# HDClarity

# Electronic Data Capture

## EHDN Biomarkers Meeting

London, 15 Jan 2016

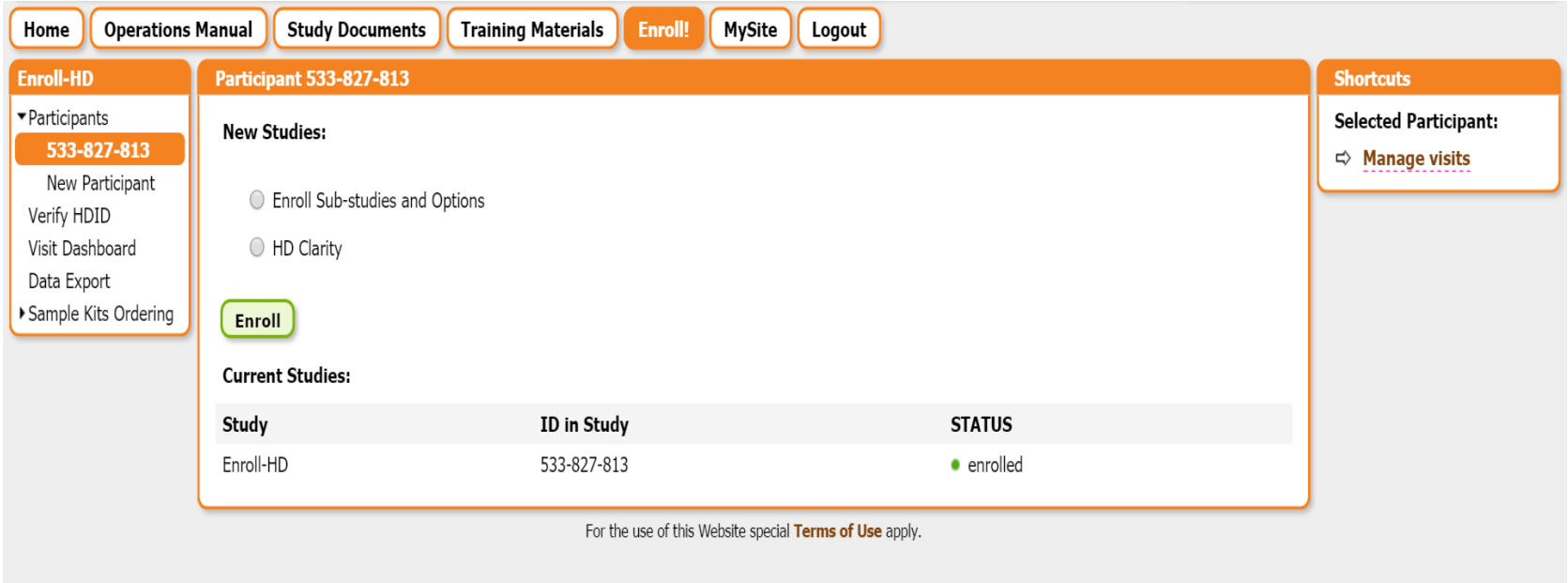
CHDI
Accelerating therapeutic development for Huntington's disease

HUNTINGTON'S DISEASE CENTRE

UCL

# Overview

- HDClarity participants are selected from Enroll-HD and the Enroll-HD electronic data capture system (EDC) is used




Enroll-HD

HDClarity

# Overview

- The HDClarity **Screening Visit** occurs 0-60 days after the Enroll-HD visit
- The HDClarity **Sampling Visit** occurs 1-30 days after screening, i.e. participants complete Enroll-HD core assessments within 3 months:
  - **Height and weight**
  - **UHDRS** (motor, functional assessment scale, independence score and TFC)
  - **Problem Behaviour Assessment** (short form)
  - **Cognitive** (catergorical verbal fluency, Stroop word and colour, and SDMT)
- Waivers may be granted at the discretion of the CI and the Enroll-HD core assessments may be performed at the **Screening Visit** if necessary

Enroll-HD

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# Overview

| HDClarity Day >-90 | HDClarity Day – 90 | HDClarity Day -30 | HDClarity Day -1 | HDClarity Day 0 | HDClarity Day 3 | HDClarity Day 56 | HDClarity Day 59 | Waiver required |
|---|---|---|---|---|---|---|---|---|
| | | | Enroll-HD & HDClarity Screening | **HDClarity Sampling** | HDClarity Phone Visit | | | No |
| | Enroll-HD | HDClarity Screening | | **HDClarity Sampling** | HDClarity Phone Visit | Optional Repeat Sampling | HDClarity Phone Visit | No |
| Enroll-HD | | HDClarity Screening | | **HDClarity Sampling** | HDClarity Phone Visit | Optional Repeat Sampling | HDClarity Phone Visit | Core assessments out of window |
| | Enroll-HD & HDClarity Screening | | | **HDClarity Sampling** | HDClarity Phone Visit | Optional Repeat Sampling | HDClarity Phone Visit | Sampling visit out of window |

Enroll-HD

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# Enroll-HD General Forms

In addition to the Enroll-HD core assessments, the following general CRFs must be checked and updated during HDClarity visits

- **Demographics**
- **Variable**
- **Comorbidities**
- **Medications**
- **Clinical Trials**

Enroll-HD

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# HDClarity Screening Visit

- There are 3 HDClarity-specific forms at the **Screening Visit**:
  - Enrollment CLR
  - Safety Lab Exam
  - Checklist

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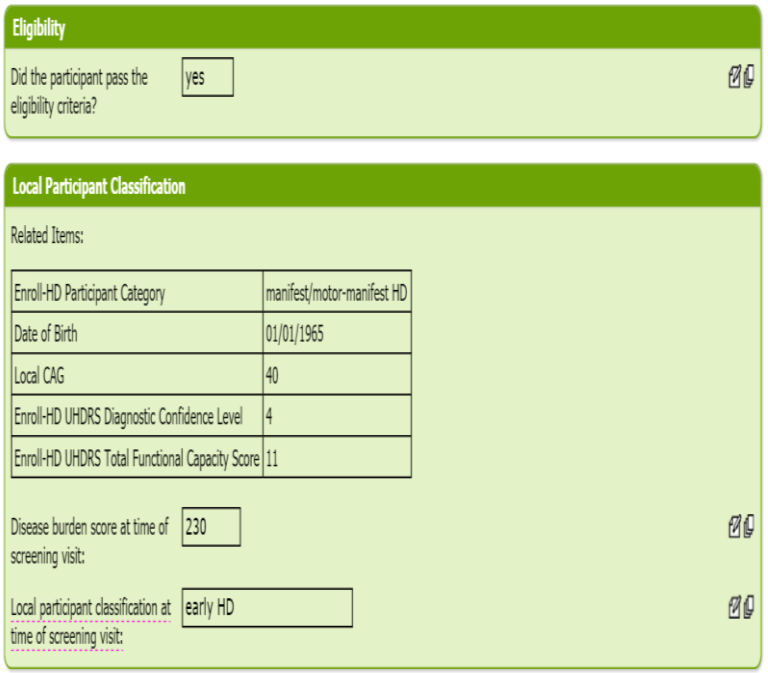
# Enrollment CLR

- Warnings are automatically generated if inclusion/exclusion criteria aren't met
- If participants do not fulfil all criteria they may be rescreened with prior approval of the CI
- If eligibility is set to 'no' then a waiver option appears
- Local Participant Classification and burden of pathology are calculated for the date of the HDClarity Screening Visit using most recent values for DOB, CAG and UHDRS



**Eligibility**

Did the participant pass the eligibility criteria? yes

**Local Participant Classification**

Related Items:

| | |
|---|---|
| Enroll-HD Participant Category | manifest/motor-manifest HD |
| Date of Birth | 01/01/1965 |
| Local CAG | 40 |
| Enroll-HD UHDRS Diagnostic Confidence Level | 4 |
| Enroll-HD UHDRS Total Functional Capacity Score | 11 |

Disease burden score at time of screening visit: 230

Local participant classification at time of screening visit: early HD

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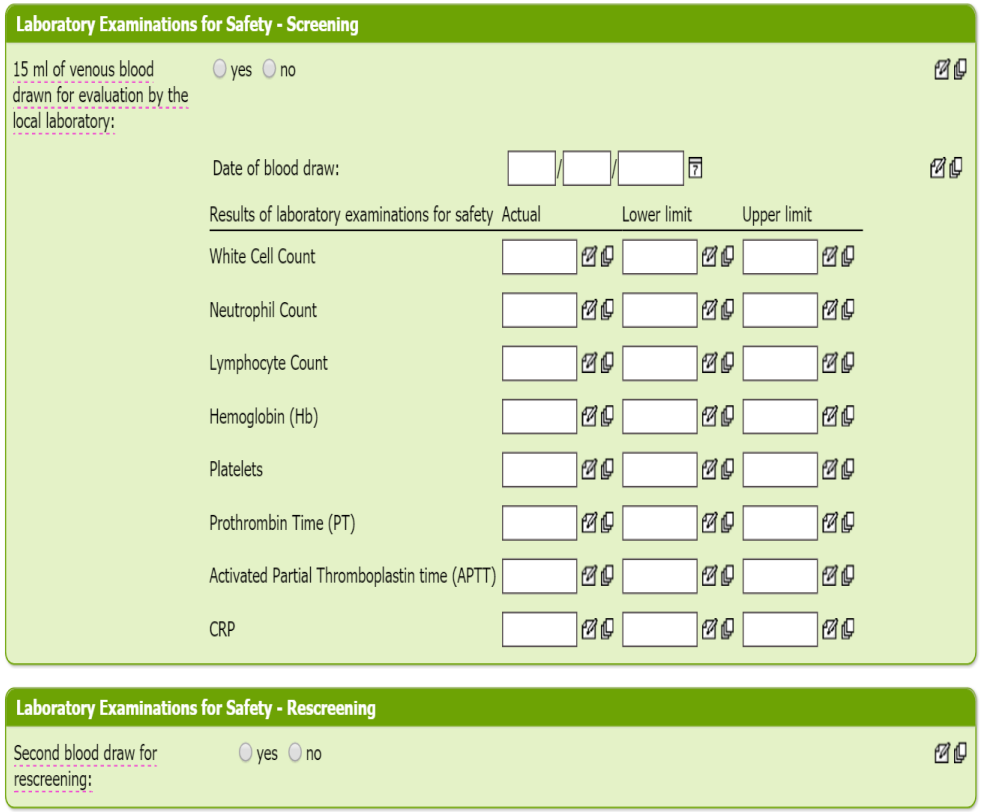
# Safety Lab Exam

- Up to 15ml venous blood:
  - Full blood count including platelet number
  - Clotting profile
  - C-reactive protein
- Upper and lower limits based on local clinical standards (≤ x2 upper limit permitted for CRP)
- If results fall out of range then re-screening may be allowed with prior approval of CI



**Laboratory Examinations for Safety - Screening**

15 ml of venous blood drawn for evaluation by the local laboratory: ○ yes ○ no

Date of blood draw: / /

| Results of laboratory examinations for safety | Actual | Lower limit | Upper limit |
|---|---|---|---|
| White Cell Count | | | |
| Neutrophil Count | | | |
| Lymphocyte Count | | | |
| Hemoglobin (Hb) | | | |
| Platelets | | | |
| Prothrombin Time (PT) | | | |
| Activated Partial Thromboplastin time (APTT) | | | |
| CRP | | | |

**Laboratory Examinations for Safety - Rescreening**

Second blood draw for rescreening: ○ yes ○ no

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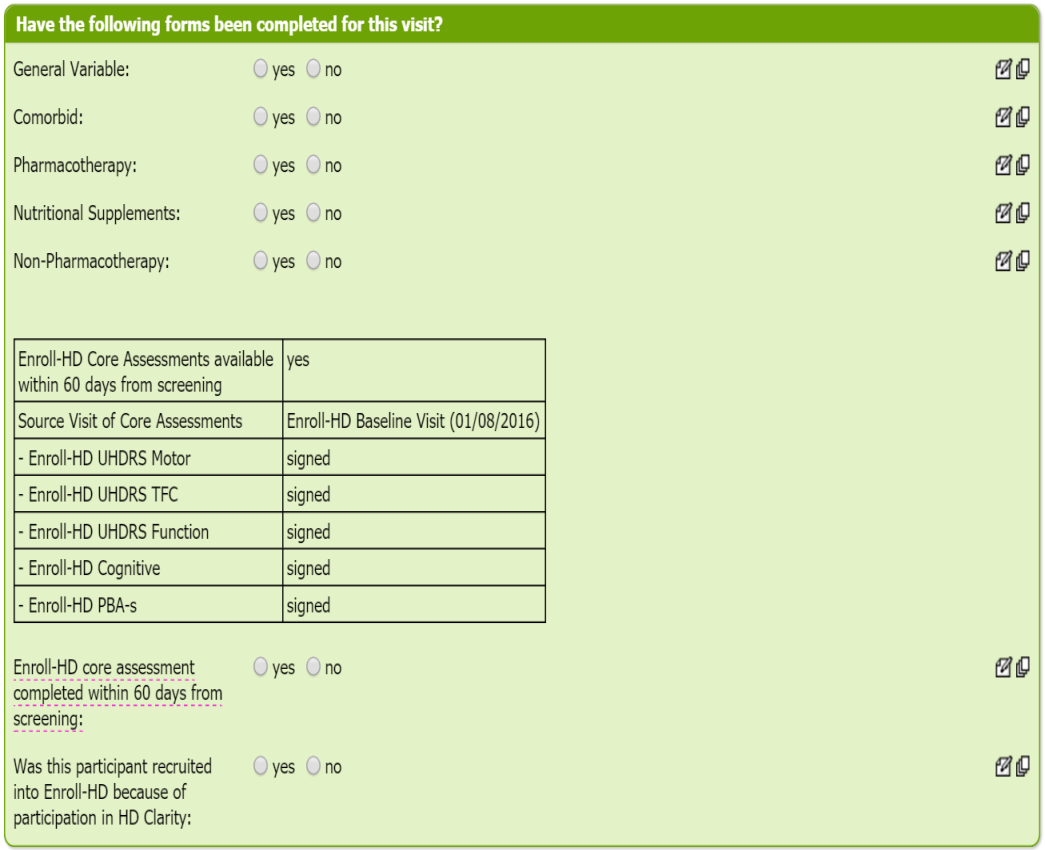
# Checklist

- If Enroll-HD core assessments are completed within the 60 day window before the **Screening Visit** the table will appear pre-populated

- If the visit is out of window, user must confirm a CI waiver granted has been given to complete the assessments on the same day



**Have the following forms been completed for this visit?**

General Variable: ○ yes ○ no

Comorbid: ○ yes ○ no

Pharmacotherapy: ○ yes ○ no

Nutritional Supplements: ○ yes ○ no

Non-Pharmacotherapy: ○ yes ○ no

| | |
|---|---|
| Enroll-HD Core Assessments available within 60 days from screening | yes |
| Source Visit of Core Assessments | Enroll-HD Baseline Visit (01/08/2016) |
| - Enroll-HD UHDRS Motor | signed |
| - Enroll-HD UHDRS TFC | signed |
| - Enroll-HD UHDRS Function | signed |
| - Enroll-HD Cognitive | signed |
| - Enroll-HD PBA-s | signed |

Enroll-HD core assessment completed within 60 days from screening: ○ yes ○ no

Was this participant recruited into Enroll-HD because of participation in HD Clarity: ○ yes ○ no

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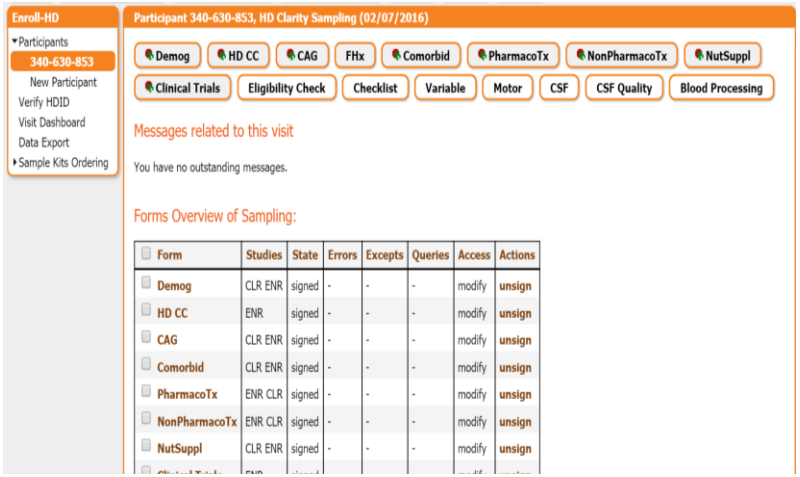
# HDClarity Sampling Visit

## To be completed within 30 days of screening

- There are 5 HDClarity-specific forms at the **Sampling Visit**:
  - Eligibility Check
  - Checklist
  - CSF
  - CSF Quality
  - Blood Processing




- Eligibility and Checklist are used to confirm consent, compliance and safety before sampling
- The Enroll-HD Variable and Motor CRFs must also be completed at the **Sampling Visit**

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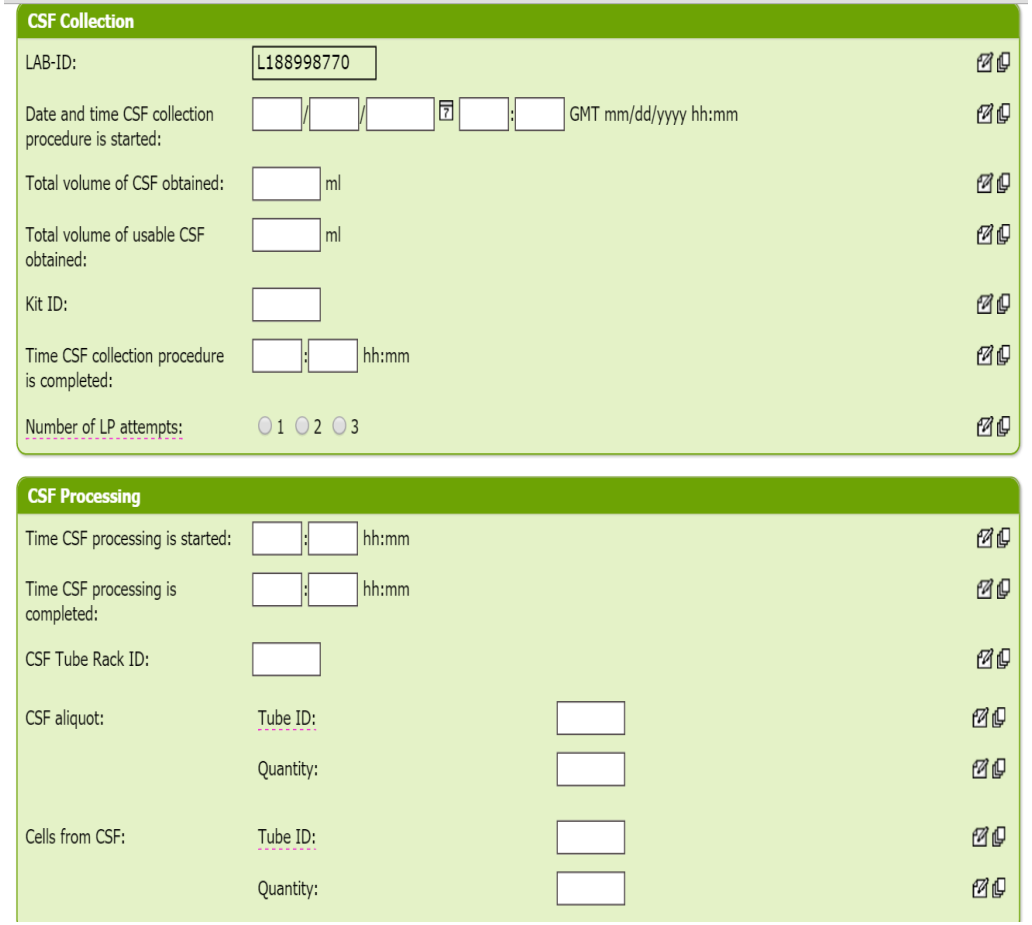
# CSF

- LP should be performed between 08:00 and 10:30
- If CSF cannot be obtained, up to three needles or adjacent space may be used (max 5 attempts)
- If 1ml CSF is macroscopically bloody, tube is discarded and CSF continued with new tube.
- Kit ID and all tube IDs are entered in CRF

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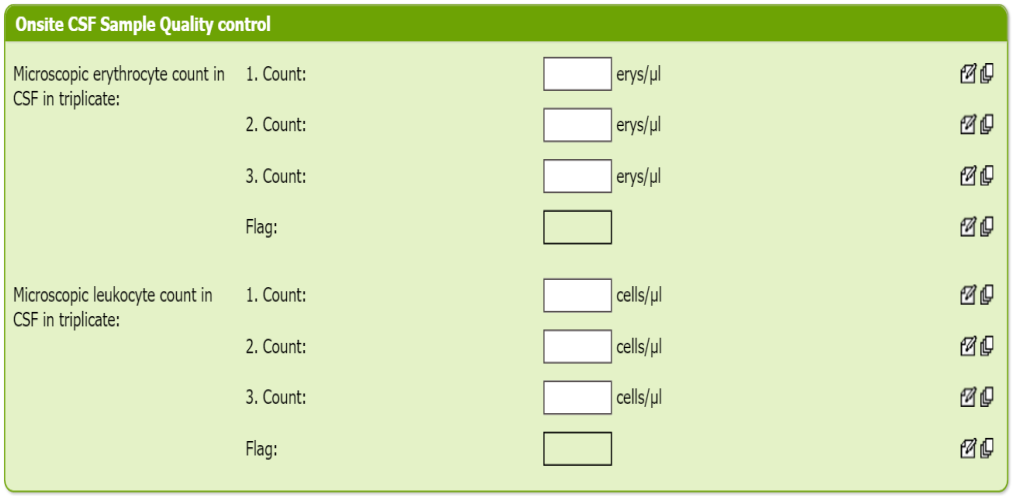
# CSF Quality

- 200 µl CSF used to determine white blood cell count and erythrocyte count per µl according to local GLP-approved laboratory practice.
- This should be done in triplicate within 60 minutes of collection and all values recorded in the CRF.

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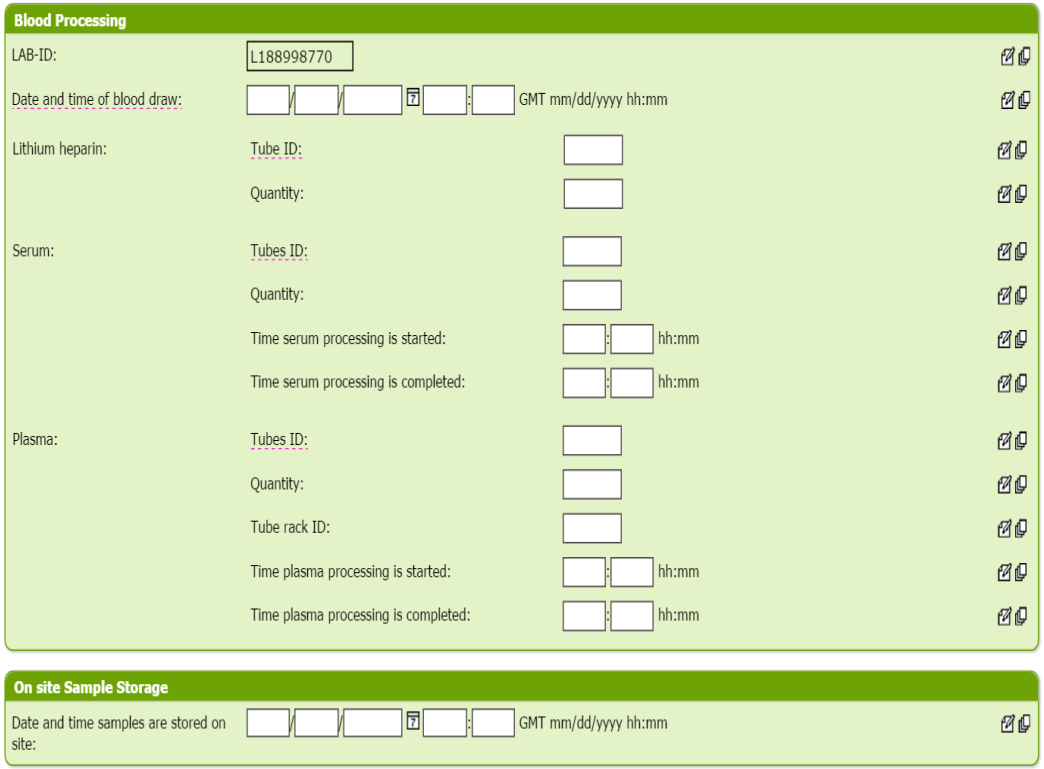
# Blood Processing

- Venous blood is drawn immediately after CSF collection is complete
  - 1 x 8.5 ml serum tube
  - 4 x 10 ml blood in lithium heparin tubes
- Tube IDs are entered in the CRF

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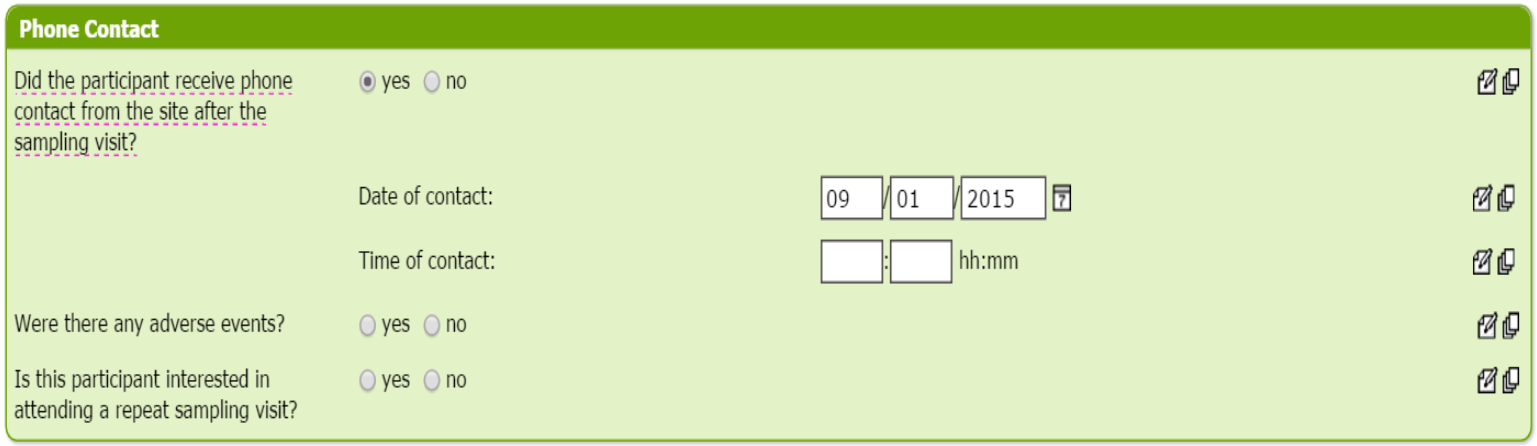
# Phone Contact
## Occurs 24-72 hours post LP

- The participant is contacted 24 to 72 hours following optional Sampling Visit to collect any AE and/or concomitant medication data

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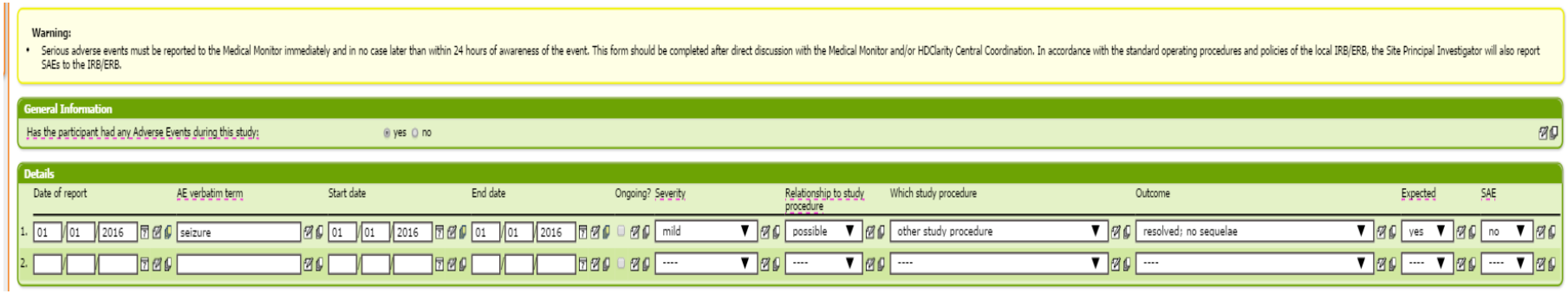
# AE Log

- AEs must be documented from the point of enrolment until procedures for the final study visit have been completed
- The AE log CRF should be completed within 48 hours of becoming aware of the event



**Warning:**

- Serious adverse events must be reported to the Medical Monitor immediately and in no case later than within 24 hours of awareness of the event. This form should be completed after direct discussion with the Medical Monitor and/or HDClarity Central Coordination. In accordance with the standard operating procedures and policies of the local IRB/ERB, the Site Principal Investigator will also report SAEs to the IRB/ERB.

**General Information**

Has the participant had any Adverse Events during this study: (•) yes ( ) no

**Details**

| | Date of report | AE verbatim term | Start date | End date | Ongoing? | Severity | Relationship to study procedure | Which study procedure | Outcome | Expected | SAE |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | 01 / 01 / 2016 | seizure | 01 / 01 / 2016 | 01 / 01 / 2016 | ☐ | mild | possible | other study procedure | resolved; no sequelae | yes | no |
| 2. | / / | | / / | / / | ☐ | ---- | ---- | ---- | ---- | ---- | ---- |

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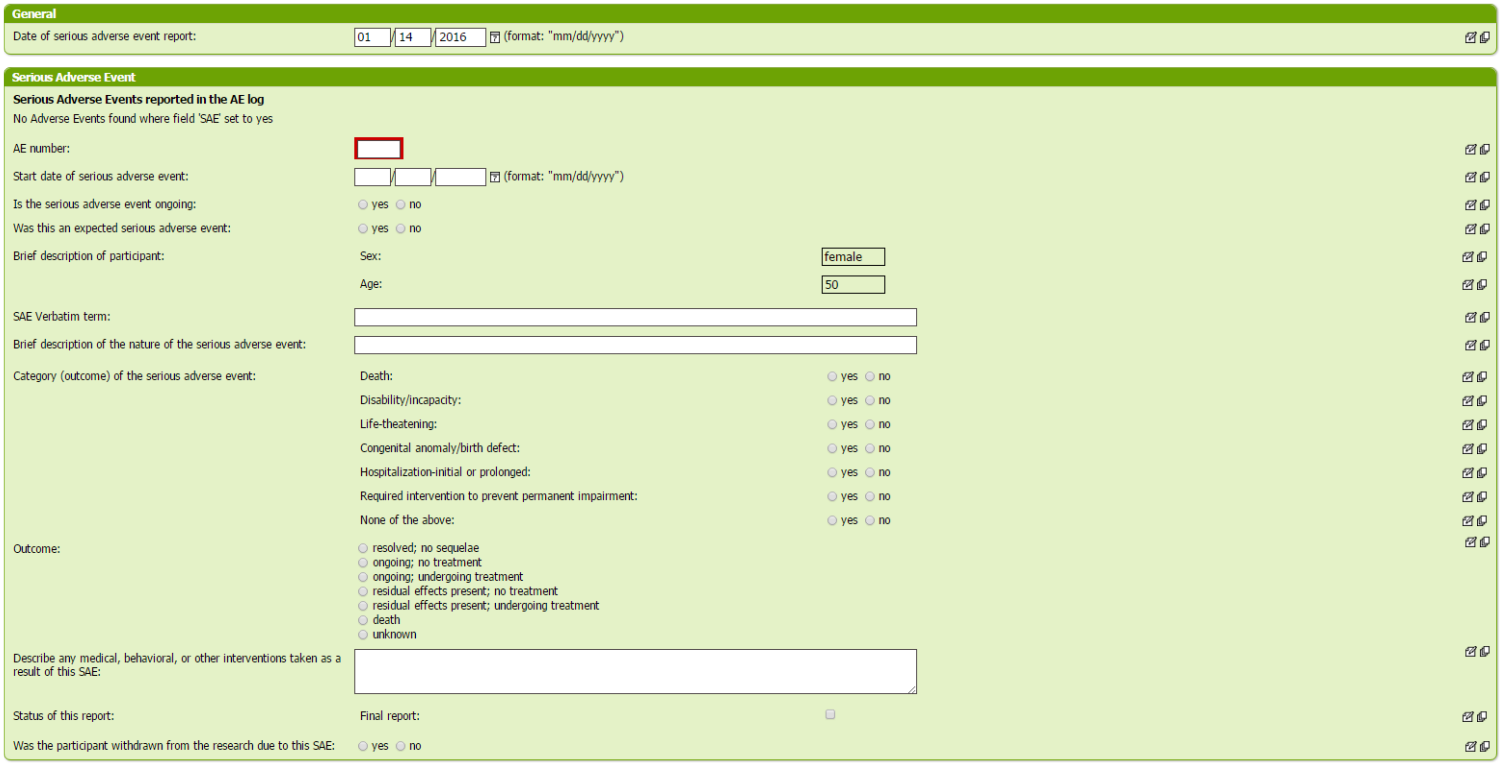
# SAEs

- SAEs must also be documented using the SAE CRF which will trigger an email to to Central Coordination, Chief Investigator, Medical Monitor and Site Principal Investigator/Coordinator



**General**

Date of serious adverse event report: 01 / 14 / 2016 (format: "mm/dd/yyyy")

**Serious Adverse Event**

**Serious Adverse Events reported in the AE log**

No Adverse Events found where field 'SAE' set to yes

AE number:

Start date of serious adverse event: / / (format: "mm/dd/yyyy")

Is the serious adverse event ongoing: yes no

Was this an expected serious adverse event: yes no

Brief description of participant: Sex: female

Age: 50

SAE Verbatim term:

Brief description of the nature of the serious adverse event:

Category (outcome) of the serious adverse event:

Death: yes no

Disability/incapacity: yes no

Life-theatening: yes no

Congenital anomaly/birth defect: yes no

Hospitalization-initial or prolonged: yes no

Required intervention to prevent permanent impairment: yes no

None of the above: yes no

Outcome:

- resolved; no sequelae
- ongoing; no treatment
- ongoing; undergoing treatment
- residual effects present; no treatment
- residual effects present; undergoing treatment
- death
- unknown

Describe any medical, behavioral, or other interventions taken as a result of this SAE:

Status of this report: Final report:

Was the participant withdrawn from the research due to this SAE: yes no

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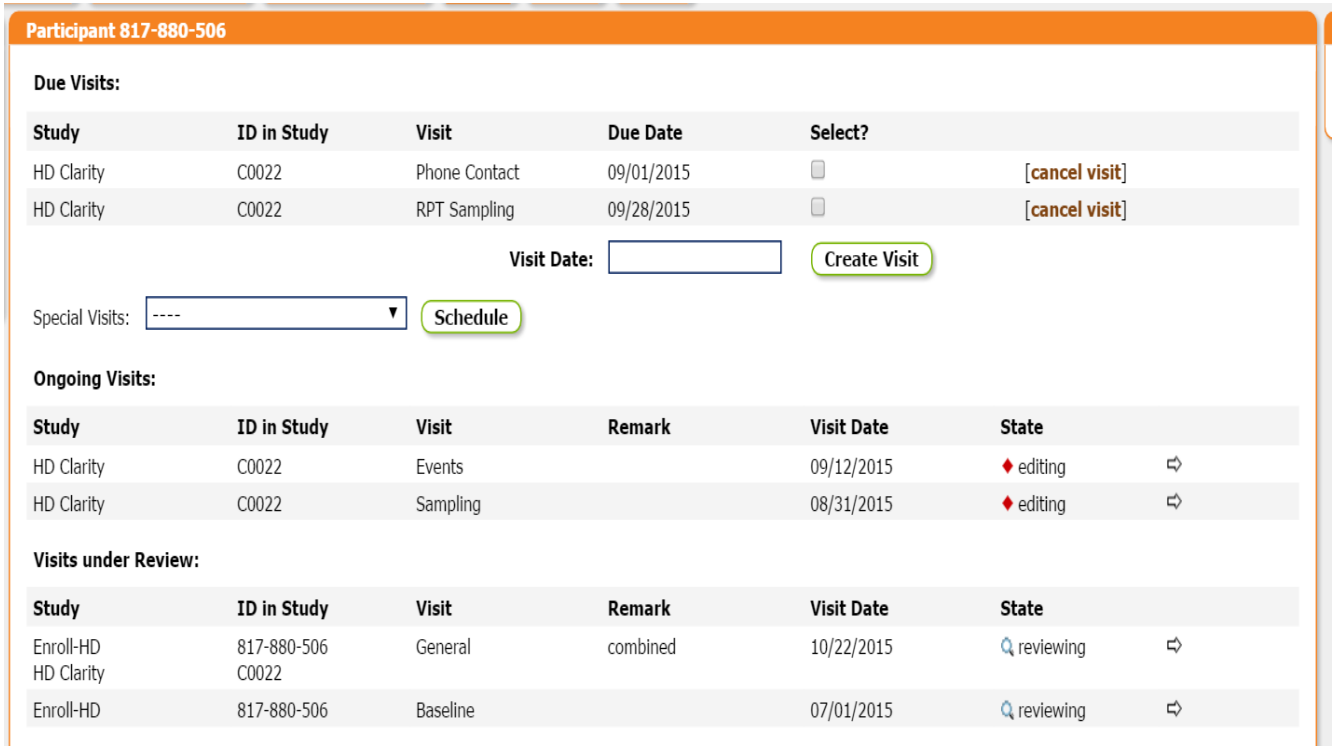
# Repeat Sampling Visit

## 4-8 weeks after initial LP

- Up to 20 participants per cohort will be invited to return for a Repeat Sampling Visit 4-8 weeks after their Sampling Visit



**Participant 817-880-506**

**Due Visits:**

| Study | ID in Study | Visit | Due Date | Select? | |
|---|---|---|---|---|---|
| HD Clarity | C0022 | Phone Contact | 09/01/2015 | ☐ | [cancel visit] |
| HD Clarity | C0022 | RPT Sampling | 09/28/2015 | ☐ | [cancel visit] |

Visit Date: Create Visit

Special Visits: ---- Schedule

**Ongoing Visits:**

| Study | ID in Study | Visit | Remark | Visit Date | State | |
|---|---|---|---|---|---|---|
| HD Clarity | C0022 | Events | | 09/12/2015 | ♦ editing | ⇨ |
| HD Clarity | C0022 | Sampling | | 08/31/2015 | ♦ editing | ⇨ |

**Visits under Review:**

| Study | ID in Study | Visit | Remark | Visit Date | State | |
|---|---|---|---|---|---|---|
| Enroll-HD<br>HD Clarity | 817-880-506<br>C0022 | General | combined | 10/22/2015 | reviewing | ⇨ |
| Enroll-HD | 817-880-506 | Baseline | | 07/01/2015 | reviewing | ⇨ |

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# Data Monitoring

- Monitoring is conducted jointly by HDClarity CC and the Enroll-HD monitoring team
- Remote data review (RDR) of Enroll-HD forms will be conducted by the Enroll-HD monitors per the Enroll-HD monitoring plan (MP)
- RDR of HDClarity-specific forms will be done by HDClarity CC
- Onsite intermin monitoring visits will be carried out by Enroll-HD monitors per the Enroll-HD MP (i.e. frequency of visits will not change), with additional time allowed for review of HDClarity SMF

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# Payment

- A participant visit should be closed and remote monitored for the payment event(s) to be triggered
- The EDC will generate monthly accounting reports for each site, documenting number and type of visits that have been remotely monitored
- Payment event(s) are triggered via the Greenphire system as for Enroll-HD with additional exceptional payments as required for unscheduled visits (e.g. rescreening)

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# Other Documents

- Standard neurological examination & brief general examination check-list
- Standard Operating Procedures; Lumbar CSF Collection, Onsite CSF Processing, Onsite Serum & Plasma Processing, Sample Storage & Shipment, AE reporting and lab manual
- Two training videos; The first will demonstrate CSF samples collection at UCL, and a second will demonstrate CSF and blood processing at the site.
- EDC User Guide (specific to HDClarity)
- Premature End of Study form

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# Biosampling Kits

## Ordering kits and shipment of samples

- HDClarity kits will be requested via the EDC
- Samples will be stored at the site at -80 $^{o}$C and must be shipped within 2 months of sampling
- Samples to be shipped include CSF, Cells from CSF, Serum, and Plasma.
- The Bulk Shipment Request form on the EDC is completed immediately after the shipment leaves the site.

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# BioKits

Each participant kit contains four sub-kits

## Lumbar Puncture sub-kit

- 4 x 50ml collection tubes
- 2 x atraumatic 22G spinal needles
- Sterile Wound pack
- 2 x 10ml syringes
- Tegaderm dressing
- Gauze
- 2 x 25G needles 2x 21G needles 2 x 18G needles


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# BioKits

## Blood Collection sub-kit

- 4 x Lithium Heparin tubes
- 1 x Serum tube
- 1 x Push-button Vacutainer blood collection set
- 2 x Vacutainers (spare)
- 2 x waterproof plasters
- 3 x Alcohol prep pads
- Tourniquet
- Sterile gauze


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# BioKits

## Blood Processing sub-kit

- 75 x cryovials labeled ‘Plasma’ + kit ID and barcode
- 3 x cryovials labeled Serum + kit ID and barcode
- 1x cryovial rack labeled Plasma + kit ID and 1D barcode
- 50 ml plasma tube
- 5 x polypropylene pipette tips
- 2 x polypropylene Pasteur pipettes with pipette teat


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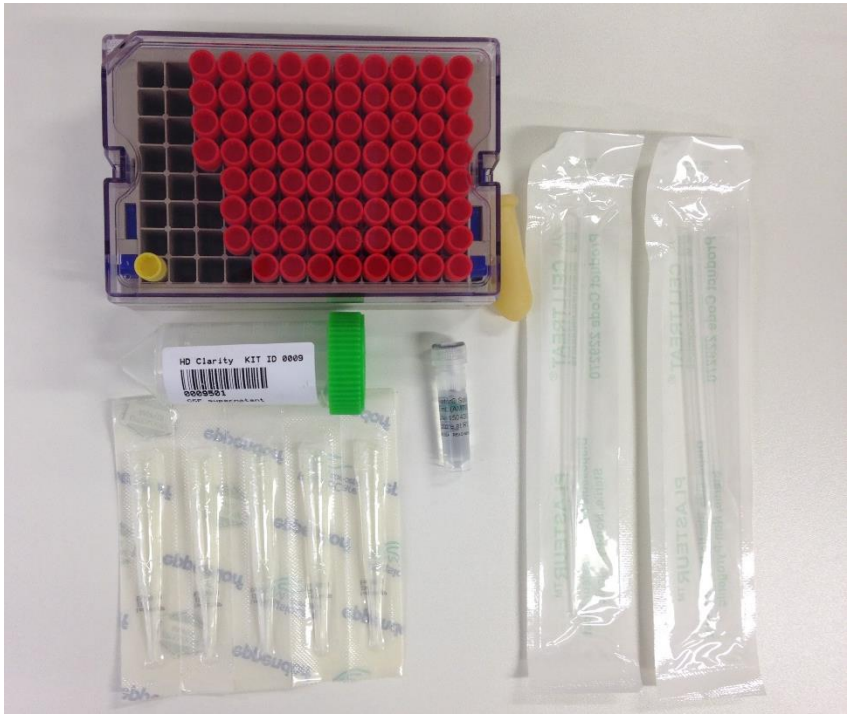
# BioKits

## CSF Processing sub-kit

- 75 x cryovials labeled ‘CSF’ + kit ID and barcode
- 1 x cryovial labeled Cells ‘CSF’ + kit ID and barcode
- Cryovial rack labeled ‘CSF’ + kit ID  and barcode
- 1.5ml RNA*later* solution
- 30ml CSF supernatant tube labelled with kit ID and barcode
- 5 x polypropylene pipette tips
- 2 x polypropylene Pasteur pipettes with pipette teat

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