# A user guide to the clinical datasets and biosamples available from Enroll-HD

**Version 2016-10-R1**

## Enroll-HD

**A worldwide observational study for Huntington's disease families**

**A CHDI Foundation Project**

# Access to Enroll-HD Data and Biosamples – Summary Guide

The Enroll-HD website hosts periodic datasets that will be made available to any researcher who is employed at a recognized research organization — universities, government institutions, nonprofit organizations, or public and private companies. This summary guide provides an overview of the policies and the accompanying documentation relevant to gaining access to the clinical data and biosamples from the Enroll-HD study. It also describes the quality control processes used for the data and the publication policy that should be adhered to by researchers.

A researcher gains access to the periodic datasets by verifying that they are employed by a recognized research organization, setting up a user account, and executing the requisite data use agreement. To encourage collaboration, researchers are asked to provide a brief description (50-200 words maximum) of their proposed project, which is automatically posted on the Enroll-HD website along with the researcher's name. In the future, the research institution and PubMed IDs will also be posted on the Enroll-HD website.

**STUDY DESCRIPTION**

Enroll-HD is a worldwide longitudinal observational study of Huntington's disease (HD) whose overarching goal is to accelerate progress towards the development of effective therapeutics for HD. Participants include individuals 18 years or older who are HD gene expansion mutation carriers independent of the phenotypical manifestation of HD and controls who do not carry the HD expansion mutation. Individuals under the age of 18 years, those with clinically diagnosed features of HD in the setting of a confirmatory family history or a positive genetic test result may be included in this study. Participants are asked to attend as many annual study visits as possible. Study sites are located in North America, Latin America, Europe, Australia and New Zealand.

The study has three main objectives:

**1. To provide a platform to support the design and conduct of clinical trials**

- Provide a resource to identify, develop and qualify novel assessment tools, clinical endpoints and biomarkers,

- Collect longitudinal data to inform disease modeling studies, and

- Facilitate the identification of potential trial participants and inform the selection of participants using data to estimate and quantify slopes/rates of disease progression (provide "run-in" data).

**2. To improve the understanding of the dynamic phenotypic spectrum and the disease mechanisms of HD**

- Collect natural history data covering the cognitive, behavioral and motor domains, enabling researchers to track rates of progression in HD and gain insights into the neurobiology of HD,

- Collect data and biologic samples to identify genetic and environmental factors influencing and/or modifying the phenotype and progression of HD, and

- Promote interrogatory studies that may provide clues to the pathogenesis of HD.

**3. To promote the development of evidence-based guidelines to inform clinical decision making and improve health outcomes for the participant/family unit**

- Assist in the identification of beneficial interventions (clinical, pharmaco-therapeutic, non-pharmacologic),

- Facilitate the dissemination and implementation of currently proposed best clinical practice,

- Provide a platform for conducting outcome research, and

- Promote exploratory data analysis projects that may identify processes to further improve the healthcare of affected individuals and their families.

To achieve these goals, Enroll-HD was designed to ensure that as many researchers as possible worldwide could access the clinical data and renewable biosamples in a rapid, transparent,

straightforward manner, lowering barriers to entry into HD research while safeguarding the identity of research participants.

Data included in the released datasets are coded, which means that the data have gone through a process of removing identifying information that could connect a participant's identity to the information.


**DATA RELEASE – PERIODIC and SPECIFIED DATASETS**

Enroll-HD clinical data consists of longitudinal data from participants' annual visits at a research site. Each participant has completed a baseline visit and a set of general forms. At least one on-site monitoring visit (see Monitoring of Data below) has been completed for each participant included in the dataset.

**Periodic datasets** are time-stamped cuts of the total Enroll-HD clinical dataset. These periodic datasets are available for download, along with accompanying documentation to aid in your use of the data. The first periodic dataset release from Enroll-HD provided all data that met the approved criteria for release as of January 1, 2015 (11am GMT).  A summary of the releases is provided in the table below.

| PDS name | Dataset derived from approved criteria | Date of release | Periodic Dataset version |
|---|---|---|---|
| Enroll-HD PDS1 | January 1, 2015 | February 28, 2015 | 2015-01-R1 |
| Enroll-HD PDS2 | October 31, 2015 | December 10, 2015 | 2015-10-R1 |
| Enroll-HD Plus PDS3 | October 31, 2016 | December 15, 2016 | 2016-10-R1 |

In addition to Enroll-HD study data, the Enroll-HD Plus PDS3 dataset includes data from a similar longitudinal observational study of HD, Registry, conducted mainly in European countries by the European Huntington's disease Network (www.ehdn.org ). The Registry study began in 2004. The Enroll-HD study started in 2012. Study sites and participants that were originally part of Registry have and continue to be transitioned to join Enroll-HD.  Registry participants who have

consented to participate in Enroll-HD have agreed to have their research data and biosamples migrated into the Enroll-HD database. This means that for a subset of Enroll-HD participants, there are additional longitudinal data available from the Registry study. Whilst the study assessment protocols are not identical between Registry and Enroll-HD, there is significant overlap of many assessments, such as the UHDRS Motor and Function, and several cognitive and behavioral rating scales. A breakdown of the assessments included in each study is provided in the [Enroll-HD Periodic Dataset Data Dictionary](#) and can also be found in the respective study protocols available on the [website](#).

Researchers may also request **specified datasets** that include Enroll-HD participant data that are excluded from the periodic datasets (see Excluded Data below), non-standard data fields, or data that are in different file formats. Such requests require completion of the [Enroll-HD Specified Dataset Information and Request Form](#). Requests for specified datasets will be referred to the Scientific Publication Review Committee for prioritization, feasibility, and approval and will therefore take time to process.


**MONITORING OF DATA**

Enroll-HD uses the following risk-based monitoring (RBM) approaches: electronic data capture (EDC) system edit checks, remote and onsite data review, medical monitoring and centralized statistical monitoring. Defined triggers are activated during the monitoring process, signaling the need for increased monitoring to mitigate increased risk. Using this strategy and combining several linked risk-based approaches in sequence improves monitoring efficiency and effectiveness. Edit checks help to identify potentially erroneous data or data entry mistakes before data are reviewed by the project team. Remote and onsite monitoring occurs sequentially (at the participant level) while medical and statistical monitoring of aggregated data and listings occur on a rolling basis.

Registry used the following monitoring approaches: electronic data capture (EDC) system edit checks, remote and onsite data review.

**DATA INCLUSION CRITERIA**

Not all the data in the Enroll-HD database are included in the periodic datasets; all of the following criteria must be met for inclusion:

1) Participant must have properly signed informed consent forms (ICF). This means that each participant's ICF is verified at the research site as part of the monitoring process.

2) The dataset includes only participants in Enroll-HD.

3) The dataset includes data obtained only from the Enroll-HD study, REGISTRY 2, REGISTRY 3 and AdHoc.

4) Participants must have a research CAG determination for inclusion.

5) Terms entered for pharmacologic therapies, indications for pharmacologic therapies, comorbid conditions, or reported events must be properly coded.

6) A participant is selected for the dataset if a Baseline visit has been performed with on-site review completed, a General visit with remote review completed, and at least one more annual visit (Follow-up, Unscheduled Visit, or Phone Contact) with remote review completed within the 15 months prior to the planned date of the data cut. The additional visit criterion applies only for participants who are enrolled more than 15 months before the data cut. Examples for the selection of participants for a potential data cut 1/2015:

   -A participant with a Baseline & General visit done in 9/2014 is included.

   -A participant with a Baseline & General visit done in 10/2013 and no additional visits is not included.

   -A participant with a Baseline & General visit done in 9/2013 and a Follow Up in 8/2014 is included.

   -A participant with a Baseline & General visit done in 6/2012 and a Follow Up in 9/2013 and no additional visits is not included.

   -A participant with a Baseline & General visit done in 6/2012 and a Phone Contact in 5/2014 is included.

7) The dataset includes data only from visits that were remotely reviewed at least once.

8) Data from participants who have discontinued from the study prematurely are included only with a completed End of Study Form.

The Enroll-HD Operations Team continually monitors these parameters to maximize the amount of data that can be published with each dataset release.

**EXCLUDED DATA**

Certain data are aggregated or withheld from the periodic dataset because they are deemed to increase the risk of potentially identifying individual participants or families, especially when combined with the broader dataset. If there are excluded data that you are interested in, please complete an Enroll-HD Specified Dataset Information and Request Form.

**BIOMATERIALS ACCESS POLICY**

Researchers can request Enroll-HD biosamples by completing the Biosamples Request Form and signing a Biosamples Use Agreement, which are available on the Enroll-HD website. Currently there is no online catalog; to enquire about the type of biosamples available, contact Biosamples@Enroll-HD.org.

Biosamples require completion of the Biosamples Request Form and will take additional time to process; non-renewable biosamples requests will also require approval from the Scientific Publication Review Committee.

**PUBLICATION POLICY**

Many people contribute to creating and making these valuable resources available to researchers. These include CHDI Foundation, clinicians, site coordination staff, raters, a worldwide operations team, EDC programmers, bio-repository personnel and scientists, assessment developers, statisticians, researchers and, most importantly, the Enroll-HD participants and their families and caregivers. In appreciation of all their efforts, we request

that each researcher adheres to the Enroll-HD publication policy when publishing work using this information (see Enroll-HD Publication Policy).

**ACCOMPANYING DOCUMENTS FOR DATASETS**

Several documents are listed in the Enroll-HD Document Index. These documents are intended to help users understand and use the Enroll-HD resources. While we hope these documents are comprehensive, you may have additional questions. Please email us at AccountSetup@Enroll-HD.org.

**Revision History**

| Version | Summary of changes |
|---------|--------------------|
| 2015-01-R1 | Initial version for the first Enroll-HD periodic dataset |
| 2015-10-R1 | Revised version for the second Enroll-HD periodic dataset |
| 2016-10-R1 | Revised version for the third Enroll-HD Plus periodic dataset |