaining consent from research participants, collecting their biological samples and contributing the data derived from such samples to the HCA Data Coordination Platform (DCP).

The third section is a series of **Study-specific discussion points** that can affect the way in which research consent is obtained from research participants on the basis of certain study-specific elements, (e.g. pediatric donors, deceased donors.) or elements that are variable across research institutions, contexts, or countries (e.g. data linkage / sharing).

The fourth section discusses the **Open Access and Managed Access** mechanisms for HCA data, and provides guidance for discussing these concepts with local research ethics boards and with research participants.

The fifth section describes the use of a **Legacy Consent Assessment Filter** to determine if previously collected data or data derived from previously collected samples can be integrated to the Human Cell Atlas, or if additional steps must first be taken.

The sixth section provides guidance on the use of **Material and Data Transfer Agreements (MDTAs)**, agreements that are used to transfer biological materials (i.e. samples) and data from one institution to another.

I. Guide to the HCA consent form templates

The HCA Ethics Toolkit contains an Ethics Submission Guidance document and a variety of Consent Form templates / Consent Clause templates that can be of help in drafting the consent materials for your study. Different consent forms are appropriate depending on the context of data collection. The descriptions below can help you determine which templates are most useful for each category of research participant taking part in your study.

1. **Consent form – main consent template**

   The main consent template is intended for the collection of samples and data **from live adult research participants (healthy and diseased).**

   Before using this consent template, it is important to ensure that the research participant has capacity to consent according to your local law and policies.

2. **Consent template (addendum) – deceased donor – anatomical gift**

   This addendum is intended to be used if tissue samples are provided as an anatomical gift (i.e. organ donation, organ procurement services), in situations where no formal research ethics review is required. This addendum supplements the main consent form template.

3. **Consent form (addendum) – deceased donor – research participant**

   This addendum is intended to be used if tissue samples are provided by a deceased donor in situations where consent to participate in research is required. Such consent can be gathered directly from the research participant prior to their death, or from the next of kin of the research participant if the research participant is deceased. This addendum supplements the main consent form template.

4. **Consent form – embryonic tissue template**

   This consent template is intended to be used if tissue samples will be derived from embryos created for fertility purposes and in excess of clinical need. This consent template replaces or supplements the main consent form template.

5. **Consent form – fetal tissue**

   This consent template is intended to be used if tissue samples will be derived from fetal tissue samples after termination of pregnancy or miscarriage. This consent template replaces or supplements the main consent form template.

6. **Consent form – leftover clinical tissue**

   This addendum is intended to be used to collect residual (leftover) tissue sampled in a clinical context. This addendum supplements the main consent form template.

7. **Consent tools – pediatrics**

   The pediatric consent tools are intended to be used to collect consent from participants from birth to the age of legal majority in your country. The pediatrics consent tools replace or supplement the main consent form template.

II. General Discussion Points

Research participants may not always have the time available, or energy, to review each page of the consent form with the researchers. Listed below are a number of important points to discuss with research participants.

Upon completion, provide all research participants with copies of the signed consent forms and other research consent documentation. Retain the original research consent form at your institution.

Introduction

Involve research participants actively in the consent process. Research participants should be encouraged to raise concerns and ask questions.

Research participants should not feel pressured to provide consent. They should feel comfortable changing their mind or, withdrawing their consent even after the research has started, or has been completed.

Research participants can take the consent materials home, or review them privately, before providing consent.

Sample language to be used in discussing the HCA with research participants:

Background

The Human Cell Atlas (HCA) is building **a reference map of all the cells in the human body, through the creation of an online database.**

Instead of representing geographical features, such as continents, countries, cities, streets, and houses, the HCA's maps of the human body will "zoom in" on molecular and organizational features of organs, tissues, and cells. To do this, the HCA is collecting tissue samples and data from donors, to help scientists from around the world understand how human cells and human genes work. Data will be derived from the samples and held on a public platform called the Data Coordination Platform (DCP).

Gene Expression Data and Cellular Information

DNA is the instruction book of the cell; it is made up of strings of molecules that code for information about how a cell works and its role in the body. When certain strings of DNA cluster together, they are called genes. 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.

Different genes are turned on in different types of cells. 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 is collecting data related to RNA and to the different ways that genes function in different parts of the human body.

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.).

Data and Sample Collection

If you choose to participate, we will collect a tissue sample from you. The sample will be used to generate your RNA and DNA.

Other data will also be collected about you. This is called metadata, and includes information such as your age, sex, and ethnicity, as well as diseases you may have, and the location in your body from which the sample was taken.

Your data will be sent to the HCA and stored on the HCA online database. The data will be held on a public platform that anyone can access. Before sending your data to the HCA, we will de-identify your data. This means that your name, address, and other directly identifying information will not be sent to the HCA.

Risks

Risks involved in collecting your sample are the risks typically associated with the type of sample, such as a bruise from a blood draw, or physical discomfort from a biopsy. If a procedure is offered, such as a skin biopsy, the specific risks associated with that procedure will be reviewed beforehand.

The risks related to your data are as follows:

- Though we will remove your name and other directly identifying information, it is never possible to guarantee perfect anonymization. There remains a risk that you could be re-identified.
- This could happen because other sources of information about you are combined with your data to identify you. This could also happen if new technologies are created that make it easier to identify you in the future.
- Though the risk is small, your genetic information could be used to discriminate against you, your family, or members of your community. Insurers, employers, or other third parties may also discriminate.
- Genetic information can reveal sensitive information about you and your biological relatives, including information about health risks and lifestyle.

Withdrawal

You can change your mind about participating in this study at any time, by contacting a member of the study team.

- If you decide that you don't want to be in the study anymore, we will try to destroy your remaining tissue samples.
- We will stop using your data in our study and will ask the HCA to remove your data from long-term storage in the HCA database.
- Some information that has been used to generate the HCA reference map will remain in the HCA even if you withdraw.
- Also, data that has already been used or published by researchers around the world cannot be removed from the HCA.

Research Results

- You will not be told which research projects have used your information stored in the HCA database. However, there will be general information available on the HCA website.
- This general information allows you to learn what kind of research has been performed using the HCA data, and the results of that research.
- Your data could be used in commercial or non-commercial research. You will not receive any of the proceeds from this research.

III. Study-Specific Considerations and Discussion Points

A. Considerations Relating to Study Design

Return of Research Results

The Human Cell Atlas (HCA) and the users of HCA data will not return information to research participants regarding the medical meaning of their results.

However, you should inform the prospective research participant whether the results of your local study will be made available to participants, and if so under which conditions (e.g. all research results, study-specific findings, material incidental findings, subsets of incidental findings …).

Sample Storage

You should inform the prospective research participant what will be done with their samples after the data from these samples has been analyzed. For instance, you should inform the prospective research participant if you intend to destroy the samples, or, if you intend to store samples in a biobank or other repository for future research use.

Data Linkage

If data is going to be collected from the medical records of research participants, or from administrative health databases, it is important to explain this to prospective research participants during the informed consent process. Participants should be informed as to what data will be collected from external sources.

B. Considerations Relating to Special Populations

Cooling-off Periods (Embryonic and Fetal Tissues)

In collecting embryonic or fetal samples from research participants, some laws or ethical frameworks can require additional steps to be taken during the consent process. Examples include the following:

- Some countries require that a period of time lapses between the presentation of the study / consent discussion and the consent of the participant.
- Some countries require that a 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

It is critical to account for such requirements in the informed consent process, (if applicable to you or to your institution). The consent process should account for such requirements and be carefully discussed with prospective research participants.

Deceased Research Participant Consent (First-person ante-mortem or next-of-kin postmortem)

In collecting consent directly from research participants or authorized representatives as concerns the use of their tissues/data prior to their death (ante-mortem), or in obtaining postmortem consent, it is important to clarify the following aspects:

- If the research participant provides ante-mortem consent, it will be possible for them to withdraw their consent to research participation up until the moment of their death. It will not be possible for the research participant's next-of-kin to withdraw such consent after the death and the instructions already given should be followed

- If the research participant's next-of-kin or authorized representative provides consent on the behalf of the research participant, such consent can be withdrawn on behalf of the research participant both prior to and following death.

Pediatric Research Participants

Pediatric research participants are generally considered to be those who have not attained the age of legal majority in your country. In some countries, it will be possible for some individuals younger than the age of legal majority to consent as though they were full adults (i.e. mature minors).

The following considerations should be accounted for in obtaining research consent from pediatric research participants:

- It is generally required to obtain assent from children (age 7 and over), and the consent of the mature minor, even if their parent or other authorized representative is providing consent on their behalf.

- In some countries, it can be required by law or ethics guidance to return actionable secondary findings (i.e. not the object of the research) to pediatric research participants. Actionable secondary findings mean that treatment or prevention are possible.

- In some countries, it can be required to recontact or re-consent pediatric research participants once they reach the legal age of majority. Notification of the existence of samples or data obtained during minority, with an option to oppose further use is also a possibility.

It is a recommended best practice to discuss with your local REB, IRB, or equivalent body prior to obtaining consent to research from children and mature minors.

IV. Open Access and Managed Access

Open Access Data

Currently, the HCA data is available through an open access mechanism. The HCA open access database provides direct access to anonymized data about the research participants to the broad public. Aggregate-level data of research participants is also used to create reference maps of human cells.

Proposed discussion language for projects using open access ***[This should be discussed in the part of the conversation concerning data and sample access]:***

Your information will be held in the part of the HCA database that anyone can access. This information is considered minimal risk. This information includes lists of genes that were activated in your cells, and limited metadata about you, such as descriptions of your biological sex and age. It has a low risk of being associated with your identity. Your information will also be combined with the data of others to make 'reference maps,' representations of the human body, that are made visible to all members of the public on the internet. These parts of the HCA data that are available to the public will not be removed from the HCA if you withdraw your consent to research.

There is ongoing discussion about the possibility of contributing coded research data to a managed access tier of the HCA (see below).

Some research projects may not be able to contribute their research data to the open access tier of the HCA. This could be the case if local ethical or legal requirements preclude the hosting of the research data collected on a platform that is available to the public.

If your data cannot be contributed to the open access tier of the HCA, you may still be able to contribute such data to the managed access tier of the HCA database in the future. The discussion language below may help to prepare for the future managed access tier of the HCA.

Managed Access Data

Currently, the HCA DCP does not accept any data that requires managed access/controlled access. In the future, however, it may be possible to integrate data to a managed access tier of the DCP that has yet to be developed.

If you are in the process of collecting data that is required to be held in managed/controlled access, you should amend the consent discussion to reflect this.

Proposed discussion language for projects using a managed/controlled access ***[This should be discussed in the part of the conversation concerning data and sample access]:***

Some parts of your data, such as genetic information and metadata, will be coded (that is, your identification removed and replaced with a code) and held on the managed part of the HCA database that is only available to approved researchers. The researchers must have been approved to access the data and have signed agreements to protect the confidentiality of the data.

V. Legacy Consent Assessment Filter

You may wish to contribute previously collected samples and data, that were not explicitly consented for contribution to the HCA database.

Depending on the consent obtained at the time of sample and data collection, it may still be possible to contribute such data to the HCA database without taking any additional steps.

Recontact of the original research participants to obtain a new consent is not always possible or practical. An ethics waiver of reconsent from your local REB may be another way to contribute legacy data to the HCA database.

In determining the approach that is most appropriate for your cohort, it will be helpful to refer to the **HCA Legacy Consent Assessment Filter**, available on the HCA website.

The Legacy Consent Assessment Filter is especially intended to guide researchers in contributing data to the HCA in following circumstances:

- Datasets that will be generated from legacy tissue samples (e.g. archival samples, samples collected for a purpose other than research, etc.), or
- Datasets that were generated before the creation of the HCA.

The following considerations are the main issues considered in determining how legacy data and data generated from legacy tissue samples can be contributed to the HCA database:

1.Can the legacy tissue sample be used to generate datasets for the HCA?

2. Is the tissue donor's consent adequate to deposit datasets in the HCA data coordination platform?

3. What is the appropriate data tier (open/managed) for the datasets?

4. If requirements for previous steps are not met, is it possible to re-consent donors or seek an ethics consent waiver?

The local policies and practices of your institution, as well as the ethical and legal requirements applicable, take precedence over the general guidance provided by the HCA Legacy Consent Assessment Filter.

VI. Material and Data Transfer Agreements (MDTAs)

In deriving data from samples to contribute them to the HCA database, you may need to transfer the biological materials or the data from your research institution to another.

For instance, this could be the case if your institution will collect the necessary tissue samples, but a different institution will perform the molecular analysis of the sample prior to the upload of data to the HCA database.

In transferring samples and data between institutions, it is important to ensure that the agreements used do not contain any provisions that could limit the contribution of the output data to the HCA database.

Some restrictions that could restrict or prevent the upload of data to the HCA include the following.

Restrictions on the use of Research Materials:

- If limitations are imposed on the use of the samples or data collected, this could create challenges to the inclusion of the data in the HCA database. These restrictions could arise from the terms of the transfer agreement, or the research consent.

- If intellectual property rights are used to protect samples or derived data, it is possible that they could create difficulties for including your data on the HCA database.

The HCA Ethics Toolkit includes a **Template Material/Data Agreement (MDTA)**. It is recommended that researchers and their institutions refer to this template in transferring materials and data between institutions prior to the upload of data to the HCA.

The use of the Template MDTA can ensure that any potential limitations on the use and transfer of biological materials or data are agreed to by the recipients. Using the Template MDTA can also help to ensure that language that could preclude the upload of data to the HCA Data Coordination Platform is not accidentally integrated to a data transfer or data sharing agreement.

If you intend to share biological materials or data with another research institution prior to contributing it to the HCA database, it is recommended to discuss this transfer with the legal staff and Technology Transfer Office at your local institution.

Providing the legal staff and Technology Transfer Office at your local institution with access to the Template MDTA may help them in ensuring that your research data can easily be contributed to the HCA Database.

The Template MDTA can be found on the HCA website.