## BioFIND Schedule of Activities

### HEALTHY CONTROL (HC) SUBJECTS

<table>
<thead>
<tr>
<th>Visit Description</th>
<th>Level #</th>
<th>Baseline V01 Day 0</th>
<th>Visit 02 Day 14</th>
<th>Telephone Call T01</th>
<th>FNL</th>
<th>Unscheduled Visit 5</th>
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1 MDS-UPDRS part 3 motor only
2 10ml plasma between 1 - 3 hours after meds
3 CBC, platelet count, PT/PTT
4 Laboratory procedures include PAXgene™ and plasma EDTA purple top
5 Assessments at the discretion of the investigator and to be recorded in source document
6 Adverse events assessed by phone 7 - 10 days following LP
7 Any AE ongoing at the 7 to 10 day reporting telephone visit should be followed until resolution or stabilization, but not more than 30 days from lumbar puncture.

9/23/2014
### BioFIND Schedule of Activities

#### PARKINSON DISEASE (PD) SUBJECTS

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<th>Level #</th>
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7. Any AE ongoing at the 7 to 10 day reporting telephone visit should be followed until resolution or stabilization, but not more than 30 days from lumbar puncture.

9/23/2014
Complete one form for each subject who has signed consent and is potentially eligible to participate in the study.

A. ☐ Check box if subject has signed consent

B. Date informed consent was signed:

C. Indicate the category for this subject: (1 = Parkinson disease, 2 = Healthy Control)

1. Date of birth:

2. Gender (0 = Female of child bearing potential, 1 = Female of non-child bearing potential, 2 = Male)

Women who are surgically sterile (hysterectomy or tubal ligation) or post-menopausal (last menstruation was 1 year or more prior to Baseline Visit) are considered to be of non-child-bearing potential.

**ETHNICITY**

3. Do you identify your ethnicity as being Hispanic or Latino (Spanish origin)? (0 = No, 1 = Yes, 2 = Unknown or not reported)

**RACE**

4.1 Do you identify yourself as being American Indian or Alaska Native? (0 = No, 1 = Yes, 2 = Unknown or not reported)

4.2 Do you identify yourself as being Asian? (0 = No, 1 = Yes, 2 = Unknown or not reported)

4.3 Do you identify yourself as being Black or African American? (0 = No, 1 = Yes, 2 = Unknown or not reported)

4.4 Do you identify yourself as being Native Hawaiian or Other Pacific Islander? (0 = No, 1 = Yes, 2 = Unknown or not reported)

4.5 Do you identify yourself as being White? (0 = No, 1 = Yes, 2 = Unknown or not reported)

4.6 Do you identify yourself with a race category not specified on this form? (0 = No, 1 = Yes, 2 = Unknown or not reported)

If Yes, please specify: ______________________

5. Projected Enrollment Date:

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6. **Referral Source:**
   - 01 = Site personnel
   - 02 = PCP
   - 04 = Family or Friend
   - 10 = Newspaper/Magazine Article
   - 11 = Newspaper/Magazine Ad
   - 14 = Radio/TV Ad
   - 15 = Radio/TV Story
   - 16 = Online News/Blog/Other
   - 17 = Out of Home Ad
   - 18 = Event
   - 30 = Advocacy Organization
   - 31 = Support Group
   - 58 = Clinicaltrials.gov
   - 59 = PDtrials.org
   - 60 = Specialist
   - 71 = MJFF Communication
   - 72 = Another PD Subject
   - 74 = Fox Trial Finder: site initiated contact with the subject
   - 75 = Fox Trial Finder: subject initiated contact with the site
   - 80 = 1-800 Call center
   - 99 = Other (specify in comments)

6a. If referred by a medical professional (02, 60), provide name:

☐ 7a. Declined

7b. **Reason for declining:**
   - 01 = Confidentiality issues
   - 03 = Protocol too restrictive
   - 04 = Protocol too time intensive
   - 05 = Travel requirements
   - 06 = Family advised declining
   - 07 = Physician advised declining
   - 08 = Enrolled in other study
   - 09 = Not interested (specify in comments)
   - 11 = Risks of Protocol
   - 12 = Did not agree to lumbar puncture
   - 13 = Other (specify in comments)

☐ 8a. Excluded

8b. **Reason for exclusion:**
   - 01 = Exclusionary medication
   - 02 = Other medical, psychiatric, or surgical condition
   - 03 = Disease too advanced
   - 04 = Dx uncertain
   - 06 = Did not meet other inclusion criteria (specify in comments)
   - 08 = Enrolled in other study
   - 12 = Abnormal Safety Labs
   - 99 = Other (specify in comments)

Comments:

__________________________________________________________________________________________________
__________________________________________________________________________________________________
__________________________________________________________________________________________________
1. Subject Education (number of years)

4. Handedness (1 = Right, 2 = Left, 3 = Mixed)
<table>
<thead>
<tr>
<th>SUBJECT ID</th>
<th>VISIT NO</th>
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<tr>
<td>INITIALS</td>
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<tr>
<td></td>
<td>DD</td>
</tr>
<tr>
<td></td>
<td>YYYY</td>
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</table>

A. Has the subject agreed to obtain a CTCC Unique ID? (0 = No, 1 = Yes)  

1. CTCC 9 digit Unique ID:  

If you have previously generated a Unique ID for this subject and have it on file, please enter it from your records.  

If you have not yet generated a Unique ID for this subject, please go to the following website to do so: https://www.ctcc.rochester.edu/uniqueid  

If you have previously generated a Unique ID for this subject, and do not have it on file, you can go to the website to reconstruct it. Please note - you will need to enter the information exactly as it was entered before to recreate the same Unique ID.
SUBJECT INCLUSION CRITERIA (0 = No, 1 = Yes)

1. Subjects must have bradykinesia and rigidity. 1.

2. Current or history of well documented resting tremor. 2.

3. Unilateral onset or persistent asymmetry, but not strictly unilateral at the time of enrollment. 3.

4. A well established response to one or more dopaminergic agents and/or amantadine (the presence of levodopa induced dyskinesia is acceptable but not required). 4.

5. Subject has progressive PD of 5 to 18 years of duration from the onset of symptoms. 5.

6. Male or female age of onset of PD 50 to 75 by history. Current ages would range from 55 to 93 based on #5 and #6 requirements. 6.

7. Ability to provide written informed consent in accordance with Good Clinical Practice (GCP), International Conference on Harmonization (ICH), and local regulations. 7.

8. Willing and able to comply with scheduled visits, required study procedures and laboratory tests. 8.

To be ELIGIBLE for study participation ALL answers to items 1-8 must be 1 = Yes.
SUBJECT EXCLUSION CRITERIA (0 = No, 1 = Yes)

3. Has other serious neurological disorders (clinically significant stroke, brain tumor, hydrocephalus, epilepsy, other neurodegenerative disorders, encephalitis, repeated head trauma).

4. Had early severe autonomic involvement. Symptomatic orthostatic hypotension or urinary incontinence within one year of onset of disease symptom.

5. Current treatment with anticoagulants (e.g., Coumadin, heparin) that might preclude safe completion of the lumbar puncture.

6. Condition that precludes the safe performance of routine lumbar puncture, such as prohibitive lumbar spinal disease, bleeding diathesis, or clinically significant coagulopathy or thrombocytopenia.

7. Any other medical or psychiatric condition or lab abnormality, which in the opinion of the investigator might preclude participation.

8. Use of investigational drugs or devices within 60 days prior to baseline (dietary supplements taken outside of a clinical trial are not exclusionary, e.g., coenzyme Q10).

9. Has lower body predominant symptoms.

10. Has supra-nuclear gaze palsy, cerebellar abnormalities, corticospinal track signs.

11. Has a history of cancer (other than basal and squamous cell skin cancers), autoimmune disorder, liver disease, or hematologic disorders within the past 5 years.

12. Has had any brain surgery including pallidotomy, thalamotomy, subthalamotomy, and deep brain stimulator (DBS) implantation.

To be ELIGIBLE for study participation ALL answers to items 3-11 and 13 must be 0 = No

To discuss questionable subject eligibility, call the CTCC Project Manager.
SUBJECT INCLUSION CRITERIA (0 = No, 1 = Yes)

1. Male or female age 55 to 93 years at Baseline visit.

7. Ability to provide written informed consent in accordance with Good Clinical Practice (GCP), International Conference on Harmonization (ICH), and local regulations.

8. Willing and able to comply with scheduled visits, required study procedures and laboratory tests.

To be **ELIGIBLE** for study participation ALL answers to items 1, 7 and 8 must be **1 = Yes**.

SUBJECT EXCLUSION CRITERIA (0 = No, 1 = Yes)

1. Family history of PD in first degree relatives.

3. Has other serious neurological disorders (clinically significant stroke, brain tumor, hydrocephalus, epilepsy, other neurodegenerative disorders, encephalitis, repeated head trauma).

4. Has a history of cancer (other than basal and squamous cell skin cancers), autoimmune disorder, liver disease, or hematologic disorders within the past 5 years.
SUBJECT EXCLUSION CRITERIA (0 = No, 1 = Yes) Continued

5. Current treatment with anticoagulants (e.g., Coumadin, heparin) that might preclude safe completion of the lumbar puncture.  
6. Condition that precludes the safe performance of routine lumbar puncture, such as prohibitive lumbar spinal disease, bleeding diathesis, or clinically significant coagulopathy or thrombocytopenia.  
7. Any other medical or psychiatric condition or lab abnormality, which in the opinion of the investigator might preclude participation.  
8. Use of investigational drugs or devices within 60 days prior to baseline (dietary supplements taken outside of a clinical trial are not exclusionary, e.g., coenzyme Q10).  
12. MoCA score less than 26.

To be **ELIGIBLE** for study participation **ALL** answers to items 1, 3 - 8 and 12 must be **0 = No**

To discuss questionable subject eligibility, call the CTCC Project Manager.
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<thead>
<tr>
<th>Subject ID</th>
<th>Visit No</th>
<th>Initials</th>
<th>Site No</th>
<th>Visit Date</th>
<th>MM</th>
<th>DD</th>
<th>YYYY</th>
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</thead>
</table>

1. Date of first symptom onset per the subject:  
   1. MM YYYY

2a. Date of Parkinson’s disease diagnosis:  
   (Leave blank if patient has a diagnosis other than PD.)  
   2a. MM YYYY

2b. 1 = Actual (ACT), 2 = Day Estimated (Day), 3 = Mon/Day Est. (MD), 4 = Month Est. (Mon)  
   2b. 

3. Were the following symptoms present at the time of diagnosis? (0 = No, 1 = Yes, U = Unknown)  
   3a. Resting Tremor  
   3b. Rigidity  
   3c. Bradykinesia  
   3d. Postural instability  
   3e. Other, specify: ____________________________  

4. Side predominantly affected at onset (1 = Left, 2 = Right, 3 = Symmetric)  
   4.
2. Most likely primary diagnosis:
   01 = Idiopathic PD
   02 = Alzheimer’s disease
   03 = Chromosome-17 frontotemporal dementia
   04 = Corticobasal degeneration
   05 = Dementia with Lewy bodies
   06 = Dopa-responsive dystonia
   07 = Essential tremor
   08 = Hemiparkinson/hemiatrophy syndrome
   09 = Juvenile autosomal recessive parkinsonism
   10 = Motor neuron disease with parkinsonism
   11 = Multiple system atrophy
   12 = Neuroleptic-induced parkinsonism
   13 = Normal pressure hydrocephalus
   14 = Progressive supranuclear palsy
   15 = Psychogenic illness
   16 = Vascular parkinsonism
   17 = No PD nor other neurological disorder
   18 = Spinocerebellar Ataxia (SCA)
   97 = Other neurological disorder(s) (specify)_________________________________
NOTE: This form starts with question 1d.

1. Has the subject ever had a significant disorder, disease or surgery of the following systems?

<table>
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<th>CATEGORIES</th>
<th>Enter all significant medical history items, including history from birth to present. Specify disorder/diagnosis and onset. For surgeries, specify reason/diagnosis. Use only one line per description. If more than 4 items, enter in ‘Additional Information’ category and indicate which category the condition falls under. DO NOT ABBREVIATE.</th>
<th>1 = Active 2 = Resolved</th>
<th>Year of Diagnosis</th>
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<tr>
<td>History?</td>
<td>2.</td>
<td></td>
<td></td>
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<tr>
<td>1f.</td>
<td>3.</td>
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</tr>
<tr>
<td>(0 = None, 1 = Yes)</td>
<td>4.</td>
<td></td>
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</tr>
</tbody>
</table>
Enter all significant medical history items, including history from birth to present. Specify disorder/diagnosis and onset. For surgeries, specify reason/diagnosis. Use only one line per description. If more than 4 items, enter in ‘Additional Information’ category and indicate which category the condition falls under. DO NOT ABBREVIATE.

<table>
<thead>
<tr>
<th>CATEGORIES</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>Year of Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td></td>
<td></td>
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<tr>
<td>History?</td>
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<td>(0 = None, 1 = Yes)</td>
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<tr>
<td>Cardiovascular</td>
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<td>2.</td>
<td>3.</td>
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<tr>
<td>History?</td>
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<td>(0 = None, 1 = Yes)</td>
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<tr>
<td>Gastrointestinal</td>
<td>1.</td>
<td>2.</td>
<td>3.</td>
<td>4.</td>
<td></td>
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<tr>
<td>History?</td>
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<tr>
<td>(0 = None, 1 = Yes)</td>
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<thead>
<tr>
<th>CATEGORIES</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>Year of Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatobiliary</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>History?</td>
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<td>(0 = None, 1 = Yes)</td>
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<tr>
<td>Renal</td>
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<tr>
<td>History?</td>
<td></td>
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<tr>
<td>(0 = None, 1 = Yes)</td>
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<tr>
<td>Gynecologic/Urologic</td>
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<tr>
<td>History?</td>
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<tr>
<td>(0 = None, 1 = Yes)</td>
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</tbody>
</table>
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<table>
<thead>
<tr>
<th>CATEGORIES</th>
<th>Year of Diagnosis</th>
<th>1 = Active</th>
<th>2 = Resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal History?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
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<td></td>
<td></td>
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<tr>
<td>2.</td>
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<td></td>
<td></td>
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<tr>
<td>3.</td>
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<td></td>
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<tr>
<td>4.</td>
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<tr>
<td>Metabolic/Endocrine History?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td></td>
<td></td>
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<td>2.</td>
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<td>3.</td>
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<tr>
<td>4.</td>
<td></td>
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<tr>
<td>Hemato/Lymphatic History?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td></td>
<td></td>
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<tr>
<td>2.</td>
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<td>3.</td>
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<td>4.</td>
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</tr>
</tbody>
</table>
Enter all **significant** medical history items, including history from birth to present. Specify disorder/diagnosis and onset. **For surgeries, specify reason/diagnosis. Use only one line per description.** If more than 4 items, enter in ‘Additional Information’ category and indicate which category the condition falls under. **DO NOT ABBREVIATE.**

<table>
<thead>
<tr>
<th>CATEGORIES</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>Year of Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologic (other than disease under study)</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>1 = Active 2 = Resolved</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
<tr>
<td>Allergy/Immunologic Please note drug allergies</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td></td>
</tr>
</tbody>
</table>

(0 = None, 1 = Yes)
Enter all significant medical history items, including history from birth to present. Specify disorder/diagnosis and onset. For surgeries, specify reason/diagnosis. Use only one line per description. If more than 4 items, enter in ‘Additional Information’ category and indicate which category the condition falls under. DO NOT ABBREVIATE.

### Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>1 = Active</th>
<th>2 = Resolved</th>
<th>Year of Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other 1s.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0 = None, 1 = Yes)</td>
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</tr>
<tr>
<td>1.</td>
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<tr>
<td>4.</td>
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</tbody>
</table>

**Additional Information**

If there are more than 4 medical history items per category, enter in ‘Additional Information’ category below. Indicate which category the condition falls under (e.g., 1a, 1b, etc.). DO NOT ABBREVIATE.
1. Have you smoked at least 100 cigarettes (about 5 packs) in your entire lifetime? (0 = No, 1 = Yes) (If No to question 1, skip to question 3)

2. Are you still smoking? (0 = No, 1 = Yes)

3. In your lifetime, have you ever drunk alcohol (beer, wine, liquor) regularly, that is, at least one drink per week for 6 months or longer? (0 = No, 1 = Yes) (If No to question 3, do not answer question 4)

4. Do you currently drink alcohol regularly? (0 = No, 1 = Yes)
<table>
<thead>
<tr>
<th>NUMBER of FAMILY MEMBERS</th>
<th>NUMBER with PD or PARKINSONISM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Biological Mother</td>
<td>1.1 1</td>
</tr>
<tr>
<td>2. Biological Father</td>
<td>2.1 1</td>
</tr>
<tr>
<td>3. Full Siblings</td>
<td>3.1 1</td>
</tr>
<tr>
<td>4. Half Siblings</td>
<td>4.1 1</td>
</tr>
<tr>
<td>5. Maternal Grandparents</td>
<td>5.1 2</td>
</tr>
<tr>
<td>6. Paternal Grandparents</td>
<td>6.1 2</td>
</tr>
<tr>
<td>7. Maternal Aunts and Uncles</td>
<td>7.1 1</td>
</tr>
<tr>
<td>8. Paternal Aunts and Uncles</td>
<td>8.1 1</td>
</tr>
<tr>
<td>9. Children</td>
<td>9.1 1</td>
</tr>
</tbody>
</table>
Cranial Nerves
0 = Normal, 1 = Abnormal (If abnormal, describe briefly), 2 = Not tested, 3 = Unable to test

1a. I

1b. II

1c. III, IV, VI

1d. V

1e. VII

1f. VIII

1g. IX, X

1h. XI

1i. XII

Motor System
2. Muscle Strength
0 = Normal, 1 = Abnormal (If abnormal, describe briefly), 2 = Not tested, 3 = Unable to test

2a. RIGHT ARM

2b. LEFT ARM

2c. RIGHT LEG

2d. LEFT LEG
3. Coordination
0 = Normal, 1 = Abnormal (If abnormal, describe briefly), 2 = Not tested, 3 = Unable to test

Finger-to-nose
3a. RIGHT HAND

3b. LEFT HAND

Heel-to-shin
3c. RIGHT LEG

3d. LEFT LEG

4. Sensation (pain, light touch, position, vibration)
0 = Normal, 1 = Abnormal (If abnormal, describe briefly), 2 = Not tested, 3 = Unable to test

4a. RIGHT ARM

4b. LEFT ARM

4c. RIGHT LEG

4d. LEFT LEG

5. Muscle Stretch Reflexes
0 = Absent, 1 = Hypoactive, 2 = Normal, 3 = Hyperactive, no clonus, 4 = Hyperactive, clonus, 5 = Not tested, 6 = Unable to test

If response is 5 or 6, describe briefly.

5a. RIGHT ARM

5b. LEFT ARM

5c. RIGHT LEG

5d. LEFT LEG

6. Plantar Response
0 = Flexor, 1 = Extensor, 2 = Indeterminate, 3 = Not tested, 4 = Unable to test

If response is 3 or 4, describe briefly.

6a. RIGHT

6b. LEFT
<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Weight (in Kilograms) - Baseline only</td>
<td>1.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Height (in Centimeters) - Baseline only</td>
<td>2.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Temperature (in Celsius)</td>
<td>3.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Arm used to measure blood pressure? (1 = Right arm, 2 = Left arm)</td>
<td>4.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Seated blood pressure: systolic/diastolic (mmHg) (to be taken after subject has been seated for 1-3 minutes)</td>
<td>7.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Seated heart rate (beats per minute) (to be taken after subject has been seated for 1-3 minutes)</td>
<td>8.</td>
<td></td>
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</tr>
</tbody>
</table>

Comments:

___________________________________________________________________________
___________________________________________________________________________
___________________________________________________________________________
1. Date of last intake of food:

2. Time of last intake of food: (24-hour clock)

3. Fasting status:
   1 = Fasted (minimum of 8 hours)
   2 = Low Fat Diet
   3 = Not Fasted, No Low Fat Diet

Comments:

____________________________________________________________________________
____________________________________________________________________________
____________________________________________________________________________
1. Is the subject on medication for treating the symptoms of Parkinson disease? (0 = No, 1 = Yes)

2. If yes, what is the subject taking: (check all that apply)
   - □ Levodopa
   - □ Dopamine Agonist
   - □ Amantadine
   - □ MAO-B Inhibitor
   - □ Other, Specify: ______________________________

Note: If subject is on multiple PD medications, answer items 4 and 5 based on the most recent dose of the subject’s medication that is of highest priority according to this list (with 1 being the highest):
   1) levodopa
   2) dopamine agonist
   3) amantadine
   4) MAO-B inhibitor

4. Date of most recent PD medication dosing prior to specimen collection and MDS-UPDRS:
   4.    MM DD YYYY

5. Time of most recent PD medication dosing prior to specimen collection and MDS-UPDRS: (24-hour clock)
   5.    :    

6. Time that the MDS-UPDRS part 3 was administered: (24-hour clock)
   6.    :    
MDS-UPDRS

The Movement Disorder Society (MDS)-sponsored new version of the UDPRS is founded on the critique that was formulated by the Task Force for Rating Scales in Parkinson’s disease (Mov Disord 2003;18:738-750). Thereafter, the MDS recruited a Chairperson to organize a program to provide the Movement Disorder community with a new version of the UDPRS that would maintain the overall format of the original UPDRS, but address issues identified in the critique as weaknesses and ambiguities. The Chairperson identified subcommittees with chairs and members. Each part was written by the appropriate subcommittee members and then reviewed and ratified by the entire group. These members are listed below.

The MDS UPDRS has four parts: Part I (non-motor experiences of daily living), Part II (motor experiences of daily living), Part III (motor examination) and Part IV (motor complications). Part I has two components: IA concerning a number of behaviors that are assessed by the investigator with all pertinent information from patients and caregivers and IB that is completed by the patient with or without the aid of the caregiver, but independently of the investigator. It can, however, be reviewed by the rater to ensure that all questions are answered clearly and the rater can help explain any perceived ambiguities. Part II is designed to be a self-administered questionnaire like Part IB, but can be reviewed by the investigator to ensure completeness and clarity. Of note, the official versions of Part1A, Part1B and Part2 of the MDS-UPDRS do not have separate on or off ratings. However, for individual programs or protocols the same questions can be used separately for on and off. Part III has instructions for the rater to give or demonstrate to the patient; it is completed by the rater. Part IV has instructions for the rater and also instructions to be read to the patient. This part integrates patient-derived information with the rater’s clinical observations and judgments and is completed by the rater.

The authors of this new version are:

Chairperson: Christopher G. Goetz
Part I: Werner Poewe (chair), Bruno Dubois, Anette Schrag
Part II: Matthew B. Stern (chair), Anthony E. Lang, Peter A. LeWitt
Part III: Stanley Fahn (chair), Joseph Jankovic, C. Warren Olanow
Part IV: Pablo Martinez-Martin (chair), Andrew Lees, Olivier Rascol, Bob van Hilten
Development Standards: Glenn T. Stebbins (chair), Robert Holloway, David Nyenhuis
Appendices: Cristina Sampaio (chair), Richard Dodel, Jaime Kulisevsky
Statistical Testing: Barbara Tilley (chair), Sue Leurgans, Jean Teresi,
Consultant: Stephanie Shaftman, Nancy LaPelle

Contact person: Christopher G. Goetz, MD
Rush University Medical Center
1725 W. Harrison Street, Suite 755
Chicago, IL USA 60612
Telephone 312-942-8016
Email: cgoetz@rush.edu

July 1, 2008
**Part I: Non-Motor Aspects of Experiences of Daily Living (nM-EDL)**

Overview: This portion of the scale assesses the non-motor impact of Parkinson's disease (PD) on patients' experiences of daily living. There are 13 questions. Part 1A is administered by the rater (six questions) and focuses on complex behaviors. Part 1B is a component of the self-administered Patient Questionnaire that covers seven questions on non-motor experiences of daily living.

Part 1A:
In administering Part IA, the examiner should use the following guidelines:

1. Mark at the top of the form the primary data source as patient, caregiver, or patient and caregiver in equal proportion.
2. The response to each item should refer to a period encompassing the prior week including the day on which the information is collected.
3. All items must have an integer rating (no half points, no missing scores). In the event that an item does not apply or cannot be rated (e.g., amputee who cannot walk), the item is marked UR for Unable to Rate.
4. The answers should reflect the usual level of function and words such as "usually", "generally", "most of the time" can be used with patients.
5. Each question has a text for you to read (Instructions to patients/caregiver). After that statement, you can elaborate and probe based on the target symptoms outlined in the Instructions to examiner. You should NOT READ the RATING OPTIONS to the patient/caregiver, because these are written in medical terminology. From the interview and probing, you will use your medical judgment to arrive at the best response.
6. Patients may have co-morbidities and other medical conditions that can affect their function. You and the patient must rate the problem as it exists and do not attempt to separate elements due to Parkinson's disease from other conditions.

**EXAMPLE OF NAVIGATING THROUGH THE RESPONSE OPTIONS FOR PART 1A**

Suggested strategies for obtaining the most accurate answer:
After reading the instructions to the patient, you will need to probe the entire domain under discussion to determine Normal vs. problematic: If your questions do not identify any problem in this domain, record 0 and move on to the next question.

If your questions identify a problem in this domain, you should work next with a reference anchor at the mid-range (option 2 or Mild) to find out if the patient functions at this level, better or worse. You will not be reading the choices of responses to the patient as the responses use clinical terminology. You will be asking enough probing questions to determine the response that should be coded.

Work up and down the options with the patient to identify the most accurate response, giving a final check by excluding the options above and below the selected response.

<table>
<thead>
<tr>
<th>Is this item normal for you?</th>
<th>‘Yes’.</th>
<th>Mark (0) Normal.</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘No, I have problems.’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider mild (2) as a reference point and then compare with slight (1).</td>
<td>‘Yes, slight is closest’.</td>
<td>Confirm and mark (1) Slight.</td>
</tr>
<tr>
<td>If mild is closer than slight.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider moderate (3) to see if this answer fits better.</td>
<td>‘No, moderate is too severe’.</td>
<td>Confirm and mark (2) Mild.</td>
</tr>
<tr>
<td>If moderate is closer than mild.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider severe (4) to see if this answer fits better.</td>
<td>‘No, severe is too severe’.</td>
<td>Confirm and mark (3) Moderate.</td>
</tr>
<tr>
<td></td>
<td>‘Yes, severe is closest.’</td>
<td>Confirm and mark (4) Severe.</td>
</tr>
</tbody>
</table>
MDS UPDRS
Part I: Non-Motor Aspects of Experiences of Daily Living (nM-EDL)

Part 1A: Complex behaviors: [completed by rater]

Primary source of information:

☐ Patient  ☐ Caregiver  ☐ Patient and Caregiver in Equal Proportion

To be read to the patient: I am going to ask you six questions about behaviors that you may or may not experience. Some questions concern common problems and some concern uncommon ones. If you have a problem in one of the areas, please choose the best response that describes how you have felt MOST OF THE TIME during the PAST WEEK. If you are not bothered by a problem, you can simply respond NO. I am trying to be thorough, so I may ask questions that have nothing to do with you.

1.1 COGNITIVE IMPAIRMENT

Instructions to examiner: Consider all types of altered level of cognitive function including cognitive slowing, impaired reasoning, memory loss, deficits in attention and orientation. Rate their impact on activities of daily living as perceived by the patient and/or caregiver.

Instructions to patients [and caregiver]: Over the past week have you had problems remembering things, following conversations, paying attention, thinking clearly, or finding your way around the house or in town? [If yes, examiner asks patient or caregiver to elaborate and probes for information]

0: Normal: No cognitive impairment.

1: Slight: Impairment appreciated by patient or caregiver with no concrete interference with the patient’s ability to carry out normal activities and social interactions.

2: Mild: Clinically evident cognitive dysfunction, but only minimal interference with the patient’s ability to carry out normal activities and social interactions.

3: Moderate: Cognitive deficits interfere with but do not preclude the patient’s ability to carry out normal activities and social interactions.

4: Severe: Cognitive dysfunction precludes the patient’s ability to carry out normal activities and social interactions.
### 1.2 HALLUCINATIONS AND PSYCHOSIS

**Instructions to examiner:** Consider both illusions (misinterpretations of real stimuli) and hallucinations (spontaneous false sensations). Consider all major sensory domains (visual, auditory, tactile, olfactory and gustatory). Determine presence of unformed (for example sense of presence or fleeting false impressions) as well as formed (fully developed and detailed) sensations. Rate the patients insight into hallucinations and identify delusions and psychotic thinking.

**Instructions to patients [and caregiver]:** Over the past week have you seen, heard, smelled or felt things that were not really there? [If yes, examiner asks patient or caregiver to elaborate and probes for information]

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No hallucinations or psychotic behaviour.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Illusions or non-formed hallucinations, but patient recognizes them without loss of insight.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Formed hallucinations independent of environmental stimuli. No loss of insight.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Formed hallucinations with loss of insight.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Patient has delusions or paranoia.</td>
</tr>
</tbody>
</table>

### 1.3 DEPRESSED MOOD

**Instructions to examiner:** Consider low mood, sadness, hopelessness, feelings of emptiness or loss of enjoyment. Determine their presence and duration over the past week and rate their interference with the patient's ability to carry out daily routines and engage in social interactions.

**Instruction to the patient (and caregiver):** Over the past week have you felt low, sad, hopeless or unable to enjoy things? If yes, was this feeling for longer than one day at a time? Did it make it difficult for you carry out your usual activities or to be with people? If yes, examiner asks patient or caregiver to elaborate and probes for information

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No depressed mood.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Episodes of depressed mood that are not sustained for more than one day at a time. No interference with patient's ability to carry out normal activities and social interactions.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Depressed mood that is sustained over days, but without interference with normal activities and social interactions.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Depressed mood that interferes with, but does not preclude, the patient's ability to carry out normal activities and social interactions.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Depressed mood precludes patient's ability to carry out normal activities and social interactions.</td>
</tr>
</tbody>
</table>
1.4 ANXIOUS MOOD

Instructions to examiner: Determine nervous, tense, worried or anxious feelings (including panic attacks) over the past week and rate their duration and interference with the patient's ability to carry out daily routines and engage in social interactions.

Instructions to patients [and caregiver]: Over the past week have you felt nervous, worried or tense? If yes, was this feeling for longer than one day at a time? Did it make it difficult for you to follow your usual activities or to be with other people? [If yes, examiner asks patient or caregiver to elaborate and probes for information.]

0: Normal: No anxious feelings.

1: Slight: Anxious feelings present but not sustained for more than one day at a time. No interference with patient's ability to carry out normal activities and social interactions.

2: Mild: Anxious feelings are sustained over more than one day at a time, but without interference with patient's ability to carry out normal activities and social interactions.

3: Moderate: Anxious feelings interfere with, but do not preclude, the patient's ability to carry out normal activities and social interactions.

4: Severe: Anxious feelings preclude patient's ability to carry out normal activities and social interactions.

SCORE

1.5 APATHY

Instructions to examiner: Consider level of spontaneous activity, assertiveness, motivation and initiative and rate the impact of reduced levels on performance of daily routines and social interactions. Here the examiner should attempt to distinguish between apathy and similar symptoms that are best explained by depression.

Instructions to patients (and caregiver): Over the past week, have you felt indifferent to doing activities or being with people? If yes, examiner asks patient or caregiver to elaborate and probes for information.

0: Normal: No apathy.

1: Slight: Apathy appreciated by patient and/or caregiver, but no interference with daily activities and social interactions.

2: Mild: Apathy interferes with isolated activities and social interactions.

3: Moderate: Apathy interferes with most activities and social interactions.

4: Severe: Passive and withdrawn, complete loss of initiative.
1.6 FEATURES OF DOPAMINE DYSREGULATION SYNDROME

Instructions to examiner: Consider involvement in a variety of activities including atypical or excessive gambling (e.g. casinos or lottery tickets), atypical or excessive sexual drive or interests (e.g., unusual interest in pornography, masturbation, sexual demands on partner), other repetitive activities (e.g. hobbies, dismantling objects, sorting or organizing), or taking extra non-prescribed medication for non-physical reasons (i.e., addictive behavior). Rate the impact of such abnormal activities/behaviors on the patient’s personal life and on his family and social relations (including need to borrow money or other financial difficulties like withdrawal of credit cards, major family conflicts, lost time from work, or missed meals or sleep because of the activity).

Instructions to patients [and caregiver]: Over the past week, have you had unusually strong urges that are hard to control? Do you feel driven to do or think about something and find it hard to stop? [Give patient examples such as gambling, cleaning, using the computer, taking extra medicine, obsessing about food or sex, all depending on the patients.

0: Normal: No problems present.
1: Slight: Problems are present but usually do not cause any difficulties for the patient or family/caregiver.
2: Mild: Problems are present and usually cause a few difficulties in the patient’s personal and family life.
3: Moderate: Problems are present and usually cause a lot of difficulties in the patient’s personal and family life.
4: Severe: Problems are present and preclude the patient’s ability to carry out normal activities or social interactions or to maintain previous standards in personal and family life.

The remaining questions in Part I (Non-motor Experiences of Daily Living) [Sleep, Daytime Sleepiness, Pain and Other Sensation, Urinary Problems, Constipation Problems, Lightheadedness on Standing, and Fatigue] are in the Patient Questionnaire along with all questions in Part II [Motor Experiences of Daily Living].
Instructions:

This questionnaire will ask you about your experiences of daily living.

There are 20 questions. We are trying to be thorough, and some of these questions may therefore not apply to you now or ever. If you do not have the problem, simply mark 0 for NO.

Please read each one carefully and read all answers before selecting the one that best applies to you.

We are interested in your average or usual function over the past week including today. Some patients can do things better at one time of the day than at others. However, only one answer is allowed for each question, so please mark the answer that best describes what you can do most of the time.

You may have other medical conditions besides Parkinson's disease. Do not worry about separating Parkinson's disease from other conditions. Just answer the question with your best response.

Use only 0, 1, 2, 3, 4 for answers, nothing else. Do not leave any blanks.

Your doctor or nurse can review the questions with you, but this questionnaire is for patients to complete, either alone or with their caregivers.

Who is filling out this questionnaire (check the best answer):

☐ Patient  ☐ Caregiver  ☐ Patient and Caregiver in Equal Proportion
### Part I: Non-Motor Aspects of Experiences of Daily Living (nM-EDL)

#### 1.7 SLEEP PROBLEMS

Over the past week, have you had trouble going to sleep at night or staying asleep through the night? Consider how rested you felt after waking up in the morning.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: Normal</td>
<td>No problems.</td>
</tr>
<tr>
<td>1: Slight</td>
<td>Sleep problems are present but usually do not cause trouble getting a full night of sleep.</td>
</tr>
<tr>
<td>2: Mild</td>
<td>Sleep problems usually cause some difficulties getting a full night of sleep.</td>
</tr>
<tr>
<td>3: Moderate</td>
<td>Sleep problems cause a lot of difficulties getting a full night of sleep, but I still usually sleep for more than half the night.</td>
</tr>
<tr>
<td>4: Severe</td>
<td>I usually do not sleep for most of the night.</td>
</tr>
</tbody>
</table>

#### 1.8 DAYTIME SLEEPINESS

Over the past week, have you had trouble staying awake during the daytime?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: Normal</td>
<td>No daytime sleepiness.</td>
</tr>
<tr>
<td>1: Slight</td>
<td>Daytime sleepiness occurs but I can resist and I stay awake.</td>
</tr>
<tr>
<td>2: Mild</td>
<td>Sometimes I fall asleep when alone and relaxing. For example, while reading or watching TV.</td>
</tr>
<tr>
<td>3: Moderate</td>
<td>I sometimes fall asleep when I should not. For example, while eating or talking with other people.</td>
</tr>
<tr>
<td>4: Severe</td>
<td>I often fall asleep when I should not. For example, while eating or talking with other people.</td>
</tr>
</tbody>
</table>
1.9 PAIN AND OTHER SENSATIONS
Over the past week, have you had uncomfortable feelings in your body like pain, aches, tingling or cramps?

0: Normal: No uncomfortable feelings.
1: Slight: I have these feelings. However, I can do things and be with other people without difficulty.
2: Mild: These feelings cause some problems when I do things or am with other people.
3: Moderate: These feelings cause a lot of problems, but they do not stop me from doing things or being with other people.
4: Severe: These feelings stop me from doing things or being with other people.

1.10 URINARY PROBLEMS
Over the past week, have you had trouble with urine control? For example, an urgent need to urinate, a need to urinate too often, or urine accidents?

0: Normal: No urine control problems.
1: Slight: I need to urinate often or urgently. However, these problems do not cause difficulties with my daily activities.
2: Mild: Urine problems cause some difficulties with my daily activities. However, I do not have urine accidents.
3: Moderate: Urine problems cause a lot of difficulties with my daily activities, including urine accidents.
4: Severe: I cannot control my urine and use a protective garment or have a bladder tube.
1.11 CONSTITUTION PROBLEMS

Over the past week have you had constipation troubles that cause you difficulty moving your bowels?

0: Normal: No constipation.

1: Slight: I have been constipated. I use extra effort to move my bowels. However, this problem does not disturb my activities or my being comfortable.

2: Mild: Constipation causes me to have some troubles doing things or being comfortable.

3: Moderate: Constipation causes me to have a lot of trouble doing things or being comfortable. However, it does not stop me from doing anything.

4: Severe: I usually need physical help from someone else to empty my bowels.

1.12 LIGHT HEADEDNESS ON STANDING

Over the past week, have you felt faint, dizzy or foggy when you stand up after sitting or lying down?

0: Normal: No dizzy or foggy feelings.

1: Slight: Dizzy or foggy feelings occur. However, they do not cause me troubles doing things.

2: Mild: Dizzy or foggy feelings cause me to hold on to something, but I do not need to sit or lie back down.

3: Moderate: Dizzy or foggy feelings cause me to sit or lie down to avoid fainting or falling.

4: Severe: Dizzy or foggy feelings cause me to fall or faint.
1.13 FATIGUE

Over the past week, have you usually felt fatigued? This feeling is not part of being sleepy or sad

0: Normal: No fatigue.

1: Slight: Fatigue occurs. However it does not cause me troubles doing things or being with people.

2: Mild: Fatigue causes me some troubles doing things or being with people.

3: Moderate: Fatigue causes me a lot of troubles doing things or being with people. However, it does not stop me from doing anything.

4: Severe: Fatigue stops me from doing things or being with people.

---

Part II: Motor Aspects of Experiences of Daily Living (M-EDL)

2.1 SPEECH

Over the past week, have you had problems with your speech?

0: Normal: Not at all (no problems).

1: Slight: My speech is soft, slurred or uneven, but it does not cause others to ask me to repeat myself.

2: Mild: My speech causes people to ask me to occasionally repeat myself, but not everyday.

3: Moderate: My speech is unclear enough that others ask me to repeat myself every day even though most of my speech is understood.

4: Severe: Most or all of my speech cannot be understood.
### 2.2 SALIVA & DROOLING

Over the past week, have you usually had too much saliva during when you are awake or when you sleep?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: Not at all (no problems).</td>
</tr>
<tr>
<td>1</td>
<td>Slight: I have too much saliva, but do not drool.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: I have some drooling during sleep, but none when I am awake.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: I have some drooling when I am awake, but I usually do not need tissues or a handkerchief.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: I have so much drooling that I regularly need to use tissues or a handkerchief to protect my clothes.</td>
</tr>
</tbody>
</table>

### 2.3 CHEWING AND SWALLOWING

Over the past week, have you usually had problems swallowing pills or eating meals? Do you need your pills cut or crushed or your meals to be made soft, chopped or blended to avoid choking?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No problems.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: I am aware of slowness in my chewing or increased effort at swallowing, but I do not choke or need to have my food specially prepared.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: I need to have my pills cut or my food specially prepared because of chewing or swallowing problems, but I have not choked over the past week.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: I choked at least once in the past week.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Because of chewing and swallowing problems, I need a feeding tube.</td>
</tr>
</tbody>
</table>
2.4 EATING TASKS

Over the past week, have you usually had troubles handling your food and using eating utensils? For example, do you have trouble handling finger foods or using forks, knives, spoons, chopsticks?

0: Normal: Not at all (No problems).

1: Slight: I am slow, but I do not need any help handling my food and have not had food spills while eating.

2: Mild: I am slow with my eating and have occasional food spills. I may need help with a few tasks such as cutting meat.

3: Moderate: I need help with many eating tasks but can manage some alone.

4: Severe: I need help for most or all eating tasks.

SCORE

2.5 DRESSING

Over the past week, have you usually had problems dressing? For example, are you slow or do you need help with buttoning, using zippers, putting on or taking off your clothes or jewelry?

0: Normal: Not at all (no problems).

1: Slight: I am slow but I do not need help.

2: Mild: I am slow and need help for a few dressing tasks (buttons, bracelets).

3: Moderate: I need help for many dressing tasks.

4: Severe: I need help for most or all dressing tasks.
### 2.6 HYGIENE

Over the past week, have you usually been slow or do you need help with washing, bathing, shaving, brushing teeth, combing your hair or with other personal hygiene?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: Not at all (no problems).</td>
</tr>
<tr>
<td>1</td>
<td>Slight: I am slow but I do not need any help.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: I need someone else to help me with some hygiene tasks.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: I need help for many hygiene tasks.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: I need help for most or all of my hygiene tasks.</td>
</tr>
</tbody>
</table>

### 2.7 HANDWRITING

Over the past week, have people usually had trouble reading your handwriting?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: Not at all (no problems).</td>
</tr>
<tr>
<td>1</td>
<td>Slight: My writing is slow, clumsy or uneven, but all words are clear.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Some words are unclear and difficult to read.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Many words are unclear and difficult to read.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Most or all words cannot be read.</td>
</tr>
</tbody>
</table>

### 2.8 DOING HOBBIES AND OTHER ACTIVITIES

Over the past week, have you usually had trouble doing your hobbies or other things that you like to do?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: Not at all (no problems).</td>
</tr>
<tr>
<td>1</td>
<td>Slight: I am a bit slow but do these activities easily.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: I have some difficulty doing these activities.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: I have major problems doing these activities, but still do most.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: I am unable to do most or all of these activities.</td>
</tr>
</tbody>
</table>
### 2.9 TURNING IN BED

Over the past week, do you usually have trouble turning over in bed?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: Normal</td>
<td>Not at all (no problems).</td>
</tr>
<tr>
<td>1: Slight</td>
<td>I have a bit of trouble turning, but I do not need any help.</td>
</tr>
<tr>
<td>2: Mild</td>
<td>I have a lot of trouble turning and need occasional help from someone else.</td>
</tr>
<tr>
<td>3: Moderate</td>
<td>To turn over I often need help from someone else.</td>
</tr>
<tr>
<td>4: Severe</td>
<td>I am unable to turn over without help from someone else.</td>
</tr>
</tbody>
</table>

### 2.10 TREMOR

Over the past week, have you usually had shaking or tremor?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: Normal</td>
<td>Not at all. I have no shaking or tremor.</td>
</tr>
<tr>
<td>1: Slight</td>
<td>Shaking or tremor occurs but does not cause problems with any activities.</td>
</tr>
<tr>
<td>2: Mild</td>
<td>Shaking or tremor causes problems with only a few activities.</td>
</tr>
<tr>
<td>3: Moderate</td>
<td>Shaking or tremor causes problems with many of my daily activities.</td>
</tr>
<tr>
<td>4: Severe</td>
<td>Shaking or tremor causes problems with most or all activities.</td>
</tr>
</tbody>
</table>

### 2.11 GETTING OUT OF BED, A CAR, OR A DEEP CHAIR

Over the past week, have you usually had trouble getting out of bed, a car seat, or a deep chair?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: Normal</td>
<td>Not at all (no problems).</td>
</tr>
<tr>
<td>1: Slight</td>
<td>I am slow or awkward, but I usually can do it on my first try.</td>
</tr>
<tr>
<td>2: Mild</td>
<td>I need more than one try to get up or need occasional help.</td>
</tr>
<tr>
<td>3: Moderate</td>
<td>I sometimes need help to get up, but most times I can still do it on my own.</td>
</tr>
<tr>
<td>4: Severe</td>
<td>I need help most or all of the time.</td>
</tr>
</tbody>
</table>
2.12 WALKING AND BALANCE

Over the past week, have you usually had problems with balance and walking?

0: Normal: Not at all (no problems).
1: Slight: I am slightly slow or may drag a leg. I never use a walking aid.
2: Mild: I occasionally use a walking aid, but I do not need any help from another person.
3: Moderate: I usually use a walking aid (cane, walker) to walk safely without falling. However, I do not usually need the support of another person.
4: Severe: I usually use the support of another person to walk safely without falling.

2.13 FREEZING

Over the past week, on your usual day when walking, do you suddenly stop or freeze as if your feet are stuck to the floor.

0: Normal: Not at all (no problems).
1: Slight: I briefly freeze but I can easily start walking again. I do not need help from someone else or a walking aid (cane or walker) because of freezing.
2: Mild: I freeze and have trouble starting to walk again, but I do not need someone’s help or a walking aid (cane or walker) because of freezing.
3: Moderate: When I freeze I have a lot of trouble starting to walk again and, because of freezing, I sometimes need to use a walking aid or need someone else’s help.
4: Severe: Because of freezing, most or all of the time, I need to use a walking aid or someone’s help.

This completes the questionnaire. We may have asked about problems you do not even have, and may have mentioned problems that you may never develop at all. Not all patients develop all these problems, but because they can occur, it is important to ask all the questions to every patient. Thank you for your time and attention in completing this questionnaire.
Part III: Motor Examination

Overview: This portion of the scale assesses the motor signs of PD. In administering Part III of the MDS-UPDRS the examiner should comply with the following guidelines:

At the top of the form, mark whether the patient is on medication for treating the symptoms of Parkinson's disease and, if on levodopa, the time since the last dose.

Also, if the patient is receiving medication for treating the symptoms of Parkinson's Disease, mark the patient's clinical state using the following definitions:

ON is the typical functional state when patients are receiving medication and have a good response.
OFF is the typical functional state when patients have a poor response in spite of taking medications.

The investigator should “rate what you see”. Admittedly, concurrent medical problems such as stroke, paralysis, arthritis, contracture, and orthopedic problems such as hip or knee replacement and scoliosis may interfere with individual items in the motor examination. In situations where it is absolutely impossible to test (e.g., amputations, plegia, limb in a cast), use the notation “UR” for Unable to Rate. Otherwise, rate the performance of each task as the patient performs in the context of co-morbidities.

All items must have an integer rating (no half points, no missing ratings).

Specific instructions are provided for the testing of each item. These should be followed in all instances. The investigator demonstrates while describing tasks the patient is to perform and rates function immediately thereafter. For Global Spontaneous Movement and Rest Tremor items (3.14 and 3.17), these items have been placed purposefully at the end of the scale because clinical information pertinent to the score will be obtained throughout the entire examination.

At the end of the rating, indicate if dyskinesia (chorea or dystonia) was present at the time of the examination, and if so, whether these movements interfered with the motor examination.

3a Is the patient on medication for treating the symptoms of Parkinson's Disease?  □ No  □ Yes

3b If the patient is receiving medication for treating the symptoms of Parkinson’s Disease, mark the patient’s clinical state using the following definitions:

□ ON: On is the typical functional state when patients are receiving medication and have a good response.
□ OFF: Off is the typical functional state when patients have a poor response in spite of taking medications.

3c Is the patient on Levodopa?  □ No  □ Yes

3.C1 If yes, minutes since last levodopa dose: ___________
3.1 SPEECH

Instructions to examiner: Listen to the patient's free-flowing speech and engage in conversation if necessary. Suggested topics: ask about the patient's work, hobbies, exercise, or how he got to the doctor's office. Evaluate volume, modulation (prosody) and clarity, including slurring, palilalia (repetition of syllables) and tachyphemia (rapid speech, running syllables together).

0: Normal: No speech problems.
1: Slight: Loss of modulation, diction or volume, but still all words easy to understand.
2: Mild: Loss of modulation, diction, or volume, with a few words unclear, but the overall sentences easy to follow.
3: Moderate: Speech is difficult to understand to the point that some, but not most, sentences are poorly understood.
4: Severe: Most speech is difficult to understand or unintelligible.

3.2 FACIAL EXPRESSION

Instructions to examiner: Observe the patient sitting at rest for 10 seconds, without talking and also while talking. Observe eye-blink frequency, masked facies or loss of facial expression, spontaneous smiling and parting of lips.

0: Normal: Normal facial expression.
1: Slight: Minimal masked facies manifested only by decreased frequency of blinking.
2: Mild: In addition to decreased eye-blink frequency, Masked facies present in the lower face as well, namely fewer movements around the mouth, such as less spontaneous smiling, but lips not parted.
3: Moderate: Masked facies with lips parted some of the time when the mouth is at rest.
4: Severe: Masked facies with lips parted most of the time when the mouth is at rest.
3.3 RIGIDITY

Instructions to examiner: Rigidity is judged on slow passive movement of major joints with the patient in a relaxed position and the examiner manipulating the limbs and neck. First, test without an activation maneuver. Test and rate neck and each limb separately. For arms, test the wrist and elbow joints simultaneously. For legs, test the hip and knee joints simultaneously. If no rigidity is detected, use an activation maneuver such as tapping fingers, fist opening/closing, or heel tapping in a limb not being tested. Explain to the patient to go as limp as possible as you test for rigidity.

0: Normal: No rigidity.
1: Slight: Rigidity only detected with activation maneuver.
2: Mild: Rigidity detected without the activation maneuver, but full range of motion is easily achieved.
3: Moderate: Rigidity detected without the activation maneuver; full range of motion is achieved with effort.
4: Severe: Rigidity detected without the activation maneuver and full range of motion not achieved.

3.4 FINGER TAPPING

Instructions to examiner: Each hand is tested separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to tap the index finger on the thumb 10 times as quickly AND as big as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

0: Normal: No problems.
1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the tapping movement; b) slight slowing; c) the amplitude decrements near the end of the 10 taps.
2: Mild: Any of the following: a) 3 to 5 interruptions during tapping; b) mild slowing; c) the amplitude decrements midway in the 10-tap sequence.
3: Moderate: Any of the following: a) more than 5 interruptions during tapping or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st tap.
4: Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.
3.5 HAND MOVEMENTS

Instructions to examiner: Test each hand separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to make a tight fist with the arm bent at the elbow so that the palm faces the examiner. Have the patient open the hand 10 times as fully AND as quickly as possible. If the patient fails to make a tight fist or to open the hand fully, remind him/her to do so. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

0: Normal: No problem.
1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) the amplitude decrements near the end of the task.
2: Mild: Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowing; c) the amplitude decrements midway in the task.
3: Moderate: Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st open-and-close sequence.
4: Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.

3.6 PRONATION-SUPINATION MOVEMENTS OF HANDS

Instructions to examiner: Test each hand separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to extend the arm out in front of his/her body with the palms down; then to turn the palm up and down alternately 10 times as fast and as fully as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

0: Normal: No problems.
1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) the amplitude decrements near the end of the sequence.
2: Mild: Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowing; c) the amplitude decrements midway in the task.
3: Moderate: Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st supination-pronation sequence.
4: Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.
### 3.7 Toe Tapping

**Instructions to examiner:** Have the patient sit in a straight-backed chair with arms, both feet on the floor. Test each foot separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to place the heel on the ground in a comfortable position and then tap the toes 10 times as big and as fast as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No problem.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the tapping movement; b) slight slowing; c) amplitude decrements near the end of the ten taps.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Any of the following: a) 3 to 5 interruptions during the tapping movements; b) mild slowing; c) amplitude decrements midway in the task.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Any of the following: a) more than 5 interruptions during the tapping movements or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) amplitude decrements after the first tap.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.</td>
</tr>
</tbody>
</table>

### 3.8 Leg Agility

**Instructions to examiner:** Have the patient sit in a straight-backed chair with arms. The patient should have both feet comfortably on the floor. Test each leg separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to place the foot on the ground in a comfortable position and then raise and stomp the foot on the ground 10 times as high and as fast as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No problems.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) amplitude decrements near the end of the task.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowness; c) amplitude decrements midway in the task.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing in speed; c) amplitude decrements after the first tap.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.</td>
</tr>
</tbody>
</table>
3.9 ARISING FROM CHAIR

Instructions to examiner: Have the patient sit in a straight-backed chair with arms, with both feet on the floor and sitting back in the chair (if the patient is not too short). Ask the patient to cross his/her arms across the chest and then to stand up. If the patient is not successful, repeat this attempt a maximum up to two more times. If still unsuccessful, allow the patient to move forward in the chair to arise with arms folded across the chest. Allow only one attempt in this situation. If unsuccessful, allow the patient to push off using his/her hands on the arms of the chair. Allow a maximum of three trials of pushing off. If still not successful, assist the patient to arise. After the patient stands up, observe the posture for item 3.13.

0: Normal: No problems. Able to arise quickly without hesitation.
1: Slight: Arising is slower than normal; or may need more than one attempt; or may need to move forward in the chair to arise. No need to use the arms of the chair.
2: Mild: Pushes self up from arms of chair without difficulty.
3: Moderate: Needs to push off, but tends to fall back; or may have to try more than one time using arms of chair, but can get up without help.
4: Severe: Unable to arise without help.

3.10 GAIT

Instructions to examiner: Testing gait is best performed by having the patient walking away from and towards the examiner so that both right and left sides of the body can be easily observed simultaneously. The patient should walk at least 10 meters (30 feet), then turn around and return to the examiner. This item measures multiple behaviors: stride amplitude, stride speed, height of foot lift, heel strike during walking, turning, and arm swing, but not freezing. Assess also for “freezing of gait” (next item 3.11) while patient is walking. Observe posture for item 3.13.

0: Normal: No problems.
1: Slight: Independent walking with minor gait impairment.
2: Mild: Independent walking but with substantial gait impairment.
3: Moderate: Requires an assistance device for safe walking (walking stick, walker) but not a person.
4: Severe: Cannot walk at all or only with another person’s assistance.
### 3.11 FREEZING OF GAIT

**Instructions to examiner:** While assessing gait, also assess for the presence of any gait freezing episodes. Observe for start hesitation and stuttering movements especially when turning and reaching the end of the task. To the extent that safety permits, patients may NOT use sensory tricks during the assessment.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No freezing.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Freezes on starting, turning or walking through doorway with a single halt during any of these events, but then continues smoothly without freezing during straight walking.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Freezes on starting, turning or walking through doorway with more than one halt during any of these activities, but continues smoothly without freezing during straight walking.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Freezes once during straight walking.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Freezes multiple times during straight walking.</td>
</tr>
</tbody>
</table>

### 3.12 POSTURAL STABILITY

**Instructions to examiner:** The test examines the response to sudden body displacement produced by a quick, forceful pull on the shoulders while the patient is standing erect with eyes open and feet comfortably apart and parallel to each other. Test retropulsion. Stand behind the patient and instruct the patient on what is about to happen. Explain that s/he is allowed to take a step backwards to avoid falling. There should be a solid wall behind the examiner, at least 1-2 meters away to allow for the observation of the number of retropulsive steps. The first pull is an instructional demonstration and is purposely milder and not rated. The second time the shoulders are pulled briskly and forcefully towards the examiner with enough force to displace the center of gravity so that patient MUST take a step backwards. The examiner needs to be ready to catch the patient, but must stand sufficiently back so as to allow enough room for the patient to take several steps to recover independently. Do not allow the patient to flex the body abnormally forward in anticipation of the pull. Observe for the number of steps backwards or falling. Up to and including two steps for recovery is considered normal, so abnormal ratings begin with three steps. If the patient fails to understand the test, the examiner can repeat the test so that the rating is based on an assessment that the examiner feels reflects the patient's limitations rather than misunderstanding or lack of preparedness. Observe standing posture for item 3.13

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No problems: Recovers with one or two steps.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: 3-5 steps, but subject recovers unaided.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: More than 5 steps, but subject recovers unaided.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Stands safely, but with absence of postural response; falls if not caught by examiner.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Very unstable, tends to lose balance spontaneously or with just a gentle pull on the shoulders.</td>
</tr>
</tbody>
</table>
### 3.13 POSTURE

Instructions to examiner: Posture is assessed with the patient standing erect after arising from a chair, during walking, and while being tested for postural reflexes. If you notice poor posture, tell the patient to stand up straight and see if the posture improves (see option 2 below). Rate the worst posture seen in these three observation points. Observe for flexion and side-to-side leaning.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No problems.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Not quite erect, but posture could be normal for older person.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Definite flexion, scoliosis or leaning to one side, but patient can correct posture to normal posture when asked to do so.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Stooped posture, scoliosis or leaning to one side that cannot be corrected volitionally to a normal posture by the patient.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Flexion, scoliosis or leaning with extreme abnormality of posture.</td>
</tr>
</tbody>
</table>

### 3.14 GLOBAL SPONTANEITY OF MOVEMENT (BODY BRADYKINESIA)

Instructions to examiner: This global rating combines all observations on slowness, hesitancy, and small amplitude and poverty of movement in general, including a reduction of gesturing and of crossing the legs. This assessment is based on the examiner's global impression after observing for spontaneous gestures while sitting, and the nature of arising and walking.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No problems.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Slight global slowness and poverty of spontaneous movements.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Mild global slowness and poverty of spontaneous movements.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Moderate global slowness and poverty of spontaneous movements.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Severe global slowness and poverty of spontaneous movements.</td>
</tr>
</tbody>
</table>

### 3.15 POSTURAL TREMOR OF THE HANDS

Instructions to examiner: All tremor, including re-emergent rest tremor, that is present in this posture is to be included in this rating. Rate each hand separately. Rate the highest amplitude seen. Instruct the patient to stretch the arms out in front of the body with palms down. The wrist should be straight and the fingers comfortably separated so that they do not touch each other. Observe this posture for 10 seconds.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No tremor.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Tremor is present but less than 1 cm in amplitude.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Tremor is at least 1 but less than 3 cm in amplitude.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Tremor is at least 3 but less than 10 cm in amplitude.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Tremor is at least 10 cm in amplitude.</td>
</tr>
</tbody>
</table>
3.16 KINETIC TREMOR OF THE HANDS

Instructions to examiner: This is tested by the finger-to-nose maneuver. With the arm starting from the outstretched position, have the patient perform at least three finger-to-nose maneuvers with each hand reaching as far as possible to touch the examiner's finger. The finger-to-nose maneuver should be performed slowly enough not to hide any tremor that could occur with very fast arm movements. Repeat with the other hand, rating each hand separately. The tremor can be present throughout the movement or as the tremor reaches either target (nose or finger). Rate the highest amplitude seen.

0: Normal: No tremor.
1: Slight: Tremor is present but less than 1 cm in amplitude.
2: Mild: Tremor is at least 1 but less than 3 cm in amplitude.
3: Moderate: Tremor is at least 3 but less than 10 cm in amplitude.
4: Severe: Tremor is at least 10 cm in amplitude.

3.17 REST TREMOR AMPLITUDE

Instructions to examiner: This and the next item have been placed purposefully at the end of the examination to allow the rater to gather observations on rest tremor that may appear at any time during the exam, including when quietly sitting, during walking and during activities when some body parts are moving but others are at rest. Score the maximum amplitude that is seen at any time as the final score. Rate only the amplitude and not the persistence or the intermittency of the tremor.

As part of this rating, the patient should sit quietly in a chair with the hands placed on the arms of the chair (not in the lap) and the feet comfortably supported on the floor for 10 seconds with no other directives. Rest tremor is assessed separately for all four limbs and also for the lip/jaw. Rate only the maximum amplitude that is seen at any time as the final rating.

Extremity ratings
0: Normal: No tremor.
1: Slight: < 1 cm in maximal amplitude.
2: Mild: > 1 cm but < 3 cm in maximal amplitude.
3: Moderate: 3 - 10 cm in maximal amplitude.
4: Severe: > 10 cm in maximal amplitude.

Lip/Jaw ratings
0: Normal: No tremor.
1: Slight: < 1 cm in maximal amplitude.
2: Mild: > 1 cm but < 2 cm in maximal amplitude.
3: Moderate: > 2 cm but < 3 cm in maximal amplitude.
4: Severe: > 3 cm in maximal amplitude.
3.18 CONSTANCY OF REST TREMOR

Instructions to examiner: This item receives one rating for all rest tremor and focuses on the constancy of rest tremor during the examination period when different body parts are variously at rest. It is rated purposefully at the end of the examination so that several minutes of information can be coalesced into the rating.

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0:</td>
<td>Normal: No tremor.</td>
</tr>
<tr>
<td>1:</td>
<td>Slight: Tremor at rest is present &lt; 25% of the entire examination period.</td>
</tr>
<tr>
<td>2:</td>
<td>Mild: Tremor at rest is present 26-50% of the entire examination period.</td>
</tr>
<tr>
<td>3:</td>
<td>Moderate: Tremor at rest is present 51-75% of the entire examination period.</td>
</tr>
<tr>
<td>4:</td>
<td>Severe: Tremor at rest is present &gt; 75% of the entire examination period.</td>
</tr>
</tbody>
</table>

DYSKINESIA IMPACT ON PART III RATINGS

A. Were dyskinesias (chorea or dystonia) present during examination?  □ No  □ Yes

B. If yes, did these movements interfere with your ratings?  □ No  □ Yes

HOEHN AND YAHR STAGE

0: Asymptomatic.

1: Unilateral involvement only.

2: Bilateral involvement without impairment of balance.

3: Mile to moderate involvement; some postural instability but physically independent; needs assistance to recover from pull test.

4: Severe disability; still able to walk or stand unassisted.

5: Wheelchair bound or bedridden unless aided.
Overview and Instructions: In this section, the rater uses historical and objective information to assess two motor complications, dyskinesias and motor fluctuations that include OFF-state dystonia. Use all information from patient, caregiver, and the examination to answer the six questions that summarize function over the past week including today. As in the other sections, rate using only integers (no half points allowed) and leave no missing ratings. If the item cannot be rated, place UR for Unable to Rate. You will need to choose some answers based on percentages, and therefore you will need to establish how many hours generally are awake hours and use this figure as the denominator for “OFF” time and Dyskinesias. For “OFF dystonia”, the total “Off” time will be the denominator. Operational definitions for examiner’s use.

Dyskinesias: Involuntary random movements
Words that patients often recognize for dyskinesias include “irregular jerking”, “wiggling”, “twitching”. It is essential to stress to the patient the difference between dyskinesias and tremor, a common error when patients are assessing dyskinesias.

Dystonia: contorted posture, often with a twisting component:
Words that patients often recognize for dystonia include “spasms”, “cramps”, “posture”.

Motor fluctuation: Variable response to medication:
Words that patients often recognize for motor fluctuation include “wearing out”, “wearing off”, “roller-coaster effect”, “on-off”, “uneven medication effects”.

OFF: Typical functional state when patients have a poor response in spite of taking medication or the typical functional response when patients are on NO treatment for parkinsonism. Words that patients often recognize include “low time”, “bad time”, “shaking time”, “slow time”, “time when my medications don’t work.”

ON: Typical functional state when patients are receiving medication and have a good response:
Words that patients often recognize include “good time”, “walking time”, “time when my medications work.”

### A. DYSKINESIAS [exclusive of OFF-state dystonia]

#### 4.1 TIME SPENT WITH DYSKINESIAS

**Instructions to examiner**: Determine the hours in the usual waking day and then the hours of dyskinesias. Calculate the percentage. If the patient has dyskinesias in the office, you can point them out as a reference to ensure that patients and caregivers understand what they are rating. You may also use your own acting skills to enact the dyskinetic movements you have seen in the patient before or show them dyskinetic movements typical of other patients. Exclude from this question early morning and nighttime painful dystonia.

**Instructions to patient [and caregiver]**. Over the past week, how many hours do you usually sleep on a daily basis, including nighttime sleep and daytime napping? Alright, if you sleep ___ hrs, you are awake ____ hrs. Out of those awake hours, how many hours in total do you have wiggling, twitching or jerking movements? Do not count the times when you have tremor, which is a regular back and forth shaking or times when you have painful foot cramps or spasms in the early morning or at nighttime. I will ask about those later. Concentrate only on these types of wiggling, jerking and irregular movements. Add up all the time during the waking day when these usually occur. How many hours ____ (use this number for your calculation).

| 0: Normal: | No dyskinesias. |
| 1: Slight: | ≤ 25% of waking day. |
| 2: Mild: | 26 - 50% of waking day. |
| 3: Moderate: | 51 - 75% of waking day. |
| 4: Severe: | > 75% of waking day. |

1. **Total Hours Awake:** ____
2. **Total Hours with Dyskinesia:** ____
3. **% Dyskinesia = ((2/1)*100):** ____
4.2 FUNCTIONAL IMPACT OF DYSKINESIAS

Instructions to examiner: Determine the degree to which dyskinesias impact on the patient’s daily function in terms of activities and social interactions. Use the patient’s and caregiver’s response to your question and your own observations during the office visit to arrive at the best answer.

Instructions to patient [and caregiver]: Over the past week, did you usually have trouble doing things or being with people when these jerking movements occurred? Did they stop you from doing things or from being with people?

0: Normal: No dyskinesias or no impact by dyskinesias on activities or social interactions.
1: Slight: Dyskinesias impact on a few activities, but the patient usually performs all activities and participates in all social interactions during dyskinetic periods.
2: Mild: Dyskinesias impact on many activities, but the patient usually performs all activities and participates in all social interactions during dyskinetic periods.
3: Moderate: Dyskinesias impact on activities to the point that the patient usually does not perform some activities or does not usually participate in some social activities during dyskinetic episodes.
4: Severe: Dyskinesias impact on function to the point that the patient usually does not perform most activities or participate in most social interactions during dyskinetic episodes.

SCORE

4.3 TIME SPENT IN THE OFF STATE

Instructions to examiner: Use the number of waking hours derived from 4.1 and determine the hours spent in the “OFF” state. Calculate the percentage. If the patient has an OFF period in the office, you can point to this state as a reference. You may also use your knowledge of the patient to describe a typical OFF period. Additionally you may use your own acting skills to enact an OFF period you have seen in the patient before or show them OFF function typical of other patients. Mark down the typical number of OFF hours, because you will need this number for completing 4.6

Instructions to patient [and caregiver]: Some patients with Parkinson’s disease have a good effect from their medications throughout their awake hours and we call that “ON” time. Other patients take their medications but still have some hours of low time, bad time, slow time or shaking time. Doctors call these low periods “OFF” time. Over the past week, you told me before that you are generally awake ____ hrs each day. Out of these awake hours, how many hours in total do you usually have this type of low level or OFF function ____ (Use this number for your calculations).

0: Normal: No OFF time.
1: Slight: ≤ 25% of waking day.
2: Mild: 26 - 50% of waking day.
3: Moderate: 51 - 75% of waking day.
4: Severe: > 75% of waking day.

B . MOTOR FLUCTUATIONS

1. Total Hours Awake: ______
2. Total Hours OFF: ______
3. % OFF = ((2/1)*100): ______
### 4.4 FUNCTIONAL IMPACT OF FLUCTUATIONS

**Instructions to examiner:** Determine the degree to which motor fluctuations impact on the patient’s daily function in terms of activities and social interactions. This question concentrates on the difference between the ON state and the OFF state. If the patient has no OFF time, the rating must be 0, but if patients have very mild fluctuations, it is still possible to be rated 0 on this item if no impact on activities occurs. Use the patient’s and caregiver’s response to your question and your own observations during the office visit to arrive at the best answer.

*Instructions to patient [and caregiver]:* Think about when those low or “OFF” periods have occurred over the past week. Do you usually have more problems doing things or being with people than compared to the rest of the day when you feel your medications working? Are there some things you usually do during a good period that you have trouble with or stop doing during a low period?

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No fluctuations or No impact by fluctuations on performance of activities or social interactions.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: Fluctuations impact on a few activities, but during OFF, the patient usually performs all activities and participates in all social interactions that typically occur during the ON state.</td>
</tr>
<tr>
<td>2</td>
<td>Mild: Fluctuations impact many activities, but during OFF, the patient still usually performs all activities and participates in all social interactions that typically occur during the ON state.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: Fluctuations impact on the performance of activities during OFF to the point that the patient usually does not perform some activities or participate in some social interactions that are performed during ON periods.</td>
</tr>
<tr>
<td>4</td>
<td>Severe: Fluctuations impact on function to the point that, during OFF, the patient usually does not perform most activities or participate in most social interactions that are performed during ON periods.</td>
</tr>
</tbody>
</table>

### 4.5 COMPLEXITY OF MOTOR FLUCTUATIONS

**Instructions to examiner:** Determine the usual predictability of OFF function whether due to dose, time of day, food intake or other factors. Use the information provided by the patients and caregiver and supplement with your own observations. You will ask if the patient can count on them always coming at a special time, mostly coming at a special time (in which case you will probe further to separate slight from mild), only sometimes coming at a special time or are they totally unpredictable? Narrowing down the percentage will allow you to find the correct answer.

*Instructions to patient [and caregiver]:* For some patients, the low or “OFF” periods happen at certain times during day or when they do activities like eating or exercising. Over the past week, do you usually know when your low periods will occur? In other words, do your low periods always come at a certain time? Do they mostly come at a certain time? Do they only sometimes come at a certain time? Are your low periods totally unpredictable?"

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal: No motor fluctuations.</td>
</tr>
<tr>
<td>1</td>
<td>Slight: OFF times are predictable all or almost all of the time (&gt; 75%).</td>
</tr>
<tr>
<td>2</td>
<td>Mild: OFF times are predictable most of the time (51-75%).</td>
</tr>
<tr>
<td>3</td>
<td>Moderate: OFF times are predictable some of the time (26-50%).</td>
</tr>
<tr>
<td>4</td>
<td>Severe: OFF episodes are rarely predictable. (&lt; 25%).</td>
</tr>
</tbody>
</table>
C. “OFF” DYSTONIA

4.6 PAINFUL OFF-STATE DYSTONIA

Instructions to examiner: For patients who have motor fluctuations, determine what proportion of the OFF episodes usually includes painful dystonia? You have already determined the number of hours of “OFF” time (4.3). Of these hours, determine how many are associated with dystonia and calculate the percentage. If there is no OFF time, mark 0.

Instructions to patient [and caregiver]: In one of the questions I asked earlier, you said you generally have ___ hours of low or “OFF” time when your Parkinson’s disease is under poor control. During these low or “OFF” periods, do you usually have painful cramps or spasms? Out of the total ___ hrs of this low time, if you add up all the time in a day when these painful cramps come, how many hours would this make?

0: Normal: No dystonia OR NO OFF TIME.
1: Slight: < 25% of time in OFF state.
2: Mild: 26-50% of time in OFF state.
3: Moderate: 51-75% of time in OFF state.
4: Severe: > 75% of time in OFF state.

Summary statement to patient: READ TO PATIENT

This completes my rating of your Parkinson’s disease. I know the questions and tasks have taken several minutes, but I wanted to be complete and cover all possibilities. In doing so, I may have asked about problems you do not even have, and I may have mentioned problems that you may never develop at all. Not all patients develop all these problems, but because they can occur, it is important to ask all the questions to every patient. Thank you for your time and attention in completing this scale with me.
### MDS UPDRS Score Sheet

**Part I**

1. A. Source of information
   - Patient
   - Caregiver
   - Patient + Caregiver

1.1. Cognitive impairment
1.2. Hallucinations and psychosis
1.3. Depressed mood
1.4. Anxious mood
1.5. Apathy
1.6. Features of DDS
1.6a. Who is filling out questionnaire
   - Patient
   - Caregiver
   - Patient + Caregiver

1.7. Sleep problems
1.8. Daytime sleepiness
1.9. Pain and other sensations
1.10. Urinary problems
1.11. Constipation problems
1.12. Light headedness on standing
1.13. Fatigue

**Part II**

2.1. Speech
2.2. Saliva and drooling
2.3. Chewing and swallowing
2.4. Eating tasks
2.5. Dressing
2.6. Hygiene
2.7. Handwriting
2.8. Doing hobbies and other activities
2.9. Turning in bed
2.10. Tremor
2.11. Getting out of bed
2.12. Walking and balance
2.13. Freezing

**Part III**

3a. Is the patient on medication?  
   - No
   - Yes

3b. Patient's clinical state
   - Off
   - On

3c. Is the patient on Levodopa?  
   - No
   - Yes

3.C1. If yes, minutes since last dose:

4.1. Time spent with dyskinesias
4.2. Functional impact of dyskinesias
4.3. Time spent in the OFF state
4.4. Functional impact of fluctuations
4.5. Complexity of motor fluctuations
4.6. Painful OFF-state dystonia

**Part IV**

3a. Is the patient on medication?  
   - No
   - Yes

3b. Patient's clinical state
   - Off
   - On

3c. Is the patient on Levodopa?  
   - No
   - Yes

3.C1. If yes, minutes since last dose:

4.1. Time spent with dyskinesias
4.2. Functional impact of dyskinesias
4.3. Time spent in the OFF state
4.4. Functional impact of fluctuations
4.5. Complexity of motor fluctuations
4.6. Painful OFF-state dystonia

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July 1, 2008

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100% Completely independent. Able to do all chores without slowness, difficulty or impairment. Essentially normal. Unaware of any difficulty.

90% Completely independent. Able to do all chores with some degree of slowness, difficulty and impairment. Might take twice as long. Beginning to be aware of difficulty.

80% Completely independent in most chores. Takes twice as long. Conscious of difficulty and slowness.

70% Not completely independent. More difficulty with some chores. Three to four times as long in some. Must spend a large part of the day with chores.

60% Some dependency. Can do most chores, but exceedingly slowly and with much effort. Errors; some impossible.

50% More dependent. Help with half, slower, etc. Difficulty with everything.

40% Very dependent. Can assist with all chores but few alone.

30% With effort, now and then does a few chores alone or begins alone. Much help needed.

20% Nothing alone. Can be a slight help with some chores. Severe invalid.

10% Totally dependent, helpless. Complete invalid.

0% Vegetative functions such as swallowing, bladder, and bowel functions are not functioning. Bedridden.

Consensus rating
(Investigator, patient, other sources) 1.

Examiner

STAFF CODE
MONTREAL COGNITIVE ASSESSMENT (MOCA)  Version 7.1 Original Version

VISUOSPATIAL / EXECUTIVE

Copy cube  Draw CLOCK (Ten past eleven) (3 points)

POINTS

/5

NAMING

FACE  VELVET  CHURCH  DAISY  RED

No points

21854

/2

MEMORY  Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

1st trial

2nd trial

ATTENTION  Read list of digits (1 digit/sec.). Subject has to repeat them in the forward order Subject has to repeat them in the backward order

Read list of letters. The subject must tap with his hand at each letter A. No points if 2 errors

FBACMNAILBFAKDEAAMOFAAB

/1

Serial 7 subtraction starting at 100

93

86

79

72

65

4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt

/3

LANGUAGE

Repeat: I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

Fluency / Name maximum number of words in one minute that begin with the letter F  

[ ] _______ (IN ≥ 11 words)  

/2

ABSTRACTION

Similarity between e.g., banana - orange = fruit train - bicycle watch - ruler

/2

DELAYED RECALL  Has to recall words WITH NO CUE

FACE  VELVET  CHURCH  DAISY  RED

Points for UNCUESD, recall only

/5

Optional

Category cue

Multiple choice cue

/orientation

Date  Month  Year  Day  Place  City

/6

TOTAL

/30

© Z.Nasreddine MD  www.mocatest.org Normal ≥ 26 / 30

Administered by: ____________________________

Add 1 point if ≥ 12 yr edu

(6/26/09)  9/18/12  Page 1 of 1
### BioFIND
**MoCA FLUENCY: LETTER “F”**

Examiners: Write responses verbatim whenever possible; substitute a check mark only when you cannot keep up. Do not count repetitions or incorrect responses. **STOP AT 60 SECONDS.**

**Instruction:** Say “I’m going to ask you to say as many words as you can that begin with a particular letter that I’ll give you in a moment. You can say any kind of word that begins with the letter, except proper nouns, like Bob or Boston (people’s names or place names), or numbers. You can only use a word once, for example, if you say “bat”, you can’t also say “batting, bats, or batter”. Any questions?”

**Scoring:** On the MoCA form, 11+ correct responses = 1; 10 or less = 0. On the MoCA page in EDC, enter the total number of correct responses for “F” phonemic fluency.

“READY? NOW SAY AS MANY WORDS THAT BEGIN WITH THE LETTER “F” AS YOU CAN IN ONE MINUTE”.

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**TOTAL CORRECT:**_________
BioFIND
MONTREAL COGNITIVE ASSESSMENT (MoCA) INSTRUCTIONS
(Refer to Operations Manual for full instructions)

**Trail Making:** Say: "Draw a line, going from a number to a letter in ascending order. Begin here [point to (1)] and draw a line from 1 then to A then to 2 and so on. End here [point to (E)]."

*Scoring:* 1 point for pattern: 1 − A- 2- B- 3- C- 4- D- 5- E, without drawing any lines that cross. Any error not immediately self-corrected earns a score of 0.

**Cube:** Say: “Copy this drawing as accurately as you can, in the space below”.

*Scoring:* 1 point is allocated for a correctly executed drawing. Drawing must be three-dimensional; All lines are drawn; No extra lines; Lines are relatively parallel and their length is similar (rectangular prisms are accepted). 0 if any of the above-criteria are not met.

**Clock:** Say: "Draw a clock. Put in all the numbers and set the time to 10 after 11".

*Scoring:* 1 point is allocated for each of the following three criteria: **Contour** (1 pt.): clock face must be a circle with only minor distortion acceptable (e.g., slight imperfection on closing the circle); **Numbers** (1 pt.): all clock numbers must be present with no additional numbers; numbers must be in the correct order and placed in the approximate quadrants on the clock face; Roman numerals are acceptable; numbers can be placed outside the circle contour; **Hands** (1 pt.): must be two hands jointly indicating the correct time; the hour hand must be clearly shorter than the minute hand; hands must be centered within the clock face with their junction close to the clock centre.

**Naming:** Point to each figure and say: “Tell me the name of this animal”.

*Scoring:* 1 point each for: (1) camel or dromedary, (2) lion, (3) rhinoceros or rhino.

**Memory:** Say: “This is a memory test. I am going to read a list of words that you will have to remember now and later on. Listen carefully. When I am through, tell me as many words as you can remember. It doesn’t matter in what order you say them”.

Examiner reads the 5 words. Check in the allocated space for each word the subject produces on this first trial. When the subject indicates that (s)he has finished (has recalled all words), or can recall no more words, read the list a second time for all subjects with the following instructions: “I am going to read the same list for a second time. Try to remember and tell me as many words as you can, including words you said the first time.” Put a check in the allocated space. Then say: “I will ask you to recall those words again at the end of the test.” *Scoring:* No points.

**Attention:** Forward Digit Span: Say “I am going to say some numbers and when I am through, repeat them to me exactly as I said them”. Read at a rate of one digit per second.

Backward Digit Span: Say: “Now I am going to say some more numbers, but when I am through you must repeat them to me in the backwards order.” Read at a rate of one digit per second.

*Scoring:* 1 point for each sequence correctly repeated (N.B.: correct backwards trial is 2-4-7).

**Vigilance:** Say: “I’m going to read a sequence of letters. Every time I say the letter A, tap your hand once. If I say a different letter, do not tap your hand”.

*Scoring:* 1 point if there is 0 to 1 errors (error is a tap on a wrong letter or a failure to tap on letter A)
Serial 7s: Say: “I want you to count by subtracting 7 from 100, and then keep subtracting 7 from your answer until I tell you to stop.” Give this instruction twice if necessary.
Scoring: 0 points for no correct subtractions, 1 point for 1 correction subtraction, 2 points for 2-to-3 correct subtractions, 3 points for 4 or 5 correct subtractions. Each subtraction is evaluated independently - if the participant responds with an incorrect number but then correctly subtracts 7 from it, give 1 pt. See manual for clarification if necessary.

Sentence repetition: Say: “I am going to read you a sentence. Repeat it after me, exactly as I say it” [pause]: I only know that John is the one to help today.” Following the response, say: “Now I am going to read you another sentence. Repeat it after me, exactly as I say it [pause]: The cat always hid under the couch when dogs were in the room.”
Scoring: 1 point for each sentence correctly repeated. Repetition must be exact. Be alert for errors that are omissions (e.g., omitting "only", "always") and substitutions/additions (e.g., "John is the one who helped today;" substituting "hides" for "hid", altering plurals, etc.).

Verbal fluency: SEE RESPONSE SHEET HEADED MoCA FLUENCY: LETTER “F” for instructions. On the MoCA form itself, write in 1 point if the subject generates 11+ words in 60 seconds. Record the subject’s responses on the separate sheet for generation of a separate raw score.

Abstraction: Ask the subject to explain what each pair of words has in common, starting with the example: “Tell me how an orange and a banana are alike”.
If the subject answers in a concrete manner, say only 1 additional time: “Tell me another way in which those items are alike”. If the subject does not give the appropriate response (fruit), say, “Yes, and they are also both fruit.” Do not give any additional instructions or clarification.

After the practice trial, say: “Now, tell me how a train and a bicycle are alike”. Following the response, say: “Now tell me how a ruler and a watch are alike”. Do not give any additional instructions or prompts.
Scoring 1 point for each correct response (transport, traveling, take trips in both; measurement). See manual.

Delayed recall: Say “I read some words to you earlier, which I asked you to remember. Tell me as many of those words as you can”.
Scoring Check for each word spontaneously recalled in the “WITH NO CUE” space. 1 point for each correctly recalled word. NOTE: We are not gathering data for the Optional cued recall trials (shaded), so there is no need to do them.

Orientation: Say: “Tell me the date today”.
If the answer is incomplete, prompt accordingly: “Tell me the (year, month, exact date, day of week)”
Then say: “Tell me the name of this place, and which city it is in.”
Scoring 1 point for each correct item. NOTE: Date responses must be exact. Place name (hospital, clinic, or office) must be exact.

Total Score: Maximum total score is 30. Add 1 point to the raw score of subjects with 12 or fewer years of formal education.
1. I sometimes have very vivid dreams. (0 = No, 1 = Yes)
2. My dreams frequently have an aggressive or action-packed content. (0 = No, 1 = Yes)
3. The dream contents mostly match my nocturnal behaviour. (0 = No, 1 = Yes)
4. I know that my arms or legs move when I sleep. (0 = No, 1 = Yes)
5. It thereby happened that I (almost) hurt my bed partner or myself. (0 = No, 1 = Yes)
6. I have or had the following phenomena during my dreams:
   6.1 speaking, shouting, swearing, laughing loudly (0 = No, 1 = Yes)
   6.2 sudden limb movements, “fights” (0 = No, 1 = Yes)
   6.3 gestures, complex movements, that are useless during sleep, e.g., to wave, to salute, to frighten mosquitoes, falls off the bed (0 = No, 1 = Yes)
   6.4 things that fell down around the bed, e.g., bedside lamp, book, glasses (0 = No, 1 = Yes)
7. It happens that my movements awake me. (0 = No, 1 = Yes)
8. After awakening I mostly remember the content of my dreams well. (0 = No, 1 = Yes)
9. My sleep is frequently disturbed. (0 = No, 1 = Yes)
10. I have/had a disease of the nervous system: (0 = No, 1 = Yes)

10a. stroke

10b. head trauma

10c. parkinsonism

10d. RLS

10e. narcolepsy

10f. depression

10g. epilepsy

10h. inflammatory disease of the brain

10i. other, specify: _________________________________
DNA Collection

Instructions: (for detailed instructions please refer to the lab manual)

DNA:
• Draw 8.5ml yellow top ACD tube.
• Send to Coriell.

1. Blood sample for DNA: (0 = Not Collected, 1 = Collected) 1.

1a. Date blood sample for DNA collected: 1a. MM DD YYYY

2. Volume of blood collected: (milliliters) 2.

3. Date DNA sample shipped: 3. MM DD YYYY
Blood Sample Collection

Instructions: (for detailed instructions please refer to the lab manual)

- Draw 10ml EDTA lavender top.
- Process per lab manual instructions.
- 1ml plasma in each (3-6) 2ml polypropylene microcentrifuge tubes.
- Send at least 3 polypropylene microcentrifuge tubes to NINDS repository and store 0-3 tubes locally.
- Pellet in one tube. Store at the local site.

4. Date blood samples collected:
6. Blood for plasma: (0 = Not collected, 1 = Collected) 6.

6a. Time of plasma sample collection: (24-hour clock) 6a.

6b. Time of centrifugation: (24-hour clock) 6b.

6c. Rate of centrifugation: (xg) 6c.

6d. Duration of centrifugation: (minutes) 6d.

6e. Indicate temperature at which tube was spun: (Celsius) 6e.

6f. Total volume of plasma aliquotted after spinning: (milliliters) 6f.

6g. Total number of plasma aliquot tubes: 6g.

6g1. Shipped to NINDS repository: 6g1.

6g2. Retained at site: 6g2.

6h. Time plasma and pellet samples placed either in freezer or on dry ice: (24-hour clock) 6h.

6i. Storage temperature: (Celsius) 6i.

6j. Was pellet tube retained at site? (0 = No, 1 = Yes) 6j.

Comments:

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
Blood Sample Collection

Instructions: (for detailed instructions please refer to the lab manual)

PAXgene™
- Draw 3 2.5ml red top tubes.
- Send 2 tubes to NINDS repository and store 1 tube locally.

Plasma
- Draw 3 10ml EDTA lavender top tubes.
- Process per lab manual instructions.
- 1ml plasma in each (9-18) 2ml polypropylene microcentrifuge tubes.
- Send 9 to NINDS repository and store 0-9 tubes locally.
- Pellet in each of 3 tubes. Send 2 tubes to NINDS repository and store 1 tube locally.

4. Date blood samples collected: ________________

(RNA – PAXgene RED TOP)

5. Blood for PAXgene/RNA: (0 = Not collected, 1 = Collected)

5a. Time of PAXgene/RNA sample collection: (24-hours at room temperature) ________________ : ________

5b. Date PAXgene/RNA samples placed in freezer: ________________

5c. Time PAXgene/RNA samples placed in freezer: ________ : ________

5d. Storage temperature: (Celsius) ________

5e. Total number of tubes: ________

5e1. Shipped to NINDS repository: ________

5e2. Retained at site: ________
(PLASMA – EDTA PURPLE TOP)

6. Blood for plasma: (0 = Not collected, 1 = Collected)
   6a. Time of plasma sample collection: (24-hour clock)
   6b. Time of centrifugation: (24-hour clock)
   6c. Rate of centrifugation: (xg)
   6d. Duration of centrifugation: (minutes)
   6e. Indicate temperature at which tubes were spun: (Celsius)
   6f. Total volume of plasma aliquotted after spinning: (milliliters)
   6g. Total number of plasma aliquot tubes:
      6g1. Shipped to NINDS repository:
      6g2. Retained at site:
   6h. Time plasma and pellet samples placed either in freezer or on dry ice: (24-hour clock)
   6i. Storage temperature: (Celsius)
   6j. Total number of pellet tubes:
      6j1. Shipped to NINDS repository:
      6j2. Retained at site:

Comments:

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
SALIVA AND URINE SAMPLES

1. Date samples collected:
   1. [ ] [ ] [ ]

2. Saliva: (0 = Not collected, 1 = Collected)
   2. [ ]

   2a. Time saliva sample collection was begun: (24-hour clock)
       2a. [ ] [: ]

   2b. Number of minutes needed to collect saliva:
       2b. [ ]

   2c. Amount of saliva collected: (ml)
       2c. [ ] .

   Saliva treated with protease inhibitor

   2d. Amount of protease inhibitor added to saliva sample: (microliters)
       2d. [ ] [ ] [ ]

   2e. Time centrifugation was begun: (24-hour clock)
       2e. [ ] [: ]

   2f. Rate of centrifugation: (xg)
       2f. [ ] [ ] [ ]

   2g. Duration of centrifugation: (minutes)
       2g. [ ] [ ]

   2h. Indicate temperature at which tubes were spun: (celsius)
       2h. [ ]

   2i. Time tubes placed in freezer: (24-hour clock)
       2i. [ ] [: ]

   2j. Storage temperature: (celsius)
       2j. [ ] -

   2k. Total number of supernatant aliquot tubes:
       2k. [ ]

       2k1. Shipped to NINDS repository:
           2k1. [ ]

       2k2. Retained at site:
           2k2. [ ]
URINE

3. Urine: (0 = Not collected, 1 = Collected)

3a. Time of urine sample collection: (24-hour clock)

3b. Time centrifugation was begun: (24-hour clock)

3c. Rate of centrifugation: (xg)

3d. Duration of centrifugation: (minutes)

3e. Indicate temperature at which tubes were spun: (celsius)

3f. Time tubes placed in freezer: (24-hour clock)

3g. Storage temperature: (celsius)

3h. Total number of urine tubes:

3h1. Shipped to NINDS repository:

3h2. Retained at site:

Comments:

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
Clinical Lab Collection

Instructions: (for detailed instructions please refer to the lab manual)
Please note: Do not use barcode labels for clinical labs. Please label clinical labs as required by the local lab.

CBC, platelets:
- Draw 10ml EDTA lavender top tube.
- Send to local lab.

PT/PTT:
- Draw 1 light blue top tube (citrate).
- Send to local lab.

1. Blood for clinical labs: (0 = Not collected, 1 = Collected)
   If Not Collected (0), provide reason in Comments.
   1a. Date sent to lab: 

Please transcribe results for the clinical labs onto the CRF

2. WBC
3. RBC
4. Hemoglobin
5. Hematocrit
6. Platelet count
7. PT
8. INR
9. PTT

INTERPRETATION

10. Clinical lab results are:
   1 = Normal (qualifies for lumbar puncture)
   2 = Abnormal, not clinically significant (qualifies for lumbar puncture)
   3 = Abnormal, clinically significant (does not qualify for lumbar puncture)

Comments: _________________________________________________________________
______________________________________________________________________
CSF Sample Collection

Instructions: (for detailed instructions please refer to the lab manual)

- Draw 50ml conical tube, mix well and then divide into 2 15ml conical tubes and spin.
- Separate into 10-18 2ml tubes.
- Send 10 tubes to NINDS repository.
- Store 0-8 tubes locally.
- Send two 1ml purple top tubes to local lab for analysis.

1. Lumbar puncture for collection of CSF:
   (0 = Not Done, 1 = Collected, 2 = Partial Collection, 3 = Attempted, no collection)
   If response is 0, 2 or 3, specify in comments.

2. Date CSF collected:

3. Indicate needle used to collect CSF:
   1 = 20g Quincke (sharp bevelled) needle
   2 = 22g Quincke (sharp bevelled) needle
   3 = 25g Quincke (sharp bevelled) needle
   4 = 22g Sprotte (atraumatic) needle
   5 = 24g Sprotte (atraumatic) needle (preferred)
   6 = 18g

4. Indicate method of collecting the CSF:
   1 = Gravity
   2 = Syringe suction

5. Lumbar puncture performed at the:
   0 = L2-L3 Interspace
   1 = L3-L4 Interspace
   2 = L4-L5 Interspace
   3 = Unknown

6. Subject position when lumbar puncture performed:
   1 = Sitting, leaned over (preferred)
   2 = Lying, curled up on side
   3 = Unknown
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<th>Question</th>
<th>Answer</th>
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<tr>
<td>7. Time CSF collection completed: (24-hour clock)</td>
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<td>8. Volume of CSF collected prior spinning: (milliliters)</td>
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<td>9. Time CSF was centrifuged: (24-hour clock) (Within 15 minutes from sample collection)</td>
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<td>10. Rate of centrifugation for the CSF sample: (xg)</td>
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<td>11. Temperature at which CSF tube was spun: (Celsius)</td>
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<td>12. Time CSF sample aliquotted: (24-hour clock)</td>
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<td>13. Total volume of CSF aliquotted after spinning: (milliliters)</td>
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<td>14. Total number of aliquot tubes:</td>
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<td>14a. Shipped to NINDS repository:</td>
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<td>14b. Retained at site:</td>
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<td>15. Was part of sample discarded due to a bloody tap? (0 = No, 1 = Yes)</td>
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<td>16. Time samples were either placed in freezer or placed on dry ice:</td>
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<td>(24-hour clock)</td>
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<td>16a. Storage temperature if placed in freezer: (Celsius)</td>
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<td>17. Was part of the sample sent to local lab for analyses? (0 = No, 1 = Yes)</td>
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<td>If No, specify in Comments.</td>
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18. What is the white blood cell count?  
18b. Indicate units:  
☐ Per cubic millimeter  ☐ Per microliter  ☐ Per liter  ☐ Other__________

19. What is the red blood cell count?  
19b. Indicate units:  
☐ Per cubic millimeter  ☐ Per microliter  ☐ Per liter  ☐ Other__________

20. What is the total protein?  
20a. Indicate units:  
☐ mg/dL  ☐ g/dL  ☐ g/L

21. What is the total glucose?  
21a. Indicate units:  
☐ mg/dL  ☐ mmol/L

22. Was a fluoroscopy performed? (0 = No, 1 = Yes)  
22a. Date of fluoroscopy:  
MM DD YYYY

23. Was a lumbar spine film performed? (0 = No, 1 = Yes)  
23a. Date of spine film:  
MM DD YYYY

24. Was an ultrasound performed? (0 = No, 1 = Yes)  
24a. Date of ultrasound:  
MM DD YYYY

Comments:
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I have reviewed all data reported for this visit and determined that they are complete, accurate, and consistent with available source documents. All data were reported by me, or by a person who has been delegated these responsibilities.

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**BioFIND**

**VISIT STATUS**

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**NOTE:** Visit Status form is required for each study visit and telephone contact whether or not the visit or call was actually performed.

1. Visit Completed: (0 = No, 1 = Yes)

   1. □

1a. If response to question 1 is Yes (1), then were the assessments performed: (1 = In person, 2 = By phone)

   1a. □

2. Visit conducted by:

   2a. Investigator (0 = No, 1 = Yes)
   2b. Sub-Investigator (0 = No, 1 = Yes)
   2c. Coordinator (0 = No, 1 = Yes)
   2d. Co-Coordinator (0 = No, 1 = Yes)

   2a. □  2b. □  2c. □  2d. □

3. Indicate why visit not done:

   1 = Scheduling issue with the subject
   2 = Scheduling issue with the staff
   3 = Family/social issues with the subject
   4 = Subject did not respond to attempts to schedule study visit
   5 = Travel distance
   6 = Medical problems
   7 = Military duty
   8 = Financial issues
   9 = Lost to follow up (complete Conclusion of Study Participation form)
   10 = Other: ________________________________
   11 = Institutionalized

   3. □

4. Were all assessments for this visit completed? (0 = No, 1 = Yes)

   If No (0), please note assessments not completed in Comments.

   4. □
In addition to the protocol required assessments specific to this visit, the following tasks were completed at this visit when applicable:

5.1  Status of Concomitant Medication Log: (1 = Updated log at this visit, 2 = No data updates to log; log is not blank, 3 = Subject has not reported taking any concomitant medications; log is blank)

5.2  Status of Adverse Event Log: (1 = Updated log at this visit, 2 = No data updates to log; log is not blank, 3 = Subject has not reported any events; log is blank)

• Reviewed reports (e.g., labs) and recorded any clinically significant values on the Adverse Event Log.

Comments:

_______________________________________________________________________
_______________________________________________________________________
_______________________________________________________________________
**BioFIND**

**ADVERSE EVENT LOG**

Record all adverse events that occur during LP through the 7-10 day follow-up period following the LP. Record disease entity as AE only if it worsens beyond what investigator expects is within normal range of fluctuation for this subject. Elicit adverse event data by asking an open-ended question, e.g., “What unusual symptoms or medical problems have you experienced since the last visit?” Record any new or change in ongoing sign or symptom as well as any event that has resolved since last evaluation. Enter each change in “severity” on new line. Date: Please specify if the Start and Stop dates are ACTUAL or ESTIMATED. If the exact date is unknown, please enter your best reasonable estimate of the date and specify which part(s) are estimated. IF EVENT IS A SERIOUS ADVERSE EVENT, please refer to the Operations Manual for reporting guidance.

<table>
<thead>
<tr>
<th>AE # (e.g., 1, 2, etc.)</th>
<th>Adverse Event (Record diagnosis if known)</th>
<th>START DATE (MM/DD/YYYY)</th>
<th>STOP DATE (MM/DD/YYYY)</th>
<th>Severity</th>
<th>SAE</th>
<th>Relationship to Study*</th>
<th>Related to Study Procedure</th>
<th>Complete when resolved or at Final Visit</th>
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<td>Primary Outcome</td>
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<td>1 = Actual (ACT)</td>
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<td>2 = Day Est. (DAY)</td>
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<td>3 = Mon/Day Est (MD)</td>
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<td>4 = Month Est. (MON)</td>
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<td>0 = No</td>
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<td>1 = Yes</td>
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</table>

* If 3, 4 or 5 are selected, complete “Related to Study Procedure”.

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Copyright © 2002 University of Rochester. All Rights Reserved.  (6/24/09) TSO  5/30/13  Page ___ of ___
<table>
<thead>
<tr>
<th>Row #</th>
<th>MEDICATION (List generic name, if possible)</th>
<th>DOSE</th>
<th>UNITS (e.g., mg, ml, units)</th>
<th>FREQUENCY (e.g., qd, BID, tid, etc.)</th>
<th>ROUTE</th>
<th>START DATE (MM/DD/YYYY)</th>
<th>STOP DATE (MM/DD/YYYY)</th>
<th>ONGOING</th>
<th>INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>paroxetine hydrochloride</td>
<td>20</td>
<td>mg</td>
<td>qd</td>
<td>3</td>
<td>10/30/2003</td>
<td>10/31/2003</td>
<td>0</td>
<td>depression</td>
</tr>
</tbody>
</table>

**Note:**
- **MEDICATION**: Record the generic name of the medication. If the generic name is unknown, record the brand name.
- **DOSE**: Specify the dose for each administration.
- **UNITS**: Indicate the units of measurement (e.g., mg, ml, units).
- **FREQUENCY**: Specify the frequency of administration (e.g., qd, BID, tid, etc.).
- **ROUTE**: Specify the route of administration (e.g., IV, IM, PO, SC, PR, Sublingual, Inhaled, Topical, Other).
- **START DATE**: Enter the start date in the format MM/DD/YYYY. Specify if the date is actual or estimated.
- **STOP DATE**: Enter the stop date in the format MM/DD/YYYY. Specify if the date is actual or estimated.
- **ONGOING**: Indicate whether the medication is still being taken at the end of the study (0 = No, 1 = Yes).
- **INDICATION**: Record the reason for use, not the drug category.
- **PD MED?**: Indicate whether the medication is a Parkinson's disease medication (0 = No, 1 = Yes).
6. Date Investigator determined and/or agreed that subject would conclude study activities:

1. Indicate subject status:
   1 = Subject completed study per protocol
   2 = Subject discontinued participation before the planned study conclusion
   3 = Subject completed study due to early conclusion of the study

4. Who was the primary person to make the decision to withdraw the subject from participation?
   01 = Subject
   02 = Investigator
   03 = Clinical Monitor
   04 = Sponsor
   05 = Primary Care Physician
   06 = Informant / Caregiver
   99 = Other, specify:______________________________

5. What was the primary reason for the subject’s early discontinuation of the study?
   01 = Death of subject
   02 = Adverse Event (complete AE Log)
   06 = Inability to continue giving consent
   07 = Unwilling/unable to commit time and/or resources, moved from area, etc.
   08 = Institutionalized
   09 = Lost to Follow-up
   12 = Reason specified by the protocol
   99 = Other, specify______________________________
If subject has ongoing AEs at 7-10 day LP follow-up call, follow for 30 days from LP or until resolved or stabilized (whichever occurs first).

<table>
<thead>
<tr>
<th>Corresponding AE# from AE Log</th>
<th>AE to be followed</th>
<th>Date of contact by site (MM/DD/YYYY)</th>
<th>Has this AE resolved since the final visit? 0 = No 1 = Yes</th>
<th>If Yes, date of resolution (MM/DD/YYYY)</th>
<th>If the AE has not resolved, is it stable/chronic? 0 = No 1 = Yes N = Resolved</th>
<th>Comments (*If No (0), comment required)</th>
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</tbody>
</table>

INVESTIGATOR'S SIGNATURE: [Signature]

DATE: 5/30/13

STAFF CODE: [Code]
<table>
<thead>
<tr>
<th>Subject ID Enrollment ID</th>
<th>CTCC Unique ID</th>
<th>Date of Enrollment</th>
<th>Initials</th>
<th>Date of Birth</th>
<th>Subject's Full Name/Address</th>
<th>Subject's Phone Number</th>
<th>Email Address (optional)</th>
</tr>
</thead>
</table>

**At Close out:**

Investigator Signature

(3/11/10)
The purpose of this log is to document the delegation of trial specific duties by the Investigator (individual responsible for the conduct of the study) to other site research personnel on the team. List individuals delegated significant study-related tasks (ICH Guideline 4.1.5). Signatures and initials are required for all individuals authorized to make entries and/or corrections on Case Report Forms (ICH Guideline 8.3.24).

<table>
<thead>
<tr>
<th>Print Full Name/ Academic Degree</th>
<th>Signature</th>
<th>Initials</th>
<th>Role in Study</th>
<th>Key Delegated Study Tasks</th>
<th>Dates of Involvement MM/DD/YYYY</th>
<th>Investigator Initials/Date</th>
</tr>
</thead>
<tbody>
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1Indicate primary role in study from this list: Investigator, Sub-investigator, Coordinator, Co-Coordinator, Back-up Coordinator, Cognitive Rater, Neuropsych Rater, Regulatory, Data Entry, Pharmacist.

2Select relevant key study tasks delegated by the Investigator:

- 1 = Assess eligibility
- 2 = Obtain informed consent
- 3 = Clinical assessments
- 4 = Obtain medical history
- 5 = Conduct physical exam
- 6 = Conduct neurological exam
- 7 = Source document/CRF completion
- 8 = Data entry
- 9 = Resolving data queries
- 10 = Regulatory document maintenance
- 11 = Specimen collection/shipping
- 12 = Assess adverse events and SAEs
- 13 = Report SAEs
Directions for Completion of the Delegation Log

• The site Investigator (individual responsible for the conduct of the study) is required to complete an entry on the log.

• The site Investigator will initial/date each entry as site research personnel are added to the form. Initials and date indicate authorization of study-specific responsibilities and confirms that site research personnel are familiar with the study details and are appropriately qualified and trained.

• If there is a change in site Investigator, the previous site Investigator will be end dated and the new site Investigator will complete an entry on the log. Any subsequent new or replacement staff must then be authorized by the new site Investigator.

• All site research personnel should be entered on the log once study-related tasks/procedures have been assigned. This would be at the time the site is selected to participate in the study, or as new/replacement staff are delegated study tasks.

• The “To” date should indicate the date the study staff ended the delegated study task(s) or at the time of database lock (whichever comes first).

• Role in study should list the site research personnel’s primary role/function in the study.

• The form should be updated during the course of the study as needed and a copy submitted to the CTCC study specific Project Manager as updates are made.

• A copy of the completed form(s) with page numbers completed will be requested by the CTCC Project Manager at the time of study close out/database lock.

• The original form should be maintained at the site in the study regulatory/study file.