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

Version 2015-10-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

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. 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 study. It also describes the quality control processes used for the data and the publication policy that should be adhered to by researchers.

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.

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. 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.

DATA RELEASE – PERIODIC and SPECIFIED DATASETS

Enroll-HD clinical data consist 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.

Dataset derived from approved criteria	**Date of release**	**Version of Periodic Dataset**
January 1, 2015	February 28, 2015	2015-01-R1
October 31, 2015	December 10, 2015	2015-10-R1

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.

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.
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 Quick Reference Guide. 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