INFORMED CONSENT FORM

(EUROPE VERSION)

I. TITLE

HDClarity: a multi-site cerebrospinal fluid collection initiative to facilitate therapeutic development for Huntington's disease

II. SPONSOR/CHIEF INVESTIGATOR/FUNDING ORGANIZATION/STUDY SITE INVESTIGATOR

HDClarity Study, a research study, is sponsored by University College London, UK (Sponsor). The chief investigator for this study is Dr. Edward Wild (Chief Investigator), who leads the Sponsor's Central Coordination team.

Funding for this study is being provided by CHDI Foundation, Inc. (CHDI), a not-for-profit foundation that only works on Huntington's disease (HD) and funds a variety of research activities aimed at developing treatments for HD.

This study's clinical procedures and assessments as well as the day-to-day management of this study will be carried out at the study sites including [_____] **[INSERT NAME OF INSTITUTION]**. The study site investigator is [_____] **[INSERT NAME OF PI]**.

III. INTRODUCTION, SCOPE AND PURPOSE OF THIS STUDY

You are being asked to participate in HDClarity, a research study. We are asking you to participate in this study because you have tested positive for the genetic mutation that causes HD or because you are a healthy control. A healthy control is a person who does not carry the genetic mutation that causes HD.

The main purpose of this study is to collect cerebrospinal fluid (CSF), the fluid that surrounds the brain and spinal cord. CSF can be used to provide information about the brain and the nervous system that is impossible to obtain in any other way. CSF is collected by a procedure called a lumbar puncture or spinal tap. This is a commonly performed procedure that takes around 30 minutes.

The CSF will be used to study HD and other conditions and to identify and evaluate biomarkers and pathways for HD and other conditions. A biomarker is something we can measure that helps us to better understand a disease. A pathway is a series of chemical reactions in a cell that play an important biological function. An increased understanding of how HD affects the brain, having better biomarkers for HD and identifying pathways relevant to HD may help in, as well as

speed up, the development of new treatments for HD. In addition, biomarkers may help design and guide future research studies and clinical trials as well as help us better understand who will most likely benefit from a particular treatment.

Two examples of biomarkers and pathways we intend to study in the CSF are (1) the huntingtin protein, which causes HD, and (2) chemicals of the kynurenine pathway – a group of chemicals produced by the brain which are thought to be involved in HD.

A blood sample will also be taken in order to make a collection of blood products matching the CSF collection. The blood sample collection will be used for the same purposes as the CSF sample collection.

In addition to the CSF and blood samples, certain information will be collected from you during this study. And, because you must first be a participant in the Enroll-HD study to participate in this study, we will also use information collected from you through your participation in the Enroll-HD study to help understand the findings from analysis of the CSF and blood samples and information collected from you in this study.

Many other important aspects of HD can be studied using these samples and information, so we will share them with other researchers for research relevant to HD.

We are asking you to donate up to 20 ml of CSF and 50 ml of blood for the purposes described above and more fully described below. And, we are asking you to donate up to another 15 ml of blood for routine safety tests.

Please read this consent form carefully. Ask the person who presents this consent form to you any questions you have before deciding whether to participate in this study. You will be given a copy of this consent form.

Your participation in this study is completely voluntary. You are completely free to choose whether or not to participate in this study. If you decide to participate, you can change your mind and withdraw from this study at any time for whatever reason. You are not required to give any reason for your decision on whether or not to participate in this study or, if you decide to participate, for your decision to withdraw from this study. Deciding not to participate in this study or deciding to withdraw from this study will not affect the current or future care that you would otherwise expect to receive. Nor will any such decision affect your participation in the Enroll-HD study.

We will not put your name, address or any other information that could directly identify you on the information and biological samples you allow us to collect from you. All information and biological samples collected from you during this study will be coded with a Huntington's disease identifier (HDID), the unique 9 digit number created for you as part of your participation in the Enroll-HD study. As you may recall, the HDID is used to protect your identity and connect your clinical information and biological samples to other HD studies in which you may participate. Only the study site staff will be aware of your identity and be able to link the information and biological samples collected from you during this study. All information and biological samples collected from you during your study visits will be stored in secure databases and repositories where they will be available now and in the future to researchers who are

trying to develop new tests for, and ways to treat HD and similar diseases, as well as other biomedical research.

IV. NUMBER OF PARTICIPANTS

Approximately 500 HD participants, at different stages of disease, and approximately 100 healthy controls will be included in this study. Approximately 30 centers will participate in this study. The locations of these centers will include, but are not limited to, the US, Canada and Europe.

V. PROCEDURES

This study consists of 2 study visits, the Screening Visit (Visit 1) and the Sampling Visit (Visit 2), not more than 30 days apart. All participants will also be contacted by telephone 1 to 3 days after the Sampling Visit to see how they are doing. Some participants may be asked to return for an additional optional study visit, the Optional Sampling Visit (Visit 3), within 8 weeks of the first Sampling Visit, in order to understand how the CSF changes over short periods of time. All participants who return for the Optional Sampling Visit will also be contacted by telephone 1 to 3 days after the Optional Sampling Visit to see how they are doing.

All costs for hotel accommodations, travel and meals are covered within specified guidelines which will be given to you prior to your visit(s).

Visit 1: Screening Visit (up to 30 days prior to Visit 2)

The study site investigator or designated study site staff will discuss the details of this study with you. You will have the opportunity to ask any questions you may have about this study. If you decide to participate, you will have to sign this form to give your informed consent to participate in this study.

In order to check to see if you are eligible to participate in this study, the study site investigator will ask you questions regarding any concurrent diseases you may have and about any medications that you have been using within the last month. A brief physical exam and a neurological exam will be performed, you will be asked questions regarding your mental and emotional wellbeing and, if you are an HD participant, your symptoms of HD will be assessed.

Since you are a participant in the Enroll-HD study, some of the above examinations and assessments may have been done as part of your most recent Enroll-HD study visit. If any of such examinations and assessments have been conducted within 2 months of your Screening Visit, they will not be repeated, and the information collected from you during your most recent Enroll-HD study visit will be used instead. Otherwise, in addition to the examinations described above, you will be asked to complete the clinical, behavioural and cognitive assessments that form the core of the Enroll-HD study as part of this study. Your height and weight will also be measured. You will probably be familiar with these from previous Enroll-HD study visits and they will take between 45 and 90 minutes. Information about the genetic mutation that causes HD, if applicable, will be collected from the Enroll-HD study.

Approximately 15 ml of blood (about 3 teaspoons) will be taken for tests to help ensure it is safe to collect the CSF. The entire procedure of collecting blood should take about 10 minutes.

The entire Screening Visit will last about 1 to 3 hours since, depending on when your most recent Enroll-HD visit was conducted, some of the above examinations and assessments may have been done as part of your most recent Enroll-HD study visit procedures and will not have to be repeated during the Screening Visit.

If the study site investigator finds you eligible for study participation, you will be scheduled for the Sampling Visit which will need to be done within 30 days of your Screening Visit.

If the study site investigator finds you are not eligible for study participation, but might become eligible within a reasonable period of time after your Screening Visit, you may be invited to return to repeat of some or all of the above examinations and assessments. If you are asked to return, you may decline to do so. If after repeating those examinations and assessments, the study site investigator finds you have become eligible for study participation, you will be scheduled for the Sampling Visit, which will need to be done within 30 days of the date of the initial part of your Screening Visit.

Visit 2: Sampling Visit

You will be asked to arrive at the study site in the morning so that the CSF collection can be done between 8:00 and 10:30 am. If it is more convenient for you, you may choose to stay at a hotel close to the study site the evening before your Sampling Visit. You will be provided with help to arrange your travel and hotel accommodations for your Sampling Visit.

You will be asked not to eat anything from midnight on the day of your Sampling Visit until after the CSF and blood sample collection is completed. You are permitted to drink water. You may also be asked to avoid certain medications prior to your appointment. If you have not followed the fasting or medication instructions, or if you are not feeling well, your Sampling Visit will need to be rescheduled.

The study site investigator will confirm that you are still willing to participate in this study. If so, a neurological exam and a brief physical exam and a motor exam will be performed, and the results of the blood testing done at your Screening Visit will be reviewed. If the study site investigator confirms that you still meet all eligibility requirements for this study, the study site staff will prepare you for the CSF collection.

You will be asked to lie on your side with your knees pulled up and your chin tucked downward. A pillow will be placed between your knees. After cleaning the skin of your lower back, local anesthetic may be injected to make the area go numb. This stings for a couple of minutes, then the skin goes numb. A very thin needle will be inserted into your lower back and up to 20 ml of CSF will be collected. Occasionally it may be necessary to try again in a different spot, or for you to sit upright, to find the right place and collect the fluid.

Once the CSF collection has been completed, approximately 50 ml of blood (the same volume as 10 teaspoons) will be taken from a vein in your arm. You will then be asked to lie flat for a

resting period of about an hour. The entire procedure of collecting CSF and blood should take about 20-45 minutes, not including the resting period.

The study site staff will check to see how you are doing during the resting period. When you are ready to leave, you will be given instructions on follow-up care.

This entire Sampling Visit will last about 3-5 hours.

Follow-Up Call: 1 to 3 Days after Sampling Visit

A member of the study site staff will call you 1 to 3 days after your Sampling Visit to see how you are doing. You will be asked how you are feeling and if you have experienced any medical conditions or symptoms since your Sampling Visit.

Visit 3: Optional Sampling Visit

Should you be asked to participate in the Optional Sampling Visit, you may decline to do so. If you do agree to participate, you will be asked to undergo a second CSF and blood sample collection as described above under Visit 2: Sampling Visit.

Follow-Up Call: 1 to 3 Days after Optional Sampling Visit

A member of the study site staff will call you 1 to 3 days after your Optional Sampling Visit to see how you are doing. You will be asked how you are feeling and if you have experienced any medical conditions or symptoms since your Optional Sampling Visit.

What must I keep in mind during this study?

During the time of this study, you are being asked to:

- Follow all instructions, including those regarding restricted medications that were given to you at your Screening Visit.
- Not eat anything on the day of your Sampling Visit or Optional Sampling Visit from midnight until the CSF and blood collection have been completed.
- Inform the study site staff of any illnesses you have had or medications you have been taking since your Screening Visit.
- Follow all instructions regarding follow-up care after your Sampling Visit or Optional Sampling Visit.

VI. PROCEDURES FOR STORING AND SHARING CODED INFORMATION AND BIOLOGICAL MATERIALS FOR RESEARCH PURPOSES

The information collected about you during this study will be entered via secure internet connections into a confidential database that is located at a data storage facility selected for this study. This facility, called a hosting facility, follows security procedures to make sure the information is safe and secure. The biological samples collected about you during this study will be stored in a biological samples repository that is located at a biological samples storage facility selected for this study.

The information collected from you and entered in the database as well as the biological samples collected from you and stored in the biological sample repository will not be associated with, or identified by, your name or other information that could directly identify you. Only the study site staff will be aware of your identity and have the key to the code that links your information and biological samples to you.

CHDI may **use,** and make available for **use** by its service providers and other organizations/researchers and their service providers, the **coded** information and/or **coded** biological samples collected from you during this study, for the following purposes:

- To generate a CSF sample collection and a blood products sample collection for identifying and evaluating biomarkers and pathways that will enable the development of new treatments for HD.
- To check the quality of the information and biological samples collected from you during this study.
- To see how different possible medicines influence biological and chemical processes that might be important in HD or other diseases.
- To design and guide future research studies and clinical trials.
- To support and enable scientific discussion and research as follows: (1) to better understand HD or other diseases being studied, (2) that furthers the development of treatments for HD or other diseases or (3) that furthers biomedical research.

CHDI may also share the **coded** information and/or **coded** biological samples collected from you during this study with the following other third parties:

- Representatives of organizations providing services in connection with this study, such as 2MT Software, the organization contracted to collect, maintain, and manage the information collected in this study and BioRep SRL, the organization contracted to store the samples collected in this study (or such other services providers as may be designated from time to time).
- Researchers at other study sites that are taking part in this study, the ethical review boards at those study sites, and other independent review boards overseeing the ethical conduct of this study.
- Representatives of national and foreign governmental and regulatory agencies and health authorities such as United States Food and Drug Administration (FDA), Health Canada and the European Medicines Agency (EMA).
- The ethics committee/review board at the site that is overseeing the ethical conduct of the study.

The Sponsor, CHDI and each of the organizations, researchers and services providers referred to above, may publish the results of their research, including coded information, in medical journals or present such results at meetings. However, your name, address or any other information that could directly identify will not be published.

CHDI may also submit coded information to be included in one or more other electronic databases for use by CHDI and the organizations, researchers and services providers referred to above for scientific discussion and research as follows: (1) to better understand HD or other

diseases being studied, (2) that furthers the development of treatments for HD or other diseases or (3) that furthers biomedical research.

The information and biological samples collected from you during this study will be used only for research purposes and will not be sold.

You can change your mind at any time about the storage and use of the biological samples collected from you during this study. Just contact the study site investigator and let him or her know that you no longer want the biological samples collected from you during this study stored and such biological samples will be removed from the storage facility and destroyed. If any of the biological samples collected from you during this study have already been distributed for use, we may not be able to locate and destroy such biological samples.

Any of the uses and activities described above may involve sending coded information and coded biological samples to other countries that may not have the same or as strict privacy laws as this country, including the United States. However, each recipient will be required to enter into an agreement under which the recipient will be required to comply with local laws applicable to their use of the information, and given that only coded information or coded biological samples are sent, the risk of unintended disclosure of identifying information is low.

Throughout this study, you have the right to ask what kind of information is recorded about you, who keeps your information, and who has access to it. You also have the right to review or ask that your information be corrected or deleted in accordance with your country's data protection laws. You understand and approve that access and corrections of information may be limited in order to ensure scientific accuracy and responsibility in accordance with applicable laws and regulations. If you choose to stop your participation in this study, no new information about you will be collected or added to the study database; however, information that was previously collected will not be removed and will be used and disclosed as set forth above.

[A description of this study will be available on http://www.clinicaltrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results of this study. You may search this website at any time.] [INCLUSION TO BE DECIDED AT TIME OF IRB SUBMISSION]

VII. DISCOMFORTS AND RISKS

Some of the possible discomforts of CSF collection include:

- The anesthetic will sting when first injected.
- You may feel a pressure sensation when the needle is inserted.
- Some people experience brief pain, either in the back or down one leg, when the needle is close to the spinal fluid. This pain usually stops after a few seconds.
- You may experience some back pain following the CSF collection.
- You may experience a headache following the CSF collection. You will be given instructions on how to manage this if it occurs. The risk of headache is about 5%. Occasionally the headache doesn't go away on its own and a second hospital procedure called a "blood

patch" may be recommended to help it resolve. This is rare – the chance is less than 1% overall.

Some of the possible discomforts of blood collection include:

- Blood collection may cause some pain and discomfort and a bruise may form at the site of the puncture with the needle.
- Fainting or feeling lightheaded may occur during or shortly following the blood collection.

Possible risks of CSF collection include:

- Hypersensitivity (allergic) reaction to the anesthetic.
- Infection caused by the needle going through the skin. This is very rare; the risk is much less than 1 in 1,000.
- Damage to the nerves in the lower back, which could cause numbness, pain or altered function in the legs, bowels, bladder or genitals. This may be caused directly by the needle or by blood leaking into the fluid. It is very rare (much less than 1 in 1,000).

Possible risks of blood collection include:

- A clot may form at the site of needle puncture and infections may occur, but these are rare.

Any adverse medical events arising from your participation in this study will be followed up and treated as deemed necessary by the study site investigator.

Possible risks of personal (private) information collection include:

- As with the collection of any personal (private) information, there is also a slight risk of accidental disclosure of information or breach of computer security. Loss of confidentiality could have a negative impact on you, your family, or other individuals or groups, including insurability, employability and/or family relationships. Safeguards are in place to minimize this potential risk.

If you are required to complete the clinical, behavioural and cognitive assessments that form the core of the Enroll-HD study as part of this study, you may experience anxiety or psychological discomfort (such as stress or fatigue) while completing these assessments. If at any time you feel you could benefit from treatment or support, you may request to be referred for appropriate care. In the course of doing questionnaires or tests you may feel tired and/or irritable. If this happens please tell your study site investigator or the study site staff and ask them to allow you time to rest or stop the testing all together.

VIII. BENEFITS

You will not have any direct benefits from participating in this study. The results of this study may contribute to new knowledge of HD.

IX. ALTERNATIVES

You do not have to participate in this study. Choosing not to participate will not affect your current or future medical care at [_____] **[INSERT NAME OF INSTITUTION]**.

X. TRAVEL EXPENSES/PAYMENT

You will receive assistance arranging travel for the study – ask your study site investigator or the study site staff for information about this. The expenses that you incur for travel, hotel and meals resulting from your participation in the study will be covered or reimbursed in accordance with the policies provided to you by your study site investigator or the study site staff.

In addition, you will receive compensation in the amount of [_____] **[INSERT AMOUNT]** after the Sampling Visit and after the Optional Sampling Visit for the invested time and discomforts arising within the scope of this study.

XI. INSURANCE AND COMPENSATION FOR INJURY

The Sponsor holds insurance in case you are harmed by your participation in this study. You may be able to claim compensation if the Sponsor has been negligent. However, [_____] **[INSERT NAME OF INSTITUTION]** continues to have a duty of care to you as a participant in the study. The Sponsor does not accept liability for any breach of the duty of care owed by [_____] **[INSERT NAME OF INSTITUTION]**, or any negligence on the part of the employees of [_____] **[INSERT NAME OF INSTITUTION]**.

The [_____] **[INSERT NAME OF INSTITUTION]** will provide medical care for any emergency medical problem that you may experience as a direct result of your participation in this study. You will not have to pay for this emergency care, but the [_____] **[INSERT NAME OF INSTITUTION]** may seek reimbursement for this care from your private health insurance carrier or government health service.

XII. FUNDING

This study and the storage of coded information and coded biological samples collected in the course of this study are supported by CHDI, a not-for-profit foundation that only works on HD and funds a variety of research activities aimed at developing treatments for HD.

XIII. COMMERCIAL USES

Successful research by us and others using your coded information and coded biological samples collected in the course of this study could result in a commercial test or therapeutic product with significant value, such as a product for the treatment of HD. You will not receive any financial benefit from such a result.

XIV. CONFIDENTIALITY

To meet regulations or for reasons related to this study, your study site investigator may share a copy of this consent form and records that identify you with the following people/oversight entities:

- Representatives of the United States, Canada and other governmental and regulatory agencies such as United States Food and Drug Administration (FDA), Health Canada and the European Medicines Agency (EMA).
- [_____] **[INSERT NAME OF PI]** and the study site staff at [_____] **[INSERT NAME OF INSTITUTION]**
- The ethical committees/review boards at study sites and other independent review boards overseeing the ethical conduct of this study (committees that make certain your rights as a participant are protected) that reviewed this study.
- Representatives of organizations providing services in connection with this study, such as 2MT Software, the organization contracted to collect, maintain, and manage the information collected in this study and BioRep SRL, the organization contracted to store the samples collected in this study (or such other services providers as may be designated from time to time).
- CHDI
- Other agents designated by the Sponsor or CHDI

XV. VOLUNTARY PARTICIPATION

Your participation in this study is completely voluntary. You are completely free to choose whether or not to participate in this study. If you decide to participate, you can change your mind and withdraw from this study at any time for whatever reason. You are not required to give any reason for your decision on whether or not to participate in this study or, if you decide to participate, for your decision to withdraw from this study. Deciding not to participate in this study or deciding to withdraw from this study will not affect the current or future care that you would otherwise expect to receive. Nor will any such decision affect your participation in the Enroll-HD study.

In the event that you do withdraw from this study, the samples collected from you during this study will continue to be stored, used, and shared in the manner described in this consent form, unless you request that the samples be removed from the storage facility and destroyed. If any of the biological samples collected from you during this study have already been distributed for use, we may not be able to locate and destroy such biological samples. In the event you withdraw from this study, the coded information collected from you during this study will continue to be stored, used, and disclosed in the manner described in this consent form. Identifying information gathered before your withdrawal may need to be used and given to others if necessary to preserve the integrity of this study.

XVI. EARLY DISCONTINUATION OF THIS STUDY

You may be withdrawn from this study if you do not follow the directions of this study or if your medical condition changes so that staying in this study might risk your health or this study. Your participation in this study may also end if funding for this study is discontinued or the Chief Investigator elects to discontinue the study.

XVII. CONTACT PERSONS

For more information concerning this research or if you believe that you have suffered a research related injury, please contact: [_____]. **[INSERT NAME AND PHONE NUMBER OF CONTACT PERSON FOR STUDY INFORMATION *NOTE: THIS PERSON IS USUALLY THE SITE'S PI]**

If you have questions about your rights as a participant, you may call [_____]. **[INSERT NAME AND PHONE NUMBER OF CONTACT PERSON FOR PARTICIPANT'S RIGHTS]**

XVIII. WHO HAS REVIEWED THIS STUDY

This study was designed jointly by the Chief Investigator (Dr Edward Wild) and CHDI with input from expert colleagues. It has been reviewed by the Sponsor (University College London) and [_____]. **[INSERT NAME OF LOCAL ETHICS REVIEW BOARD]**

XIX. CONSENT TO PARTICIPATE IN THIS STUDY

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I agree to the uses and disclosures of my identifying information as described above. I understand that I will be given a signed copy of this form for my records and future reference.

_____	_____	_____
Signature of Participant	Printed Name	Date
_____	_____	
Signature of Authorized Representative	Relationship to Participant	
_____	_____	
Print Name of Authorized Representative	Date	

For Study Site Staff:

Person Obtaining Consent

I have read this form to the participant/authorized representative and/or the participant/authorized representative has read this form. An explanation of this study was given and questions from the participant/authorized representative were solicited and answered to the participant/authorized representative's satisfaction. In my judgment, the participant/authorized representative has demonstrated comprehension of the information.

_____	_____	_____
Signature of Person Obtaining Consent	Printed Name and Title	Date

Assent Signatures, For Participants with a Legally Authorized Representative

Signature of Person Conducting Assent Discussion Date

Note: This section cannot be used for translations into another language. A translated consent form is necessary for enrolling participants who do not speak English.

---------- **Use this witness section only if applicable** ----------

If this consent form is read to the participant because the participant (or legally authorized representative) is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant (or the participant's legally authorized representative). The participant (or the participant's legally authorized representative) freely consented to be in this study.

Signature of Impartial Witness Date

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling participants who do not speak English.