EURO **HUNTINGTON'S DISEASE** NETWORK

Protocol of Euro-HD-Registry

Version 1.1

1. Background and study objectives

A. Specific aims and objectives

Registry is the core study of the European Huntington's disease Network (Euro-HD). The aim of the Registry study is to build up a database of Huntington's disease (HD) patients and HD mutation carriers who are willing to participate in clinical trials throughout Europe.

The aim is to find out more about HD mutation carriers and the phenotypical characteristics of the disease using standardised assessment tools (e.g. UHDRS). This will allow:

- The identification and recruitment of participants for clinical trials in a far more expedite way.
- The identification and recruitment of participants with defined phenotypical characterisation for biomarker trials.

Since serial assessments are planned the Registry study will contribute to the understanding of the natural course of HD.

In addition Registry will provide information about the impact of HD on health care costs (economic impact), quality of life and caregivers.

B. Background and Significance

Huntington's disease is an autosomal dominant neurodegenerative disorder that results from an unstable expansion of the trinucleotide repeat CAG in the HD gene IT-15. HD has a prevalence of 5-10 per 100,000 in the general population. The clinical features of HD usually emerge in adulthood (mean age of 37 years) with a movement disorder (typically chorea), cognitive dysfunction and psychiatric symptoms. The course of HD is relentless, leading to functional disability and death over a period of 10-30 years. To date, there is no treatment which has been shown to alter the progression of the disease.

With genetic testing (following genetic counselling) it is possible to predict that a person will develop HD a long time before clinical symptoms and signs develop.

As HD is a rare disease, extensive cooperation is essential to be able to include the number of participants required for conclusion well powered studies.

With the Registry study recruitment of patients and mutations carriers in order to learn more about the progress of the disease and patients who are eligible for clinical trials will be facilated.

2. Participant selection criteria

Participants who are willing to participate in regular evaluations conducted by the investigators and have a diagnosis of Huntington's diseas, are HD mutation carriers or persons at risk.

A. Inclusion criteria

1. Diagnosed Huntington's disease (CAG repeat expansion >35 on larger allele), presymptomatic patients or persons at risk for Huntington's disease (one parent must have been diagnosed with Huntington's disease).
2. Written informed consent by patient or legal representative (e.g. for minors and patients with HD who are unable to give informed consent).

B. Exclusion criteria

1. Participants who are unable to understand the study protocol and give informed consent, and have no legal representative.
2. Participants with choreatic movement disorder other than HD.

3. Observation schedules

There are no fixed observation schedules, but investigators should evaluate participants at least once a year. The study calls for annual assessments. If the participant has to be seen more often for medical reasons, assessments can be conducted more frequently.

4. Methods of participant evaluation

Participant evaluation is carried out clinically using the Unified Huntington Disease Rating Scale (UHDRS 1999) and questionnaires. The UHDRS is divided into four parts: a motor score, a behavioural scale for evaluating psychiatric symptoms, a cognitive score and a score of total functional capacity (TFC). For further evaluation there are supplementary questionnaires: Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (Ham-D), Global Clinical Impression (GCI), SF-36 health survey, Caregiver questionnaire and Clinical Service Receipt Inventory (CSRI). The Ham-D and the GCI are filled out by the investigator. For the Ham-D the investigators are requested to give their impressions about the severity of depressive symptoms. For the GCI, the investigators should rate their overall impression concerning the severity of disease.
The BDI, the SF-36 Health survey and the CSRI must be filled out by the patient assisted by a caregiver. With the BDI patient should answer questions about the severity of depressive symptoms. The SF-36 health survey examines how ill and debilitate a patient feels. The CSRI evaluates what health service resources the patient needs.
The Caregiver questionnaire needs to be filled out by a caregiver. The questionnaire evaluates the caregiver's role in order to measure the patient's disability.
On each visit the following assessments are obligatory: the UHDRS motor score, TFC score, medical history and the concomitant medication. Whilst the other questionnaires are optional, the investigator should aim to obtain as much of the information as possible.
(see appendix 2. hardcopy of electronic case report form).

5. Registration of the participant / data security

Participant data is entered after creating a unique pseudonym for each individual, based on unchanging information (date of birth, birth name, place of birth and mother's maiden name). The pseudonym is a nine figure number created by a secure one-way algorithm, e.g.: **Christine Mustermann**, Date of Birth: **13 April 1964**, Place of Birth: **Berlin**, Birth name: **Maier**; Mother´s maiden name: **Schmidt.**
These data give the pseudonym: **344-259-192**

The identifying data are never stored electronically. The investigator must store the original data and the pseudonym in the source documents (patient file) and in the investigator file.

6. Participant consent

Before consenting to participate in this study, all patients will be provided with sufficient information in the form of a Patient Information Sheet (see appendix A) prepared in the local language and approved by the responsible IRB.
The participant or the legal representative must give written and dated informed consent. (See appendix 1 Patient information and informed consent)

7. Participant risk

Since Registry is an observational study, participants do not undergo specific risks by participating. Therefore no medical insurance is required.

8. End of study/withdrawals

There is no fixed end of study. After patient death the 'Death Report form' (study form) must be completed by the investigator. If the participant does not want to continue, the participant can every time leave the study.
The 'End of Study form' must be completed by the investigator, detailing the reasons for withdrawal´(eg. marking "patient request").
If the participant is withdrawn by the investigator the 'End of Study form' must also be completed.
On the participant's request the coordination centre can anonymise all information obtained so far.

9. Monitoring trial progress

For data control there will be continuous evaluation of data for plausibility. There will be additional on-site monitoring to check source documents and data entry. During the site visits, the study monitor should review original patient records and compare them with the electronic CRF.
The investigator should allocate adequate time for these visits and should ensure that the monitor is given direct access to the patient source documents (e.g. hospital files).
Between on-site monitoring visits the monitor should regularly check the electronic data for completeness and plausibility of the data.
Missing data will be marked. If the basic data comprising medical history, CAG repeats, concomitant medication and at least one UHDRS are missing, the participant must be deleted from the database by the coordination centre and the data can not be used for statistical evaluation.

10. Forms and data handling

A complete CRF is attached in the Appendix. The data are entered electronically via internet-based technology. The web-portal is separated into several parts with different access rules. An investigator is only allowed to see their own patients' data.
Central Coordination is allowed to view all data of all centres for plausibility checks, quality control and monitoring.
By order of the Board of Directors, Central Coordination is permitted to statistically evaluate the whole data set. The whole database is saved in the portal.

11. Modification of the protocol

Any modification of the protocol which may have an impact on the conduct of the study, including study objectives, study design, participant population, study procedures or significant administrative aspects, will require a formal amendment to the protocol.
The Euro-HD Network, the investigator and the IRB will agree upon such amendments prior to implementation.

12. Administrative responsibilities

The Investigator is responsible for the adequate medical care of the participant during the study. The Investigator must follow GCP Guidelines and is responsible for the safety and the medical care of the participant.

Sponsor of the Registry study is the Euro-HD network.

The Euro-HD network and Central Coordination are responsible for monitoring and data control. Central Coordination is responsible for the monitoring performed by the language coordinators and auditing.
The Board of Directors is responsible for the scientific background and decisions about who has access to the database.

13. Appendix

A. Patient/Companions Information and Patient Informed Consent

Participant Information

Name of study: Registration for participation in the European Huntington's Disease Network ('REGISTRY').

Dear Participant

You are either suffering from Huntington's disease (HD) or belong to a family at risk for HD. The clinician treating you has asked you whether you are willing to participate in a study which aims to recruit people with HD across Europe. This will enable you to enrol in studies relating to the natural progression of HD and interventional studies aimed at delaying this progression. Therefore, it is important that you are interviewed and examined by experienced clinicians in order to record how much, or how little, you are affected or impaired by HD. The results of the examinations will be entered onto an electronic database which is available to the network. Your name, address or any other information which could allow personal identification will not be recorded in the database. Your data will be 'pseudonymised', i.e. recorded under a 'code name', which is a series of 9 digits. Therefore, nobody but the clinicians treating you know your identity (for a detailed explanation see page 3: 'Information regarding data processing, data protection and data safety').

The European Huntington's Disease Network (Euro-HD Network) is a network supported by an American charity (´High-Q´) and is in the process to build up an electronic database of patients with HD and their relatives. The aim of the network is to carry out clinical research into HD, to improve knowledge of the natural course of the disease, and facilitate the recruitment of suitable candidates for future pharmacological studies. Your consent relates solely to the electronic registration of your data; any further research requires the provision of subsequent details and your explicit written consent.

At each clinic examination, your physical and mental ability will be assessed by clinicians; these examinations are no different from those you are already familiar with from previous consultations. In addition, you will be asked to complete questionnaires assessing your wellbeing. Relatives or individuals involved in the care of HD patients will be asked to complete questionnaires relating to both the possible economic consequences of HD and their estimation of the level of care needed for HD patients.

There are no specific risks arising from your participation in the study given that it is an observational study. If you are willing to participate it is important that you (and a person accompanying you) attend a follow-up examination at least once a year.

Data entry and the use of this database will be carried out using the internet. The database is held at Central Coordination, Ulm University, Ulm, Germany. To ensure that nobody other than the clinician treating you can trace back your identity, any details which could identify you are <u>not</u> saved on the database.

To enable the clinician treating you to separate your data from your identity, a pseudonym will be given during study registration under which your data will be recorded ('pseudonymised') (see section 'EURO-HD Network: information regarding data processing, data protection and data safety' below for issues relating to data security, for example, the reassurance that only

authorised persons have access to the data and that there can be no mishandling of data during communication via the internet).
In addition to the use of the website for data storage, there are chat rooms that enable patients and relatives to contact other people affected by HD (anonymously if you wish).

Evaluation and publication of study results will be carried out anonymously and in the form of statistics. As a result, none of your personal data will ever be made public.

VOLUNTEERING
Your participation in this research project is voluntary. You are free to withdraw from the study at any time and without giving reason. This potential withdrawal does not affect your continuing medical treatment.

INSURANCE
Because `REGISTRY` is neither a pharmacological study nor a study to test new diagnostic procedures, there are no additional health risks and the participants therefore do not need insurance.

CLINICIAN CONTACT
Should you have any questions at anytime during the course of the research project you can reach *(local investigator*) on telephone number (*telephone number of local investigator)* at any time during working hours. For emergencies out of hours, ring (*local emergency number*).

CONFIDENTIALITY/DATA PROTECTION
All clinicians and related medical staff involved in looking after you during this clinical study abide by medical confidentiality and are obliged to comply with data protection.

Research results relating to this study are intended for use in an anonymous form in scientific publications.

As far as is necessary for ensuring correct data entry, authorized individuals (e.g. the sponsor, the university) are permitted to review your medical records.

If individuals authorized to view records are not bound by medical confidentiality as mentioned above, personal data that come to their attention during checks are confidential under the Data Protection Act.

Place; date Name of the consenting clinician

EURO-HD-Network:
Information regarding data processing, data protection and data security.

An essential safety aspect of the project is the processing of my data in an exclusively pseudonymised manner. What does that mean and how is it carried out?

During your first visit, your clinicians will enter certain data about you into the computer. From these personal data a unique code name ('pseudonym') is calculated, consisting of a series of 9 digits. The following personal data are used: first name, birth name (surname), date of birth, place of birth and mother's maiden name.

Example:
Maria, Miller nee Mustermann, born 10.11.1964 in Ulm, mother's maiden name Schmidt.
This information generates the code ('pseudonym'): 425-491-326.

Importantly, the pseudonym is created on the basis of a hash-algorithm. This is where a unique value is assigned during a complicated procedure. The mathematical algorithm ensures that this can only take place in one direction, i.e. the resulting value (the 'pseudonym') cannot be traced back to your person by anybody (not even the system programmer).

The personal data transmitted during the registration process are held only for the calculation of the pseudonym for a short time in the memory of a large computer ('server'). Viewing personal data during this time is impossible. These data are then erased so that no identification details remain. Following this, all data entry and use of data is exclusively carried out under the assigned pseudonym.

Which data do I have to reveal apart from the registration data in the course of the Registry study and subsequent studies?

During the course of the Registry study, some health and/or medical data will be recorded as well as your personal details (see Participant Information Sheet for further details). If you are participating in any subsequent studies, your clinician will give you detailed information about the study and the data required for it accordingly. Each subsequent study requires separate patient consent.

Who can see and use my data?

1.You
if you wish, you can gain access rights with which you can call up your data. If you don't have access to your stored data, you can view the data stored about you through the clinician treating you.

2. The clinician treating you
As your contact with the EURO-HD Network, the clinician treating you locally is the only person apart from you who can link your pseudonym and personal details. After the initial registration, however, data entry and viewing by your treating clinicians is carried out via the pseudonym assigned to your person.
Your clinician can use your personal information to contact you as and when future studies arise for which you are a suitable candidate.

3. EURO-HD staff
EURO-HD staff analyse your stored data in order to: 1) contact the treating clinician and 2) to co-ordinate projects with the data. EURO-HD investigators can only view and use pseudonymised data entered on the EURO-HD network.

For the purpose of data control, investigators of the EURO-HD-Network ('monitors' and 'auditors') are allowed to check with clinicians treating you that the data entered onto the network matches with the data found in your medical records. Naturally, monitors/auditors are bound by confidentiality during this, and no personal data will be recorded outside the documentation belonging to clinicians treating you.

4. Scientists
This only includes scientists who are involved in Huntington's disease research. The scientists have to apply to the Board of Directors (a group of eight experienced clinicians and scientists) for authorisation to use the data. These scientists can only view and use the pseudonymised data. They are also required to ensure that any further use of the data and any publications are carried out in an anonymised form (i.e. not even using the pseudonym).

5. System Administrators
In order to safeguard the EURO-HD-Network central database, a small number of authorised system administrators can view pseudonymised data.

6. Other groups and Individuals
No-one other than the groups and individuals mentioned above can gain access to or receive the data stored about you.

What reassurance do I have that unauthorised individuals cannot gain access to my data via the Internet?*

During data entry, the data processing is encrypted. The server where the database is stored is located behind a 'firewall'. This sophisticated security system ensures that only authorised computers and individuals can access the database. Furthermore, the central database holds no record of your personal identity as it is pseudonymised).

How long is my data stored for?

All data will remain stored for the foreseeable future. A complete deletion of data is impossible because the data is likely to have become part of a scientific study. The reason for this is because the researchers responsible have to be able to prove that the relevant study was carried out in accordance with regulations, even years after the research was completed. Alternatively, complete anonymisation can be carried out in the following cases:

- If you withdraw your consent for participation in the entire project and request that your data is anonymised.
- If you withdraw from participation in a particular study and request complete anonymisation of past data relating to that study.
- If you did not participate in any study for at least 10 years (excluding Registry).
- 10 years after your death

Following anonymisation, data can can never ever be linked to your person.

Location, date Name of the informing clinician

Consent Form

Name of the study: Registration for participation in the European Huntington´s Disease Network (`REGISTRY`)

Content, procedures, risks and aims of the research project named above as well as the right to view the data recorded has been explained to me in sufficient detail by Dr… …..

I have had the opportunity to ask questions and have received answers to them.

I have had sufficient time to decide whether to participate in the project.

I have received a copy of the patient information and consent form.

Information and consent form regarding Data Protection

During scientific studies, personal data and medical findings about you are recorded. The storage, analysis and communication of data relating to the study are carried out according to legal requirements and entail the following consent before participating in the study:

1. I agree that data /medical data taken during the course of this study can be recorded in questionnaires and on electronic data carriers and processed without providing personal identity.

2. I also agree that an authorised person who is bound by confidentiality (e.g. from the sponsor, or the University) can view the personal data recorded as far as it is necessary for data control of the project. For this aim, I release the clinician from the requirement for medical confidentiality.

Name of the Participant

……

Place, date……

Signature of the participant

Participant Information (Companions)

Name of study: Registration for participation in the European Huntington's Disease Network ('REGISTRY').

Dear Participant,

You are a companion of a person affected by HD (either a patient or a mutation carrier) who has asked you whether you are willing to assist in a research project recruiting people with HD across Europe.
Since the symptoms of HD are noticed differently by companions and the affected persons themselves, and the disease of a close one also has an impact on companions, we would like to ask you to complete two questionnaires at each visit. These questionnaires ask about (1) the impact of the illness on you as a companion and (2) the economic consequences of suffering from HD including an estimation of the level of care needed by HD patients (e.g. travel costs to the clinic, loss of salary, etc.).The completed questionnaires will be entered onto an electronic database which is available to the network.
Your name, address or any other information which could allow personal identification will not be recorded in the database. The European Huntington's Disease Network (Euro-HD Network) is a network supported by an American charity ('High-Q') and is in the process to build up an electronic database of people affected by HD. The aim of the network is to carry out clinical research into HD, to improve knowledge of the natural course of the disease, and facilitate the recruitment of suitable candidates for future studies including Drug trials. The consent relates solely to an electronic registration of data.
If you are willing to participate it is important that you as a companion attend follow-up examinations at least once a year.

Data entry and the use of this database will be carried out using the internet. The database is held at Central Coordination, Ulm University, Ulm, Germany. To ensure that nobody other than the clinician treating HD patients/mutation carriers can trace back their identity, any details which could identify them, are <u>not</u> saved on the database.

To enable the clinician treating HD patients/mutation carriers to separate their data from their identity, a pseudonym will be given during study registration under which their data will be recorded ('pseudonymised') (see section 'EURO-HD Network: information regarding data processing, data protection and data safety below for issues relating to data security).
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- If you withdraw your consent for participation in the entire project and request that your data is anonymised.
- If you withdraw from participation in a particular study and request complete anonymisation of past data relating to that study.
- If you did not participate in any study for at least 10 years (excluding Registry).
- 10 years after your death

Following anonymisation, data can can never ever be linked to your person.

Location, date Name of the informing clinician

B. Hardcopy of the CRF

[test-3] Medical History

General

Date data obtained: . . (in format "dd.mm.yyyy")

Demographics

Date of birth: . . (in format "dd.mm.yyyy")

Gender: ○ female ○ male

Ethnicity:
- ○ white
- ○ black
- ○ Hispanic
- ○ Asia of Pacific Islander
- ○ American Indian or Alaskan Native
- ○ other
- ○ unknown

Other ethnicity:

Years of education: years

Handness: ○ right ○ left ○ mixed

Weight: kg

Height: cm

BMI:

Occupation during most of career:
- ○ professional and technical worker
- ○ manager, administrator, clerical worker, sales worker
- ○ craftsman and foreman
- ○ service worker, farmer, farm manager, domestic worker
- ○ labourer, farm labourer, and farm foreman
- ○ not in labour force

Marital status: ○ single ○ married ○ divorced

Past Medical History

Birth trauma or serious neonatal illness: ○ yes ○ no

Childhood (birth to 12 years) serious illness: ○ yes ○ no

Adolescent (13-17 years) serious illness: ○ yes ○ no

Adult (18+ years) serious illness: ○ yes ○ no

Major surgery requiring general anaesthesia:	○ yes ○ no
History of alcohol abuse:	○ never abused alcohol ○ ex-alcohol abuser ○ currently abuses alcohol
History of drug abuse:	○ never abused drugs ○ ex-drug abuser ○ currently abuses drugs
History of smoking tobacco:	○ never smoked ○ ex-smoker ○ currently smokes
Is the subject naturally or surgically sterile?	○ yes ○ no

Comorbid Conditions

Dermatological:	○ yes ○ no
	Condition:
Ophthalmological:	○ yes ○ no
	Condition:
Pulmonary:	○ yes ○ no
	Condition:
Cardiovascular (including HTN):	○ yes ○ no
	Condition:
Gastrointestinal:	○ yes ○ no
	Condition:
Hepatic:	○ yes ○ no
	Condition:
Urological:	○ yes ○ no
	Condition:
Gynaecological:	○ yes ○ no
	Condition:
Musculoskeletal:	○ yes ○ no
	Condition:
Neurologic (other than HD):	○ yes ○ no

	Condition:
Endocrine/Metabolic:	○ yes ○ no
	Condition:
Other:	○ yes ○ no
	Condition:
Does the subject have any allergies?	○ yes ○ no
	Please list allergies:
Does subject wear dentures?	○ yes ○ no
	If yes is answered for 31a, do the dentures fit properly per the subject? ○ yes ○ no

Psychiatric History

Depression:	○ yes ○ no
OCD:	○ yes ○ no
Psychosis:	○ yes ○ no
Suicidal ideation:	○ yes ○ no
Suicide attempts:	○ yes ○ no

Family History

Mother affected:	○ yes ○ no
	Age at onest of symptoms in mother: years
Father affected:	○ yes ○ no
	Age at onest of symptoms in father: years

HD History

Symptoms first noted by subject:	month: year:
Symptoms first noted by family:	month: year:

Rater's estimate of symptom onset: month: year:

HD diagnosed: month: year:

What are these symptoms?:

	motor	cognitive	psychiatric	oculomotor	other	mixed
Initial major symptom noted by subject	○	○	○	○	○	○
Initial major symptom noted by family	○	○	○	○	○	○
Rater's judgement of initial major symptom	○	○	○	○	○	○

Comments: ○ yes ○ no

Enter comment:

[test-4] CAG Analysis

General

Date data obtained: . . (in format "dd.mm.yyyy")

CAG Analysis

Specimen type: blood brain (postmortem)

CAG analysis results (number of CAG repeats):

Were the exact repeat lengths given in the laboratory report? yes no

Allele 1 CAG repeat length (smaller allele):

Allele 2 CAG repeat length (larger allele):

Is the exact CAG repeat length (larger allele) known to:

The physician: yes no unknown

The subject: yes no unknown

The family: yes no unknown

Analyzing laboratory :

Comments: yes no

Enter comment:

[test-6] Concomitant Medication Log

Medication Log

Drug name	Indication1	Indication2	Dose/Unit	Frequency	Start date	Stop date
					. .	. .

[test-14] Study End and Death

End of Study

Date of last evaluation: . . (in format "dd.mm.yyyy")

Specify primary reason for patient´s premature discontinuation from study:
- Death
- Event or intercurrent illness of a nature requiring withdrawal
- Request of primary care physician, site investigator
- Subject´s request
- Failure of subject to return to follow-up visit and failure to be located by investigator
- Institutionalized (will not be followed further)
- Other, please specify:

Other reason:

Death Report Form

Date of death: . . (in format "dd.mm.yyyy")

Place of death:
- home
- hospital
- nursing home
- hospice care
- unknown

Cause of death:
- pneumonia
- other infection
- cancer
- stroke
- trauma
- suicide
- other, please specify:

Other cause:

Was an autopsy performed? no yes unknown

Result of autopsy:

Information obtained primarily from:
- spouse/family
- friend
- physician/nurse
- subject´s chart
- obituary in newspaper
- death certificate
- other

Other:

Comments? no yes

Comment:

[test-0] Huntington's Disease Rating Scale '99 - Motor Assessment

General

Date data obtained: . . (in format "dd.mm.yyyy")

Motor score:

Motor Assessment

Ocular pursuit:

Horizontal	Vertical	
○	○	0 = complete (normal)
○	○	1 = jerky movement
○	○	2 = interrupted pursuits/full range
○	○	3 = incomplete range
○	○	4 = cannot pursue

Saccade initiation:

Horizontal	Vertical	
○	○	0 = normal
○	○	1 = increased latency only
○	○	2 = suppressible blinks or head movements to initiate
○	○	3 = unsupressable head movements
○	○	4 = cannot initiate saccades

Saccade velocity:

Horizontal	Vertical	
○	○	0 = normal
○	○	1 = mild slowing
○	○	2 = moderate slowing
○	○	3 = severely slow, full range
○	○	4 = incomplete range

Dysarthria:
- ○ 0 = normal
- ○ 1 = unclear, no need to repeat
- ○ 2 = must repeat to be understood
- ○ 3 = mostly incomprehensibe
- ○ 4 = anarthria

Tongue protrusion:
- ○ 0 = can hold tongue fully protruded for 10 sec
- ○ 1 = cannot keep fully protruded for 10 sec
- ○ 2 = cannot keep fully protruded for 5 sec
- ○ 3 = cannot fully protrude tongue
- ○ 4 = cannot protrude tongue beyond lips

Finger taps:

Right	Left	
○	○	0 = normal (≥15/5 sec.)
○	○	1 = mild slowing, reduction in amplitude (11-14/5 sec.)
○	○	2 = moderatly impaired (7-10/5 sec.)
○	○	3 = severly impaired (3-6/5 sec.)
○	○	4 = can barly perform task (0-2/5 sec.)

Pronate/supinate-hands:

Right	Left	
○	○	0 = normal
○	○	1 = mild slowing and/or irregular
○	○	2 = moderate slowing and irregular
○	○	3 = severe slowing and irregular
○	○	4 = cannot perform

Luria:
- ○ 0 = ≥4 in 10 sec, no cue
- ○ 1 = <4 in 10 sec, no cue
- ○ 2 = ≥4 in 10 sec with cues
- ○ 3 = <4 in 10 sec with cues
- ○ 4 = cannot perform

Rigidity-arms:

Right	Left	
○	○	0 = absent
○	○	1 = slight or present only with activation
○	○	2 = mild to moderate
○	○	3 = severe, full range of motion
○	○	4 = severe with limited range

Bradykinesia-body:
- ○ 0 = normal
- ○ 1 = minimally slow (?normal)
- ○ 2 = mildly but clearly slow
- ○ 3 = moderately slow, some hesitation
- ○ 4 = markedly slow, long delays in initiation

Maximal dystonia:

Trunk	RUE	LUE	RLE	LLE	
○	○	○	○	○	0 = absent
○	○	○	○	○	1 = slight/intermittent
○	○	○	○	○	2 = mild/common or moderate/intermittent
○	○	○	○	○	3 = moderate/common
○	○	○	○	○	4 = marked/prolonged

Maximal chorea:

Face	BOL	Trunk	RUE	LUE	RLE	LLE	
○	○	○	○	○	○	○	0 = absent
○	○	○	○	○	○	○	1 = slight/intermittent
○	○	○	○	○	○	○	2 = mild/common or moderate/intermittent
○	○	○	○	○	○	○	3 = moderate/common
○	○	○	○	○	○	○	4 = marked/prolonged

Gait:
- ○ 0 = normal gait, norrow base
- ○ 1 = wide base and/or slow
- ○ 2 = wide base and walks with difficulty
- ○ 3 = walks only with assistance
- ○ 4 = cannot attempt

Tandem walking:
- ○ 0 = normal for 10 steps
- ○ 1 = 1 to 3 deviations from straight line
- ○ 2 = >3 deviations
- ○ 3 = cannot complete

	○ 4 = cannot attempt
Retropulsion pull test:	○ 0 = normal ○ 1 = recovers spontaneously ○ 2 = would fall if not caught ○ 3 = tends to fall spontaneously ○ 4 = cannot stand

[test-2] Huntington's Disease Rating Scale '99 - Behavioral Assessment

General

Date data obtained: . . (in format "dd.mm.yyyy")

Behavioral score:

Behavioral Assessment

Depressed mood:

Frequency:
- 0 = never or almost never
- 1 = seldom, less than once a week
- 2 = sometimes, at least once a week
- 3 = frequently, several times a week
- 4 = very frequently, most of the time

Severity:
- 0 = no mood disturbance
- 1 = questionable or equivocal
- 2 = mild, responds to redirection and reassurance
- 3 = moderately depressed, expresses distress
- 4 = severe, significant suffering and loss of functioning

Low self-esteem/guilt:

Frequency:
- 0 = never or almost never
- 1 = seldom, less than once a week
- 2 = sometimes, at least once a week
- 3 = frequently, several times a week
- 4 = very frequently, most of the time

Severity:
- 0 = no evidence
- 1 = questionable or equivocal
- 2 = mild, definitely present
- 3 = moderate, some distress
- 4 = severe

Anxiety:

Frequency:
- 0 = never or almost never
- 1 = seldom, less than once a week
- 2 = sometimes, at least once a week
- 3 = frequently, several times a week
- 4 = very frequently, most of the time

Severity:
- 0 = no evidence
- 1 = questionable or equivocal
- 2 = mild, responds to reassurance
- 3 = moderate, impacts on everyday life
- 4 = severe, causing a profound restriction of activities

Suicidal thoughts:

Frequency:
- 0 = not thinking about suicide or self harm
- 1 = seldom thinking about suicide - less than once a month
- 2 = sometimes thinking abou suicide - at least once a month
- 3 = frequently thinking about suicide - at least once a week

- 4 = often thinks about suicide - sometimes for days and weeks on end

Severity:

- 0 = no suicidal thoughts
- 1 = no thoughts at current time, but person talks about suicide as a potential option
- 2 = fleeting thoughts about it
- 3 = seriously considered suicide but has no plan
- 4 = has a plan and is actively preparing

Disruptive or aggressive behavior:

Frequency:

- 0 = never or almost never
- 1 = seldom, less than once a month
- 2 = sometimes, at least once a month
- 3 = frequently, at least once a week
- 4 = very frequently, everyday

Severity:

- 0 = behavior well-controlled
- 1 = verbal threats or intimidating behavior
- 2 = mild physically or verbally threatening behavior
- 3 = clear physical threat (moderately aggressive), bumping, shoving, verbal outburst
- 4 = clear physical threat (severe aggression) striking/hitting, or definite intention to cause injury

Irritable behavior:

Frequency:

- 0 = never or almost never
- 1 = seldom, less than once a week
- 2 = sometimes, at least once a week
- 3 = frequently, several times a week
- 4 = very frequently, most of the time

Severity:

- 0 = behavior well-controlled
- 1 = questionable or equivocal
- 2 = definite but mild
- 3 = moderate, others change their behavior to avoid irritating subject
- 4 = severe irritability

Perseverative/obsessional thinking:

Frequency:

- 0 = never or almost never
- 1 = seldom, less than once a week
- 2 = sometimes, at least once a week
- 3 = frequently, several times a week
- 4 = very frequently, most of the time

Severity:

- 0 = thinking is always flexible
- 1 = questionable or equivocal
- 2 = gets stuck on certain ideas but can be easily redirected
- 3 = moderate - gets stuck on certain ideas, difficult to redirect
- 4 = severe - gets stuck on certain ideas, and does not respond to redirection

Compulsive behaviour:

Frequency:
- ○ 0 = never or almost never
- ○ 1 = seldom, less than once a week
- ○ 2 = sometimes, at least once a week
- ○ 3 = frequently, several times a week
- ○ 4 = very frequently, most of the time

Severity:
- ○ 0 = behaviour always well-controlled
- ○ 1 = equivocal - has a mild impulse not sufficient to act on
- ○ 2 = mild - has impulse, acts on impulse, but can stop
- ○ 3 = moderate - has impulse, acts on it and sometimes cannot stop
- ○ 4 = severe - has impulse, acts on it and cannot stop

Delusions:

Frequency:
- ○ 0 = no evidence
- ○ 1 = seldom, less than once a month
- ○ 2 = sometimes, at least once a month
- ○ 3 = frequently, at least once a week
- ○ 4 = very frequently, sometimes for days on end

Severity:
- ○ 0 = no evidence
- ○ 1 = has delusional idea(s), not sure it is true
- ○ 2 = convinced of idea(s) but allows that the idea is not true
- ○ 3 = utterly convinced of the idea(s)
- ○ 4 = utterly convinced of the idea(s), behavior is determined by the delusion(s)

Hallucinations:

Frequency:
- ○ 0 = no evidence of hallucinations
- ○ 1 = seldom, less than once a month
- ○ 2 = sometimes, at least once a month
- ○ 3 = frequently, at least once a week
- ○ 4 = often, sometimes for days on end

Severity:
- ○ 0 = no evidence
- ○ 1 = has hallucinations, but doubts they are real
- ○ 2 = convinced of the reality of the hallucinations, but allows that it is possible that they are not real
- ○ 3 = utterly convinced of the hallucinations being real, but not acting on them
- ○ 4 = severe - has hallucinations that are vivid, subject is utterly convinced they are real and the hallucinations severely disrupt behavior

Apathy:

Frequency:
- ○ 0 = never
- ○ 1 = seldom apathetic, less than once a week
- ○ 2 = sometimes, at least once a week
- ○ 3 = frequently, several times a week
- ○ 4 = very frequently, most of the time

,

	Severity:	○ 0 = no evidence ○ 1 = equivocal ○ 2 = mild apathy - subject not initiating conversation or activity but is responsive ○ 3 = moderate apathy - sometimes responds to efforts to get involved in conversation/activities ○ 4 = severe apathy - generally unresponsive to attempts to involve subject in activities or conversation	
Other questions:			
	Does the examiner believe the subject is confused?	○ yes ○ no	
	Does the examiner believe the subject is demented?	○ yes ○ no	
	Does the examiner believe the subject is depressed?	○ yes ○ no	
	Does the subject require pharmacotherapy for depression?	○ yes ○ no	
	Does the subject require pharmacotherapy for irritability?	○ yes ○ no	
Information sources:			
	Was the behavioral assessment information obtained from:	○ 1 = subject only ○ 2 = subject and family/companion	

[test-1] Huntington's Disease Rating Scale '99 - Cognitive Assessment

General

Date data obtained: . . (in format "dd.mm.yyyy")

Cognitive score:

Cognitive Assessment

Verbal fluency test:

Symbol digit modality test:

Stroop Interference Test:

Colour naming:

Word reading:

Interference:

[test-5] Huntington's Disease Rating Scale '99 - Functional Assessment and Independance Scale

General

Date data obtained: . . (in format "dd.mm.yyyy")

Functional Assessment Score:

Independence scale in %:

Functional Assessment

	yes	no
Could subject engage in gainful employement in his/her accustomed work	○	○
Could subject engage in any kind of gainful employment?	○	○
Could subject engage in any kind of volunteer or non gainful work?	○	○
Could subject manage his/her finances (monthly) without any help?	○	○
Could subject shop for groceries without help?	○	○
Could subject handle money as a purchaser in a simple cash (store) transaction?	○	○
Could subject supervise children without help?	○	○
Could subject operate an automobile safely and independently?	○	○
Could subject do his/her own housework without help?	○	○
Could subject do his/her own laundry (wash/dry) without help?	○	○
Could subject prepare his/her own meals without help?	○	○
Could subject use the telephone without help?	○	○
Could subject take his/her own medications without help?	○	○
Could subject feed himself/herself without help?	○	○
Could subject dress himself/herself without help?	○	○
Could subject bathe himself/herself without help?	○	○
Could subject use public transportation to get places without help?	○	○
Could subject walk to places in his/her neighborhood without help?	○	○
Could subject walk without falling?	○	○
Could subject walk without help?	○	○
Could subject comb hair without help?	○	○
Could subject transfer between chairs without help?	○	○
Could subject get in and out of bed without help?	○	○
Could subject use toilet/commode without help?	○	○
Could subject`s care still be provided at home?	○	○

Information sources:

Was the functional assessment information obtained from:
- ○ 1 = Subject only
- ○ 2 = Subject and family/companion

Independence Scale

Subject's independence in %:
- ○ 100 = no special care needed
- ○ 95
- ○ 90 = no physical care needed if difficult tasks are avoided
- ○ 85
- ○ 80 = pre-disease level of employment changes or ends;cannot perform household chores to pre-disease level, may need help with finances
- ○ 75

- ○ 70 = self-care maintained for bathing, limited household duties (cooking and use of knives), driving terminates; unable to manage finances
- ○ 65
- ○ 60 = needs minor assistance in dressing, toileting, bathing; food must be cut for subject
- ○ 55
- ○ 50 = 24-hour supervision appropriate; assistance required for bathing, eating, toileting
- ○ 45
- ○ 40 = chronic care facility needed; limited self feeding, liquified diet
- ○ 35
- ○ 30 = subject provides minimal assistance in own feeding, bathing, toileting
- ○ 25
- ○ 20 = no speech, must be fed
- ○ 15
- ○ 10 = tube fed, total bed care
- ○ 5

[test-15] Huntington's Disease Rating Scale '99 - Functional Capacity

General

Date data obtained: . . (in format "dd.mm.yyyy")

Functional score:

Functional Capacity

Occupation:
- 0 = unable
- 1 = marginal work only
- 2 = reduced capacity for usual job
- 3 = normal

Finances: 0 = unable | 1 = major assistance | 2 = slight assistance | 3 = normal

Domestic chores: 0 = unable | 1 = impaired | 2 = normal

ADL:
- 0 = total care
- 1 = gross tasks only
- 2 = minimal impairment
- 3 = normal

Care level: 0 = full time skilled nursing | 1 = home or chronic care | 2 = home

Information Sources:

Was the information obtained from:
- 1 = subject only
- 2 = subject and family/companion

[test-7] Huntington's Disease Rating Scale '99 - Clinical Summary

General

Date data obtained: . . (in format "dd.mm.yyyy")

Clinical Summary

What was the purpose of this visit?
- 1 = subject in an at risk study
- 2 = subject in a manifest HD study
- 3 = presymptomatic genetic testing
- 4 = determine if person is symptomatic
- 5 = known manifest HD
- 6 = other

Other pupose of visit:

Since your last assessment of the subject, in your opinion, has the subject:
- 1 = improved
- 2 = worsened
- 3 = stayed about the same
- 4 = not applicable (never seen before)

Since your last assessment does the subject feel:
- 1 = improved
- 2 = worsened
- 3 = stayed about the same
- 4 = not applicable (never seen before)

Do you believe that this subject has manifest HD?
- yes
- no

Comments:

[test-9] Becks Depression Scale

General

Date data obtained: . . (in format "dd.mm.yyyy")

Becks Score:

Beck - Depression Inventory (BDI)

A:
- I do not feel sad
- I feel sad
- I am sad all the time and cannot snap out of it
- I am sad or unhappy that I cannot stand it

B:
- I am not particularly discouraged about the future
- I feel discouraged about the future
- I feel I have nothing to look forward to
- I feel that the future is hopeless and that things cannot improve

C:
- I do not feel like a failure
- I feel I have failed more than the average person
- As I look back on my life, all I can see is a lot of failure
- I feel I am a complete failure as a person; I do not feel sad

D:
- I get as much satisfaction out of things as I used to
- I do not enjoy things the way I used to
- I do not get real satisfaction out of anything anymore
- I am dissatisfied or bored with everything

E:
- I do not feel particularly guilty
- I feel guilty a good part of the time
- I feel quite guilty most of the time
- I feel guilty all of the time

F:
- I do not feel I am being punished
- I feel I may be punished
- I expect to be punished
- I feel I am being punished

G:
- I do not feel disappointed in myself
- I am disappointed in myself
- I am disgusted with myself
- I hate myself

H:
- I do not feel I am worse than anybody else
- I am critical of myself for my weaknesses or mistakes
- I blame myself all the time for my faults
- I blame myself for everything bad that happens

I:
- I do not have any thoughts of killing myself
- I have thoughts of killing myself, but I would not carry them out
- I would like to kill myself
- I would kill myself if I had the chance

J:
- I do not cry any more than usual
- I cry more than I used to
- I cry all the time now
- I used to be able to cry, but now I cannot cry even though I want to

K:
- I am no more irritated by things than I ever am
- I am slightly more irritated now than usual
- I am quite annoyed or irritated a good deal of the time
- I feel irritated all the time now

L:
- I have not lost interest in other people
- I am less interested in other people than I used to be
- I have lost most of my interest in other people

	○ I have lost all of my interest in other people
M:	○ I make decisions about as well as I ever could ○ I put off making decisions more than I used to ○ I have greater difficulty in making decisions than before ○ I can not make decisions at all anymore
N:	○ I do not feel that I look any worse than I used to ○ I am worried that I am looking old or unattractive ○ I feel that there are permanent changes in my appearance that make me look unattractive ○ I believe that I look ugly
O:	○ I can work about as well as before ○ it takes an extra effort to get started at doing something ○ I have to push myself very hard to do anything ○ I cannot do any work at all
P:	○ I can sleep as well as usual ○ I do not sleep as well as I used to ○ I wake up 1-2 hours earlier than usual and find it hard to get back to sleep ○ I wake up several hours earlier than I used to and cannot get back to sleep
Q:	○ I do not get tired more than usual ○ I get tired more easily than I used to ○ I get tired from doing almost anything ○ I am too tired to do anything
R:	○ my appetite is no worse than usual ○ my appetite is not as good as it used to be ○ my appetite is much worse now ○ I have no appetite at all anymore
S:	○ I have not lost much weight, if any, lately ○ I have lost more than five pounds ○ I have lost more than ten pounds ○ I have lost more than fifteen pounds
T:	○ I am no more worried about my health than usual ○ I am worried about physical problems such as aches or pains, or upset stomach or constipation ○ I am very worried about physical problems and it is hard to think of much else ○ I am so worried about my physical problems that I cannot think about anything else
U:	○ I have not noticed any recent change in may interest in sex ○ I am less interested in sex than I used to be ○ I am much less interested in sex now ○ I have lost interest in sex completely

[test-8] Hamilton Rating Scale for Depression

General

Date data obtained: . . (in format "dd.mm.yyyy")

Hamilton Rating Scale

Depressed mood:
- absent
- these feeling states indicated only on questioning
- these feeling states spontaneously reported verbally
- communicates feeling states non-verbally - i.e., through facial expression, posture, voice, and tendency to weep
- patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

Feelings of guilt:
- absent
- self reproach, feels he has let people down
- ideas of guilt or rumination over past errors or sinful deeds
- present illness is a punishment. Delusions of guilt
- hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

Suicide:
- absent
- feels life is not worth living
- wishes he were dead or any thoughts of possible death to self
- suicidal ideas or gesture
- attempts at suicide (any serious attempt rates 4)

Insomnia early:
- no difficulty falling asleep
- complains of occasional difficulty falling asleep - i.e., more than 1/2 hour
- complains of nightly difficulty falling asleep

Insomnia middle:
- no difficulty
- patient complains of being restless and disturbed during the night
- waking during the night - any getting out of bed rates 2 (except for purposes of voiding)

Insomnia late:
- no difficulty
- waking in early hours of the morning but goes back to sleep
- unable to fall asleep again if he gets out of bed

Work and activities:
- no difficulty
- thoughts and feelings of incapacity, fatigue or weakness related to activities; work or hobbies
- loss of interest in activity; hobbies or work - either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities)
- decrease in actual time spent in activities or decrease in productivity
- stopped working because of present illness

Retardation: Psychomotor:
- normal speech and thought
- slight retardation at interview
- obvious retardation at interview
- interview difficult
- complete stupor

Agitation:
- none
- fidgetiness
- playing with hands, hair, etc.
- moving about, can't sit still
- hand wringing, nail biting, hair-pulling, biting of lips

Anxiety:	○ no difficulty ○ subjective tension and irritability ○ worrying about minor matters ○ apprehensive attitude apparent in face or speech ○ fears expressed without questioning
Anxiety somatic:	○ absent ○ mild ○ moderate ○ severe ○ incapacitating
Somatic symptoms:	○ none ○ loss of appetite but eating without encouragement from others. Food intake about normal ○ difficulty eating without urging from others. Marked reduction of appetite and food intake
Somatic symptoms general:	○ none ○ heaviness in limbs, back or head. Backaches, headache, muscle aches. Loss of energy and fatigability ○ any clear-cut symptom rates 2
Genital symptoms:	○ absent ○ mild ○ severe
Hypochondriasis:	○ not present ○ self-absorption (bodily) ○ preoccupation with health ○ frequent complaints, requests for help, etc. ○ hypochondriacal delusions
Loss of weight:	○ no weight loss ○ probably weight loss associated with present illness ○ definite (according to patient) weight loss ○ not assessed
Insight:	○ acknowledges being depressed and ill ○ acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc. ○ denies being ill at all
Diurnal variation:	
Time of variation:	○ no variation ○ worse in A.M. ○ worse in P.M.
Severity of variation:	○ none ○ mild ○ severe
Depersonalization and derealization:	○ absent ○ mild ○ moderate ○ severe ○ incapacitating
Paranoid symptoms:	○ none ○ suspicious ○ ideas of reference ○ delusions of reference and persecution
Obsessional and compulsive symptoms:	○ absent ○ mild ○ severe

[test-11] Care Giver Questionaire

General

Date data obtained: . . (in format "dd.mm.yyyy")

Caregiver Questionnaire

	not at all	only a little	quite a lot	a lot	completely
My relative needs my help to perform many tasks	○	○	○	○	○
My relative is dependent on me	○	○	○	○	○
I have to watch my relative constantly	○	○	○	○	○
I have to help my relative constantly	○	○	○	○	○
I don't have a minute's break from my caregiving duties	○	○	○	○	○
I feel that I am missing out on life	○	○	○	○	○
I wish I could escape from this situation	○	○	○	○	○
My social life has suffered	○	○	○	○	○
I feel emotionally drained due to caring for my relative	○	○	○	○	○
I expected that things would be different at this point in my life	○	○	○	○	○
I am not getting enough sleep	○	○	○	○	○
My health has suffered	○	○	○	○	○
Caregiving has made me physically ill	○	○	○	○	○
I am physically tired	○	○	○	○	○
I don't get on with other family members as well as I used to	○	○	○	○	○
My caregiving efforts aren't appreciated by others in my family	○	○	○	○	○
I've had problems with my marriage	○	○	○	○	○
I don't do as good a job at work as I used to	○	○	○	○	○
I feel resentful of other relatives who could, but do not, help	○	○	○	○	○
I feel embarrassed by my relative's behaviour	○	○	○	○	○
I am ashamed of my relative	○	○	○	○	○
I resent my relative	○	○	○	○	○
I am uncomfortable when I have friends over	○	○	○	○	○
I feel angry about my interactions with my relative	○	○	○	○	○

[test-12] SF-36 Heath Survey

General

Date data obtained: . . (in format "dd.mm.yyyy")

SF-36 Health Survey

In general, would you say your health is: ○ excellent ○ very good ○ good ○ fair ○ poor

Compared to one year ago, how would you rate your health in general now:
- ○ much better
- ○ somewhat better
- ○ about the same
- ○ somewhat worse
- ○ much worse

During the past 4 weeks to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups:
- ○ not at all
- ○ slightly
- ○ moderately
- ○ quite a bit
- ○ extremely

During the past 4 weeks how much bodily pain have you had: ○ none ○ very mild ○ mild ○ moderate ○ severe ○ very severe

During the past 4 weeks how much did pain interfere with your normal work:
- ○ not at all
- ○ a little bit
- ○ moderately
- ○ quite a bit
- ○ extremely

During the past 4 weeks how much of the time has your physical health or emotional problems interfered with your social activities like visiting friends, relatives, etc:
- ○ all of the time
- ○ most of the time
- ○ sometimes
- ○ a little of the time
- ○ none of the time

Does your health now limit you in these activities:

	yes, a lot	yes, a little	not at all
Vigorous activities, such as running, lifting heavy object, participating in strenuous sports	○	○	○
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	○	○	○
Lifting and carrying groceries	○	○	○
Climbing several flights of stairs	○	○	○
Climbing one flight of stairs	○	○	○
Bending, kneeling or stooping	○	○	○
Walking more than a mile	○	○	○
Walking several blocks	○	○	○
Walking one block	○	○	○
Bathing or dressing yourself	○	○	○

During the past 4 weeks have you had any of the following problems with your work or other regular daily activities as a result of your physical health:

Cut down on the amount of time you spent on work or other activities:	○ yes	○ no
Accomplished less than you would like:	○ yes	○ no
Were limited in the kind of work or other activities:	○ yes	○ no
Had difficulty performing the work or other activities:	○ yes	○ no

During the past 4 weeks have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems:

Cut down on the amount of time you spent on work or other activities:	○ yes	○ no
Accomplished less than you would like:	○ yes	○ no
Didn't do work or other activities as carefully as usual:	○ yes	○ no

How did you feel during the past 4 weeks:

	all of the time	most of the time	a good bit of the time	some of the time	a little of the time	none of the time
Did you feel full of life?	○	○	○	○	○	○
Have you been a very nervous person?	○	○	○	○	○	○
Have you felt so down in the dumps that nothing could cheer you up?	○	○	○	○	○	○
Have you felt calm and peaceful?	○	○	○	○	○	○
Did you have a lot of energy?	○	○	○	○	○	○
Have you felt downhearted and low?	○	○	○	○	○	○
Did you feel worn out?	○	○	○	○	○	○
Have you been a happy person?	○	○	○	○	○	○
Did you feel tired?	○	○	○	○	○	○

How true or false is each of the following statements for you?:

	definitely true	mostly true	don't know	mostly false	definitely false
I seem to get sick a little more than other people	○	○	○	○	○
I am as healthy as anybody I know	○	○	○	○	○
I expect my health to get worse	○	○	○	○	○
My health is excellent	○	○	○	○	○

[test-13] Client Service Receipt Inventory

General

Date data obtained: . . (in format "dd.mm.yyyy")

Hospital and Residential Services

Neurology outpatient visit: yes no

Number of attendances received in the last 6 months:

Other hospital outpatient visit: yes no

Number of attendances received in the last 6 months:

Day hospital (neurology dept): yes no

Number of attendances received in the last 6 months:

Nursing or residential home: yes no

Number of residential days received in the last 6 months:

Neurology inpatient ward: yes no

Number of inpatient days received in the last 6 months:

Cardiology inpatient ward: yes no

Number of inpatient days received in the last 6 months:

Urology inpatient ward: yes no

Number of inpatient days received in the last 6 months:

Intensive care unit: yes no

Number of inpatient days received in the last 6 months:

Other inpatient ward: yes no

(specify):

Number of inpatient days received in the last 6 months:

Primary and Community Care Services

General practitioner (GP): yes no

Usual location: care practice home

Total number of contacts:

Average duration: minutes

Neurologist: yes no

	Usual location: ○ care practice ○ home
	Total number of contacts:
	Average duration: minutes
Other doctor (e.g. cardiologist):	○ yes ○ no
	Usual location: ○ Care practice ○ Home
	Total number of contacts:
	Average duration: minutes
Physiotherapist:	○ yes ○ no
	Usual location: ○ care practice ○ home
	Total number of contacts:
	Average duration: minutes
Social worker:	○ yes ○ no
	Usual location: ○ care practice ○ home
	Total number of contacts:
	Average duration: minutes
Nurse:	○ yes ○ no
	Usual location: ○ care practice ○ home
	Total number of contacts:
	Average duration: minutes
Speech therapist:	○ yes ○ no
	Usual location: ○ care practice ○ home
	Total number of contacts:
	Average duration: minutes
Home help:	○ yes ○ no
	Usual location: ○ care practice ○ home
	Total number of contacts:
	Average duration: minutes
Other service:	○ yes ○ no
	(specify):
	Usual location: ○ care practice ○ home
	Total number of contacts:
	Average duration: minutes

Investigations / Diagnostic Tests	
Magnetic Resonance Image (MRI):	○ yes ○ no
	Total number of investigations in the last 6 months:
	Description (if necessary):
CT/CAT scan:	○ yes ○ no

	Total number of investigations in the last 6 months:	
	Description (if necessary):	
Electroencephalogram (EEG):	○ yes ○ no	
	Total number of investigations in the last 6 months:	
	Description (if necessary):	
Blood test:	○ yes ○ no	
	Total number of investigations in the last 6 months:	
	Description (if necessary):	
Other investigations/tests:	○ yes ○ no	
	Total number of investigatons in the last 6 months:	
	Description (if necessary):	

Aids or Devices		
Wheelchair:	○ yes ○ no	
Crutches/sticks:	○ yes ○ no	
Stroller/zimmer frame:	○ yes ○ no	
Other:	○ yes ○ no	
	(please specify):	

Adaptations to the Home		
Stairlift:	○ yes ○ no	
Shower/bath relocation:	○ yes ○ no	
Toilet relocation:	○ yes ○ no	
Redesign kitchen:	○ yes ○ no	
Medicalised bed:	○ yes ○ no	
Concrete ramp:	○ yes ○ no	
Other (e.g. move home):	○ yes ○ no	
	(please specify):	

Informal Care		
Personal care (e.g. bathing, dressing):	○ yes ○ no	
	Relationship of carer to the patient:	
	Average number of hours care per week:	
Help inside the home (e.g. cooking, cleaning):	○ yes ○ no	
	Relationship of care to the patient:	

	Average number of hours care per week:
Help outside the home (e.g. shopping):	○ yes ○ no
	Relationship of carer to the patient:
	Average number of hours care per week:
Other:	○ yes ○ no
	(specify):
	Relationship of carer to the patient:
	Average number of hours care per week:
What is the principal reason for extra care?	○ HD ○ other illness
Have any friends and relatives stayed off work to assist with the patients`s care because of HD?	○ yes ○ no
	For how long have they stayed off work? total weeks
	Please estimate average income lost per week:
	Currency: ○ UK-£ ○ € ○ SFR
	Amount:

Journeys	
Private transport (car):	○ yes ○ no
	Number of journeys:
	Number of travellers:
	Average distance of each return trip: (km)
	Average cost of each journey per person:
Public transport (train, bus, etc.):	○ yes ○ no
	Number of journeys:
	Number of travellers:
	Average distance of each return trip: (km)
	Average cost of each journey per person:
Hospital transport (taxi/car):	○ yes ○ no
	Number of journeys:
	Number of travellers:
	Average distance of each return trip: (km)

C. Examination Guidelines for the Unified Huntington's DiseaseRating Scale '99

Produced and revised by The Huntington Study Group, June 11, 1999

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I. Motor Assessment

 # 1 Ocular Pursuit - Ocular pursuit should be assessed over a range of approximately 20° with a target passing slowly at ≤ 10° per second, which corresponds to about 2 seconds for moving an object from one shoulder to the other.

#2-3 Saccade initiation and velocity - Saccade initiation should be tested over a 20° range, as for ocular pursuits. Saccade movement should be elicited by a sound (snapping fingers) or movement (wiggle fingers, but not by a verbal command to look to the right or left. Saccade velocity should be tested at a larger range of approximately 30° so as to be able to detect incomplete range.

#4-5 Dysarthria and tongue protrusion -

#6 Finger Taps - Subject taps thumb with index finger in rapid succession with widest amplitude possible, each hand separately.

#7 Pronate/Supinate hands - This task requires the subject to alternately hit the palmar and dorsal surface of one hand against the palm of the opposite hand. Use the palm of the opposite hand as a target instead of some other surface such as the subject's leg or the table surface. The subject should do this task as quickly as possible over a five-second interval. The task is graded according to the degree of slowing and irregularity.

#8 Luria- Fist-hand-palm sequencing - Say "Can you do this?" Examiner puts hand into fist on flat surface (or in lap) and sequences as follows: fist, side, flat (DO NOT REPEAT THIS OUT LOUD). Watch to make sure that subject can mimic each step. Continue to practice Luria 3-step for 1 - 2 minutes. When subject is able to join you then say "Very good, now keep going, I am going to stop." Rest hand and start timing subject's sequences. A sequence is considered correct only if it is unaided by examiner model and in the correct order. Count completed sequences and score. If subject was unable to complete any sequences over a 10-second period, then continue as follows. Say "Now lets try it again. Put your hands like this. FIST; SIDE; FLAT". Watch to make sure the subject can mimic each step. Using the verbal labels, begin the sequences again and ask the subject to "Do as I do, Fist, Side, Flat" (repeat this as you continue). Continue to perform Luria 3-step. When subject is able to join you say "Very good, now keep going, I am going to stop". Rest hand and start timing subject's sequences. A sequence is considered correct if it is unaided by examiner model and in the correct order. Count completed sequences and score as above.

#9 Rigidity - Arms - Rigidity is judged on passive movement of the arms with the subject relaxed in the sitting position.

#10 Body bradykinesia - Observe the subject during spontaneous motion such as walking, sitting down, arising from a chair, and executing the tasks required during the examination. This rating reflects the examiner's overall impression of bradykinesia.

#11-12 Maximal dystonia (Tendency toward a posture, posturing along an axis) and maximal Chorea (movement) - Observe the subject during the examination; i.e., no particular maneuvers are required to illicit these features. Maximal dystonia and chorea are typically observed during demanding motor tasks such as tandem gait. Both dystonia and chorea are rated by specific regions. "BOL" refers to buccal-oral-lingual. Facial dystonia includes blepharospasm, jaw opening and closing. When rating dystonia (question #11) BOL and facial dystonia should be included in your assessment of the truncal region.

#13 Gait - Observe the subject walking approximately ten yards as briskly as they can, then turning and returning to the starting point.

#14 Tandem gait - The subject is requested to walk ten steps in a straight line with the foot placed (accurately but not quickly) such that the heel touches the toe of the other foot. Deviations from a straight line are counted.

#15 Retropulsion Pull Test - The subject's response to a sudden posterior displacement produced by a pull on the shoulder while the subject is standing with eyes open and feet slightly apart is assessed. The shoulder pull test must be done with a quick firm tug after warning the subject. The test may be repeated if the subject did not have sufficient warning or did not understand the test. The subject should be relaxed with feet apart and should not be learning forward. If the examiner feels pressure against his/her hands when placed on the subject's shoulders, the examiner should instruct the subject to stand up straight and not lean forward. The examiner should instruct the subject to take a step backward to avoid falling.

Examiners must catch subjects who begin to fall. To prevent either individual from falling to the floor, examiners should brace themselves with one foot back and/or stand between subject and a wall. However, adequate room is needed to test retropulsion and recovery. Subjects should be told that taking one step backwards is acceptable.

#16 Weight - Self-explanatory.

#17 Diagnostic confidence level

0 = Normal (no abnormalities)

1 = non-specific motor abnormalities (less than 50 % confidence)

2 = motor abnormalities that *may* be signs of HD (50 - 89 % confidence)

3 = motor abnormalities that are *likely* signs of HD (90 - 98 % confidence)

4 = motor abnormalities that are *unequivocal* signs of HD ≥ 99 % confidence)

The diagnosis of HD is based on the unequivocal presence of an otherwise unexplained extrapyramidal movement disorder (e.g., chorea, dystonia, bradykinesia, rigidity) in a subject at risk for HD.

The grade assigned by the investigator represents a level of confidence for the diagnosis of the HD in a particular subject. Grade 1 represents a < 50 % confidence level for a particular subject who may have non-specific motor abnormalities. Such abnormalities could include mild clumsiness or slowness that might be normal findings, or non-specific changes such as distal weakness. Grade 2 implies a 50 - 89 % confidence level and should be assigned to a subject with suggestive but not definitive clinical findings. Such findings could include mild slowness and clumsiness with minimal non-specific oculomotor abnormalities. Grad 3 should be assigned to a subject that has motor abnormalities that are likely signs of HD (90 - 98 % confidence). Such abnormalities could include intermittent movements that could represent chorea in the setting of mild motor slowing. Grade 4 should be assigned only to a subject with an unequivocal extrapyramidal movement disorder in the presence of a confirming family history or known positive gene test, when the examiner is ≥ 99 % confident (only errs 1 in a 100 such instances) that the subject has HD. Such findings would include the presence of definite chorea or dystonia, usually with accompanying motor slowing.

II. Cognitive Assessment

Overview

The cognitive assessment portion of the Unified Huntington's Disease Rating Scale (UHDRS) consists of the Verbal Fluency, Symbol Digit Modalities and Stroop Interference Tests. The cognitive section of the UHDRS is estimated to take approximately 7 - 10 minutes, including instructions. The following instructions are provided to ensure inter-site consistency. Specific questions or problems administering this battery should be directed to Peter G. Como, Ph.D., University of Rochester Medical Center, phone 001-716-275-5130, fax 001-716-473-4678.

General Testing Guidelines

1. The neuropsychological test battery should be given only to subjects aged 17 years or older whose primary language is English.
2. Memorize the instructions for each cognitive test. You should always focus the majority of your attention on the subject to ensure proper comprehension of test instructions.
3. Be sure the subject is ready for each test and fully comprehends the test instructions. If you have any doubt regarding this, re-instruct the subject.
4. During test administration, be attentive to potential sources of distraction (e.g., extraneous noises, interruptions by others, etc.). If, in your judgement, the subject is distracted by an extraneous source, re-administer the test and note this on the data form in the comments section.
5. Many subjects will ask for feedback regarding their performance. It is important that you refrain from giving direct feedback. Reassurance that they are performing well is recommended. Non-specific statements such as "there are no right or wrong answers to these tests" and/or "it is not possible to fail these tests" will often alleviate test-taking anxiety. Negative feedback can potentially influence performance on subsequent tasks. If a subject becomes upset over an inability to complete a task, give a short break and continue on. Never force subjects into completing a task if they absolutely refuse.
6. Be certain to adhere carefully to the time limits for each test (see below).
7. Make sure you have all the necessary testing materials and equipment arranged in advance (e.g., stopwatch, pencils, test materials, etc.).
8. Ensure that subjects who require glasses or other aides have them available for testing. If the subject forgets to bring these aides, note this in the comments section of the data form.
9. Caregivers or significant others should not be present in the testing room during the neuropsychological examination, as they may be a source of anxiety or distraction.

Equipment and Supplies

You will need a stopwatch, pencils, and a quiet, comfortable room with table and chairs. Master copies of all test answer forms as well as the Stroop Interference Test Plates will be provided by the Huntington Study Group Coordination Center. You will need to make a sufficient number of quality copies to allow for administration to each subject.

Case Report Form Coding

Please try to administer all tests. Use the "R" code for tests the subject refused to complete. Use the "C" code if the subject was unable to do all or part of the battery. Use the "U" code for tests that were not administered, data unavailable; form must have explanation in the comments section.

Order of Tests

The order of test administration must be the same for each subject at each evaluation session. The order in which tests are to be administered is as follows:

1. Verbal Fluency Test (F-A-S)
2. Symbol Digit Modalities Test (SDMT)
3. Stroop Test

Instructions for Administration and Scoring

1. Verbal Fluency Test (#19)

For this task subjects are asked to produce as many words as possible beginning with a specified letter in one minute. Say, *"I am going to say a letter of the alphabet. Then I want you to tell me as many words as you can think of that start with that letter. For instance, if I say "R", you might give me "rice", "radio", or "relish"... I do not want you to use words that start with capital letters, like "Richard" or "Rochester". Also do not use the same word again with a different ending - if you say "run", don't also say "running". "Any questions?"* Answer any questions the subject has about this task, then say, *"The first letter is "F" go ahead".* Begin timing. Write down all words given by the subject in the order they are produced, even if they are incorrect or repetitions. Should the subject give up before the end of the minute, encourage him/her to generate more words. If the subject is silent for more than 15 seconds, say, *"Remember, tell me words that begin with the letter ....."*.(and tell them the letter). Stop the subject at the end of one minute.

Continue by saying, *"Now, I would like you to tell me all the words you can think of that start with the letter "A"*. Start timing, reminding the subject if necessary that proper nouns and different verb forms are not allowed. Administer the final letter ("S") the same way.

Scoring: The score is the sum of admissible responses across all three trials. Proper nouns and words not beginning with the specified letter are not counted as correct. If the subject repeats a word, count only the first occurrence of the word as correct. If multiple forms of a word are given, count only one form toward the subject's total. Vernacular or commonly accepted slang words (e.g., "munchies") are permissible. Homonyms (e.g., "see", "sea") are counted separately only if the subject indicates the alternate usage. Words that are also proper nouns (e.g., "ford") are acceptable only if the subject indicated the proper usage of the word. Since rapid transcription of words is often sloppy, scoring at a later time may be problematic due to difficulty reading

one's handwriting; thus this task is best scored immediately, while the subject's responses are fresh in mind.

2. Symbol Digit Modalities Test (#20)

Hand the test form to the subject and say, *"Please look at the boxes at the top of the page. Each box in the upper row has a symbol in it, and each box below it has a number. Now look at the next line of boxes* (point to the first line of boxes without numbers). *Notice that the boxes on the top have symbols, but boxes beneath are empty. You are to fill in each empty box with the number that goes with each symbol according to the way they are paired at the top of the page. For example, if you look at the first symbol* (point to the first symbol in the row beneath the key), *and then look up at the key, you see that his symbol is paired with number "one"* (show the pairing). *So you would write a "one" in this box* (write a "1" in the first box). *This next symbol* (point to the next symbol *is paired with five. So you would put a "five" in this box* (write "5" in the second box). *Now what number goes in this box* (point to third box) ?" Subject should say "two". If not, explain the subject's error.

When the subject appears to comprehend the task, say, *"Good, now for practice, fill in the boxes up to this double line, and then stop"* Correct immediately any errors made during the practice period, explaining the subject's error. Repeat the instructions and review the correct coding of the practice boxes as necessary until the subject understands the task. Occasionally a subject will not be able to comprehend the nature of the task. Do not administer the remainder of the test if a subject can not complete any of the practice items.

Continue with the test by saying, *"When I say "go" write in the numbers just like you have been doing as fast as you can until I say "stop". Work as quickly as you can. Moving from one line to the next without skipping any boxes. If you make a mistake, don't erase it. Just write the correct answer over the mistake. Remember to work as quickly as you can. Ready? Go!"* Start timing. At the end of 90 seconds, say *"Stop!"* Be sure that the subject does not continue working after the time limit is reached. Do not allow the subject to skip any boxes.
Scoring: The score is the number of correct responses in 90 seconds. Do not include the practice sample in the total score.

3. Stroop Interference Test (#21 - 23)

This test has three parts: first the subject names colors (red, green or blue). Next the subject reads the names of the colors ("red", "green", "blue") that appear in black print. Finally the subject reads the interference card in which the words are printed in non-corresponding colors (e.g., "red" printed in blue ink), with the instructions to ignore the printed words and report only the color of ink in which each word is printed.

Color naming: Hand the card with the colored rectangles to the subject and say; *"Please read across the top line, naming the colors you see, either red, green, or blue".* Occasionally a subject will incorrectly identify a color (e.g., call a blue spot "purple"). Indicate to the subject that the three colors used in the test are red, green and blue. If the subject cannot discriminate the colors, terminate this test. Continue by pointing to the second line and say, *"Begin here, and go across the rows from left to right without skipping any. Tell me the colors as quickly as you can. Go!"* Begin timing, stop after 45 seconds.

Scoring: Count the total number of words correctly read.

Interference Task: Hand the card with words printed in different colors to the subject. Say, *"This card has words written in colored ink, but you can see that each word is in the wrong color of ink. For example, here the word "red" is written in blue ink* (point to the first word of the top line). *Please read across the top line, telling me the color of ink that each word is written in. Ignore the words, just tell me the color of ink you see".* Some subjects may be slow to acquire the necessary "cognitive set" and will read the word instead of reporting the ink color. Additional review of the instructions to name ink colors and not read the words may be necessary. Should the subject fail to show an understanding of the task after several attempts, discontinue the task. Note, however, that most subjects will make one or two errors on the practice line as they acquire the proper "test set". Do not consider such minor slips to be indication of failure to comprehend the task. When it is clear that the subject understands what he/she is to do (even if he/she can not do it flawlessly), continue by pointing to the second line and say, *"Begin here, and go across the rows from left to right without skipping any. Remember to ignore the words, and simply tell me the colors of ink that you see. Go!"* Begin timing, stop after 45 seconds.

Scoring: Count the total number of colors correctly identified.

III. Behavioral Assessment (#25 - 35)

Guidelines for Administration of Behavioral Assessment

The following guidelines have been developed to clarify the use of the severity and frequency ratings. Ratings should be based on all information available including the clinician's impression and the report of the subject and the informant for the past month. Be sure to ask questions about each specific item that will allow you to make ratings of severity and

frequency. Words in ***italics*** are useful for framing questions to the subject or informant, other descriptions are useful ideas of behaviors to look for in your observation.

#25 **Depressed Mood:** *In the past month have you been feeling sad (or down or "blue")? Has your mood affected your daily activities? Have you found yourself doing something you would ordinarily enjoy and realized you weren't having any fun?* Evidence of sad mood from behavioral observation includes sad voice or expression, tearfulness.

#26 **Low self-esteem/guilt:** *In the past month have you been feeling badly about yourself? Have you found yourself thinking or saying that you are a failure, or blaming yourself for things?* Evidence of low self-esteem/guilt includes self- blame without justification, self-deprecation including feelings of being a bad or unworthy person, feeling like a failure.

#27 **Anxiety:** *In the past month have you found yourself feeling worried about things?* Evidence if anxiety includes worrying, panic, feeling frightened or fearful for no apparent reason.

#28 **Suicidal thoughts:** *Since your last visit, have you found yourself thinking that life is not worth living or that you would be better off dead? Have you thought about hurting yourself or killing yourself? Are you planning to hurt yourself or kill yourself? Have you taken any steps toward carrying out your plan?*

#29 **Disruptive or aggressive behavior:** *Since the last visit, have you had any emotional or temper outbursts? Have you had times when you lost control of yourself? Have you hit or shoved or thrown things or expressed your temper in a physical way? Have you used threats or hostile words?* This item is used to rate loss of temper and impaired self-restraint. Threatening behavior includes physical violence or aggression, verbal outbursts, threatening, foul or abusive language.

#30 **Irritable Behavior:** *In the past month, have you felt impatient? Do you behave in a demanding way? Do other say you behave in a demanding way or have a short fuse or are overly sensitive?* Note that this item is used to rate the ease with which the subject loses his/her temper rather than how extreme the behavior is once self-control is lost.

#31 **Perseverative/Obsessional Thinking:** *Within the past month, have you found yourself getting stuck on certain ideas? Within the past month, have you been bothered by thoughts, images or fears that keep coming back even if you try not to*

have them? This item is used to rate inflexibility or perseveration of thinking. The content of the thinking need not be worries, but can be for example about making a

#32 **Compulsive Behavior:** *In the past month, have you found yourself doing certain things over and over again? Are you unable to resist doing some of these things? For example, do you wash your hands again and again, or count up to a certain number, or check that that door is locked over and over to make sure that you've done it correctly?* This item is used to rate repetitive, purposeful, and intentional behaviors.

#33 **Delusions:** *I' am going to ask you about unusual experiences that people sometimes have. Since the last visit, has it ever seemed like people are out to get you or peroöe are controlling you? Has it seemed like you have any special powers or importance, or that books, TV, and radio statements are referring to you? Are there any other unusual things you experience that I have not asked about?* Delusions are fixed false beliefs that are not culturally shared.

#34 **Hallucinations:** *Since the last visit, have you heard things that other people couldn't hear, such as noises or the voices of people whispering or talking? Did you ever have vision or see things that other people could not see? How about any other strange sensations in your body: skin, smell, or taste?* Hallucinations are perceptions without a physical stimulus (e.g., hearing voices when no one is in the room).

#35 **Apathy:** *Within the past month, have you found that you have lost interest in things that used to be important to you? Do you sit around a lot doing nothing? Are you just as interested as always in trying new things, starting new projects?* Apathy is a lack of interest or emotional involvement in things, and can be distinguished from anhedonia which refers to inability to experience pleasure. Apathy is reflected behaviorally by neglecting hygiene, being inactive, sitting around doing nothing, doing nothing unless told to do it by someone else, saying little in conversation, failing to initiate conversation. This question should definitely be addressed to an informant if possible.

Questions '36 – 39

Items **# 36 - 39** assess whether the subject has reached certain behavioral milestones. **Confusion** is defined as intermittent or persistent disorganized thinking, perceptual disturbances or disorientation to time, place, or person. **Dementia** is defined as progressive impairment in memory, abstract thinking or judgement that interferes with work or usual social activities and relationships. **Depression** is defined as persistent depressed mood, anhedonia, or vegetative signs sufficient to interfere with daily functioning.

IV. Functional Assessment (#43 - 67)

The functional assessment consists of three principal sections. In the first series of questions which may only be answered YES (1) or NO (2), the clinician must judge whether the subject has the capacity to perform the task, not if the subject actually performs the task. This assessment is based on the clinician's impression of disability due to any cause, whether cognitive or physical.

General Guidelines for Administration of Functional Assessment checklist (items 43 through 67)

1. Because insight may be impaired in people with HD, it is best to interview an informant in addition to the subject. Sometimes, it is helpful to have the subject sitting in front of the informant. In that case, if an informant disagrees with the subject he/she can nod his head yes/no without the subject's knowledge. Alternatively, you may want to interview the subject and the informant separately. If there is disagreement between the subject and informant, the investigator must use his/her judgement to determine the most likely answer.
2. The time frame for the answers to these questions is the day of the assessment. It is not the time since the last visit or performance over the last week or month.
3. Functional capacity should be judged according to the investigator's opinion of capacity to perform the activity rather than the actual performance of this activity. If the subject or informant reports that the subject never does or does not want to do the activity, ask: "Could they do it if they had to?" the investigator might also ask what would happen if the subject were alone and had to complete the task. For example, if the spouse says that the subject has never managed the monthly finances, the investigator should ask, "If you (informant) were away for a week, would the monthly bills be paid, or would they pile up until you came home?"
4. Impairment of any of the functional activities may be based on any cause, i.e., cognitive impairment, physical impairment or psychiatric impairment. For example, chorea might impair someone's ability to do housework. Not doing housework might also be due to cognitive impairment such as inability to plan and organize the activity or psychiatric impairment such as severe apathy associated with lack of initiative.
5. In general, if there is some doubt about the accuracy of the response, ask for specific examples of the ability or inability to perform a given activity. Include enough probes to determine the reason for the problem.
6. An informant or a subject may report that he/she has always had difficulty with the activity, i.e., the subject has always had difficulty managing monthly finances without any help. To help the informant determine whether the subject could perform this activity unassisted, the probe might be: "Compared to today, do you think he/she could have managed the monthly finances better a year ago?"

Alternatively, the probe could be, "Do you think he/she could have managed the monthly finances better before he/she had some of the symptoms/signs of HD?" these probes which highlight change in function may help the informant determine the subject's capacity to perform the activity at the present time.

7. For many of the responses, the key feature is the ability to do these activities without any help, i.e., alone. Therefore, if the subject has some difficulty doing the laundry, i.e., it takes longer to put the clothes into he washing machine, but the subject can do the laundry unassisted, the answer to the question "Could the subject do his/her laundry but does not use the washer or dry, the answer would be no. If there is some doubt, to probe further, the investigator can ask the caregiver, "If you were away for a week, would the subject do his/her laundry?"
8. All answers should be answered yes or no. Only use U or N as specified.

Guidelines for Specific Functional Assessment Questions

#43 If the subject is no longer able to work at the job he/she had for the majority of his/her life, answer "no". For example, if the person worked in a fast food chain as a cashier and after developing HD was forced to leave that job and worked in a less demanding job, the answer would be "no" to gainful employment in accustomed work. If the subject is a homemaker who never worked for pay, the probe for this person might be: "Can the subject manage the household today as well as he/she always has or must they have assistance to do so?" If assistance is now required, the answer would be "no".

#44 Gainful employment means that the person is paid for their services. This is judged as potential capacity, not whether the person is actually working.

#45 Volunteer or non-gainful work means the person is not paid for their services.

#46 Refer to General Guidelines #6.

#47 Shopping for groceries without help means going into the store obtaining groceries without assistance. If the subject requires help carrying bundles, but can otherwise handle the task, the answer is "yes".

#48 The person should be able to go to a store and come back with the correct change.

#49 Supervising children means physically as well as cognitively caring for children who could not otherwise be left alone. This does not mean infants.

#50 Operating an automobile safely and independently means the subject can drive without others feeling afraid to drive with the subject and showing good judgment. If the person has never learned how to drive, the answer should be "N" (Not applicable) since it is difficult to judge potential in this situation.

#51 Housework activities might include cooking, vacuuming, dusting, taking out the trash, and doing dishes. If a subject never did any housework, ask about picking up after themselves (e.g., doing light dusting or making the bed) and hanging up his/her clothes. Housework might also extend to light yard work if that was the subject's responsibility.

#52 If the subject only folds laundry and does nothing else, the answer is "no".

#53 Preparing meals can include making a sandwich, heating up soup or using the microwave, as long as the person does it himself/herself. A probe might be "if the subject were left alone, would he/she able to prepare his/her own meals?"

#54 Using a telephone without help means the ability to make outgoing calls and answer the telephone.

#55 If the subject has the pills in a dispenser but he/she is able to remember to take them by himself/herself, then the answer is "yes". If the subject cannot physically handle medications without assistance, the answer is "no".

#56 If the subject cannot cut his/her own food without assistance, then the answer to ability to feed himself/herself without help is "no".

#57 If the subject must have clothes laid out, but he/she can dress properly (i.e., enough to be presentable), the answer is "yes".

#58 If the subject requires assistance getting into the shower/tub, but then bathes himself/herself, the answer is "yes".

#59 Public transportation includes bus and train. If there is no public transportation the question should be; "public transportation were available, could he/she use it without assistance?"

#60 Walking to places in the neighborhood without help implies not getting lost. A probe might be "would he/she be able to find his/her way home if he/she was out on one of the streets in the neighborhood?"

#61 Falling should occur at least once a week for a "no" answer. A one-time fall does not indicate a "no" answer.

#62 Required use of a walker or a cane is "help". In other words, if the subject cannot walk without an assistive device, the answer is "no".

#63-66 Self explanatory.

#67 Care at home implies only whether the person is capable of living at home, rather than in the equivalent of institutional care.

V. INDEPENDENCE SCALE (#69)

Guidelines for administration of the Independence Scale

The Independence Scale is intended to assess the ability of the subject to function independently in activities of daily living across the full spectrum of the disease since the last visit. As with the Total Functional Capacity (TFC), it is best to interview an informant in addition to the subject. The scale makes inquiry of a general of level of functioning representative of the capabilities of the subject as judged by the investigator. By using specific tasks as benchmarks, this scale attempts to quantify a subject's general level of function. However, in some instances these tasks may not pertain to the experiences of a particular subject and the clinician will have to make a judgement as to the ability of the subject to perform that task if he or she were required to do so.

It is acceptable to score a subject as intermediate between two levels (e.g., 75) when the subject maintains some attributes of the upper level but not others.

100 No special care needed.

The subject shows no decline in ability to perform at pre-disease levels in any sphere of activity. This score is generally reserved for an assessment of persons at-risk and asymptomatic.

90 No physical care needed if difficult tasks are avoided.

The subject functions at an apparently unimpaired level in employment, interpersonal relationships, and personal finances so long as he or she is not confronted with an unusual challenge or high stress circumstance.

80 Pre-disease level of employment changes or ends; cannot perform household chores to pre-disease level; may need help with finances.

Subjects who have been gainfully employed are not able to continue in the same position and must either stop working altogether or accept a position of lesser responsibility. For subjects who have generally not worked outside the home, the ability to manage and perform their daily tasks such as grocery shopping, cleaning and home maintenance, and child care, is lessened. The ability to oversee income tax preparation and more complex aspects of personal finances (e.g. investment or retirement plans) will also lessen at this stage for subjects who have been involved in these activities previously.

70 Self-care maintained for bathing, limited household duties (cooking and use of knives), driving terminates; unable to manage finances.
Some aspects of personal hygiene and other activities of daily living although may be impaired although the basic capacity to bathe remains. Generally employment or supervision of household chores will have ceased and, although the individual is still at home, his or her ability to perform household duties is limited. Tasks requiring manual and cognitive dexterity such as cutting food or using a stove are impaired. By this time the subject has or should have stopped driving, and can no longer manage his/her finances although still able to use money for simple purchases.

60 Needs minor assistance dressing, food must be cut for subject.

The subject can no longer function with total independence for basic tasks of dressing and eating. Modifications to the home may include a change to clothes that are more easily put on and removed, or use of finger foods or foods that can be eaten with a spoon alone as opposed to knife and fork.

50 24-hour supervision appropriate; assistance required for bathing, eating, toilette.

The subject may not necessarily reside in a nursing facility or chronic care facility but such a placement would not be considered inappropriate. In accordance with such a placement, the subject would benefit from supervision and assistance for essential activities of daily living.

40 Chronic care facility needed; limited self-feeding, liquefied diet.

The subject either resides in a chronic care facility or is cared for in manner consistent with such placement at home. The subject is able to eat finger foods or can use utensils only with great difficulty. The texture of food items may have been modified to include softer or pureed foods.

30 Subject provides minimal assistance in own feeding, bathing, toileting.

The subject requires significant assistance with all activities, but is still able to sit in a chair.

20 No speech, must be fed.

The subject provides no assistance for any activities. There is no recognizable speech, although the subject may vocalize.

10 Tube feeding; total bed care.

The subject is never out of bed and requires total care for all personal care and can be appropriately considered a candidate for tube feeding although this may not actually have been instituted.

VI FUNCTIONAL CAPACITY (#70 - 74)

Guidelines For Assessing (Total) Functional Capacity (TFC)

The HD Functional Capacity (HDFC) Scale, also referred to as Total Functional Capacity (TFC) or the Shoulson-Fahn scale, was designed so that a health professional experienced with HD could evaluated a subject based on a brief interview involving the subject and a close family member or friend familiar with the subject's functioning. The scale has undergone extensive validity and reliability testing in large populations of HD subjects [1].

The HDFC scale focuses on assessment of the subject's capacity rather than actual performance. This places the emphasis on the clinician's judgement and does not require rigorous documentation of performance. The examiner is required to arrive at a clinical rating of the subject's capabilities -- a judgement that the clinician commonly makes in the day-to-day evaluation of disability. An examination of the subject's actual motor or cognitive performance is only required to the extent that it aids in arriving at a realistic assessment of the subject's capabilities. Accordingly, the TFC should take

into account a global assessment of the subject's motor and cognitive capabilities but does not require formal assessment of motor or cognitive performance.

On the basis of a 5 - 10 minute interview, the clinician rates the subject in each of the 5 categories according to what the subject is judged capable of doing. The scale should reflect current capacity and should be assessed independent of prior examinations. The subject may over-estimate capacity and the interview involving family or friend helps to confirm actual function.

Guidelines for Specific Functional Capacity Questions

#70 Engagement in Occupation

The subject's capacity to engage satisfactorily in gainful or voluntary works is assessed regardless of whether or not the subject is actually working. *Normal* refers to gainful employment, actual or potential, with usual work expectations. *Reduced capacity* refers to full or part-time gainful employment with lower than usual work expectation (relative to the subject's training and education), but with satisfactory performance. *Marginal* refers to a capacity only for part-time employment, actual or potential with low work expectations. *Unable* refers to a subject who would be unable to carry out these financial tasks, even with considerable assistance and oversight.

#71 Capacity to Handle Financial Affairs

Functional capacity is assessed by surveying the subject's involvement in personal and family finances including balancing a checkbook, paying bills, budgeting, shopping, etc. *Normal* capacity refers to satisfactory handling of these basic financial tasks. *Requires slight assistance* refers to mild difficulties which would require the assistance/oversight of a family member or financial advisor. *Requires major assistance* refers to a subject who would require extensive supervision in handling routine financial tasks. *Unable* refers to a subject who would be unable to carry out these financial tasks, even with considerable assistance and oversight.**#72 Capacity to Manage Domestic Responsibilities**

This category refers to the subject's capacity to carry out routine domestic tasks such as cleaning, laundering, dishwashing, table setting, cooking, lawn care, answering mail, maintaining a calendar, etc. *Normal* capacity refers to a full capacity without assistance. *Impaired* refers to impaired

capacity requiring only slight assistance or supervision. *Unable* refers to marked incapacity requiring major assistance.

#73 Capacity to Perform Activities of Daily Living

This category refers to the traditional areas of "activities of daily living" including eating, dressing and bathing. *Normal* refers to full capacity. *Minimal impairment* refers to impaired capacity requiring only slight assistance. *Gross tasks only* refers to requiring moderate assistance and supervision. *Total care* refers to major incapacity requiring total assistance and supervision.

#74 Level of Care

This category refers to the most appropriate care environment to meet the subject's capacity, whether at *home*, at *home or chronic care facility or full skilled nursing care (24 hours a day supervision).*

VI. CLINICAL SUMMARY (#80)

#80 To answer this question the examiner must take into account all aspects of the UHDRS (Motor, Cognitive, Behavioral and Functional components) and to decide with a confidence level ≥99 % whether the subject has manifest HD.

References:

1. Shoulson I, Kurlan R, Rubin A, Goldblatt D, Behr J, Miller C, Kennedy J, Bamford K, Caine E, Kido D, Plumb S, Odoroff C: Assessment of functional capacity in neurodegenerative movement disorders: Huntington's disease as a prototype, in *Quantification of Neurologic Deficit,* T Munsat (ed), Butterworths, Stoneham, MA., pp. 271 - 283, 1989.

D. Amendments

a) Amendment 1.0 to 1.1

Change of patient and relatives (now: companions) information, Amendment of the Patient Informed Consent. Hardcopy of CRF still not finished.

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