

Form D1c: Biological and Clinical Staging

ADRC: _____ PTID: _____

Form date: ____/____/____

Visit #: _____

Examiner's
initials: _____
 Language:
☐ 1 English
☐ 2 Spanish

Was this form completed?

☐ 1 Completed☐ 0 Not completed (reason): _____

Key (not completed reason):

88 = Optional

Section 1 – Categorization of fluid analyte and imaging biomarkers

Biomarkers are categorized in this section based on four criteria:

1. Identify three broad mechanistic groupings
2. Subclassify based on the proteinopathy or pathophysiologic pathway that each biomarker measures (e.g., A,T,N, etc.)
3. Within the Core category, distinguish between Core 1 and Core 2 biomarkers
4. Imaging and fluid analyte biomarkers are listed separately within each category

Core Biomarkers

Core 1

A (A β proteinopathy) and T₁ (phosphorylated and secreted AD tau)

CSF or plasma analytes

Plasma

1. Were plasma biomarkers used in the etiologic diagnosis?
- ☐
- 0 No (SKIP TO QUESTION 2)
- ☐
- 1 Yes

If yes, select all plasma biomarkers that were used:

- 1a.
- ☐
- 1 p-tau 217

If checked:

1a1. p-tau 217 result

☐ 0 Normal☐ 1 Abnormal

1a2. Where were the p-tau 217 values used in the diagnosis analyzed?

☐ 1 Analyzed by NCRAD☐ 2 Analyzed in-house or elsewhere☐ 9 Unknown

1a3. Was the plasma p-tau 217 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?

☐ 0 No☐ 1 Yes☐ 9 Unknown

- 1b.
- ☐
- 1 %p-tau 217

If checked:

1b1. %p-tau 217 result

☐ 0 Normal☐ 1 Abnormal

1b2. Was the plasma %p-tau 217 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?

☐ 0 No☐ 1 Yes☐ 9 Unknown

*%p-tau values not currently analyzed by NCRAD; only available in-house or elsewhere

- 1c.
- ☐
- 1 Other plasma biomarker (SPECIFY): _____

If checked:

1c2. Other plasma biomarker result

☐ 0 Normal☐ 1 Abnormal

1c3. Where were the other plasma biomarker values used in the diagnosis analyzed?

☐ 1 Analyzed by NCRAD☐ 2 Analyzed in-house or elsewhere☐ 9 Unknown

1c4. Was the plasma sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?

☐ 0 No☐ 1 Yes☐ 9 Unknown

CSF or plasma analytes*continued...***CSF**

2. Were CSF biomarkers used in the etiologic diagnosis?
- ☐
- 0 No (
- SKIP TO QUESTION 3**
-)
- ☐
- 1 Yes

If yes, select all CSF biomarkers that were used:

- 2a.
- ☐
- 1 p-tau 181/ A
- β
- 42

If checked:

- 2a1. p-tau 181/ A
- β
- 42 result
- ☐
- 0 Normal
- ☐
- 1 Abnormal

- 2a2. Where were the p-tau 181/ A
- β
- 42 values used in the diagnosis analyzed?
- ☐
- 1 Analyzed by NCRAD
-
- ☐
- 2 Analyzed in-house or elsewhere
-
- ☐
- 9 Unknown

- 2a3. Was the CSF p-tau 181/ A
- β
- 42 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?
- ☐
- 0 No
-
- ☐
- 1 Yes
-
- ☐
- 9 Unknown

- 2b.
- ☐
- 1 t-tau / A
- β
- 42

If checked:

- 2b1. t-tau / A
- β
- 42 result
- ☐
- 0 Normal
- ☐
- 1 Abnormal

- 2b2. Was the CSF t-tau / A
- β
- 42 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?
- ☐
- 0 No
-
- ☐
- 1 Yes
-
- ☐
- 9 Unknown

**t-tau values not currently analyzed by NCRAD; only available in-house or elsewhere*

- 2c.
- ☐
- 1 A
- β
- 42 / 40

If checked:

- 2c1. A
- β
- 42 / 40 result
- ☐
- 0 Normal
- ☐
- 1 Abnormal

- 2c2. Where were the A
- β
- 42 / 40 values used in the diagnosis analyzed?
- ☐
- 1 Analyzed by NCRAD
-
- ☐
- 2 Analyzed in-house or elsewhere
-
- ☐
- 9 Unknown

- 2c3. Was the A
- β
- 42 / 40 sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?
- ☐
- 0 No
-
- ☐
- 1 Yes
-
- ☐
- 9 Unknown

- 2d.
- ☐
- 1 Other CSF biomarker (
- SPECIFY**
-): _____

If checked:

- 2d2. Other CSF biomarker result
- ☐
- 0 Normal
- ☐
- 1 Abnormal

- 2d3. Where were the other CSF biomarker values used in the diagnosis analyzed?
- ☐
- 1 Analyzed by NCRAD
-
- ☐
- 2 Analyzed in-house or elsewhere
-
- ☐
- 9 Unknown

- 2d4. Was the CSF sample used in the diagnosis from a date within +/- 12 months of the current UDS visit?
- ☐
- 0 No
-
- ☐
- 1 Yes
-
- ☐
- 9 Unknown

Imaging**Amyloid PET**

3. Was Amyloid PET used in the etiologic diagnosis?
- ☐
- 0 No (
- SKIP TO QUESTION 4**
-)
- ☐
- 1 Yes

- 3a. Amyloid PET result:
- ☐
- 0 Not elevated
- ☐
- 1 Elevated

- 3b. How were amyloid PET results obtained (
- select all that apply*
-)?
- ☐
- 1 Visual read
- ☐
- 1 Quantitative

- 3c. Where were amyloid PET results obtained?
- ☐
- 1 Central (CLARiTi, ADNI, LEADS, SCAN)
-
- ☐
- 2 Local or other interpretation (e.g., other clinical trials)
-
- ☐
- 9 Unknown

- 3d. Was the amyloid PET scan used in the diagnosis from a date within +/- 12 months of the current UDS visit?
- ☐
- 0 No
-
- ☐
- 1 Yes
-
- ☐
- 9 Unknown

Core 2**T₂** (AD tau proteinopathy)

4. Was tau PET used in the etiologic diagnosis? ☐ 0 No (**SKIP TO QUESTION 5**) ☐ 1 Yes

MTL

- 4a. Tau PET MTL result: ☐ 0 Not elevated ☐ 1 Elevated
- 4b. How were tau PET MTL results obtained (*select all that apply*)? ☐ 1 Visual read ☐ 1 Quantitative
- 4c. Where were tau PET MTL results obtained? ☐ 1 Central (CLARiTi, ADNI, LEADS, SCAN)
☐ 2 Local or other interpretation (e.g., other clinical trials)
☐ 9 Unknown

Neocortical

- 4d. Tau PET Neocortical result: ☐ 0 Not elevated ☐ 1 Elevated
- 4e. How were tau PET neocortical results obtained (*select all that apply*)? ☐ 1 Visual read ☐ 1 Quantitative
- 4f. Where were tau PET neocortical results obtained? ☐ 1 Central (CLARiTi, ADNI, LEADS, SCAN)
☐ 2 Local or other interpretation (e.g., other clinical trials)
☐ 9 Unknown
- 4g. Was the tau PET scan used in the diagnosis from a date within +/- 12 months of the current UDS visit? ☐ 0 No
☐ 1 Yes
☐ 9 Unknown

Biomarkers of non-AD co-pathology**V** (vascular brain injury)**Infarction on MRI or WMH consistent with ischemia**

5. Was infarction on MRI or WMH consistent with ischemia or blood products consistent with CAA used in the etiologic diagnosis? ☐ 0 No (**SKIP TO QUESTION 6**) ☐ 1 Yes
- 5a. Imaging result: ☐ 1 Infarction on MRI (*select all that apply below*)
☐ 1 Lacunar
☐ 1 Cortical
☐ 1 Microbleeds
☐ 1 WMH
☐ 1 Superficial siderosis
☐ 1 Other (**SPECIFY**): _____
- 5b. Was the imaging scan used in the diagnosis from a date within +/- 12 months of the current UDS visit? ☐ 0 No
☐ 1 Yes
☐ 9 Unknown

S (α-synuclein)**αSyn-SAA***

6. Was αSyn-SAA used in the etiologic diagnosis: ☐ 0 No (**SKIP TO QUESTION 7**) ☐ 1 Yes
- 6a. αSyn-SAA result: ☐ 0 Normal ☐ 1 Abnormal
- 6b. αSyn-SAA assay: ☐ 1 CSF
☐ 2 Other (**SPECIFY**): _____
- 6c. Where were αSyn-SAA values obtained? _____
- 6d. Was the αSyn-SAA sample used in the diagnosis from a date within +/- 12 months of the current UDS visit? ☐ 0 No
☐ 1 Yes
☐ 9 Unknown

* If a fluid analyte is presently informative only when measured in CSF this is denoted by (*), if informative with plasma or CSF then no specific notation added

Biomarkers of non-AD co-pathology*continued...*

7. Did the participant meet the AA biological biomarker criteria for Alzheimer's based on a positive Core 1 biomarker? ☐ 0 No (**END FORM HERE**)
☐ 1 Yes

8. Which Core 1 biomarker was used to make this determination (*select all that apply*)?

Imaging:☐ 1 Amyloid PET**Plasma:**☐ 1 p-tau217☐ 1 %p-tau217**CSF:**☐ 1 p-tau181/A β 42☐ 1 t-tau/A β 42☐ 1 A β 42/40**Other (SPECIFY):****Section 2 – Biological staging for individuals on the Alzheimer's disease continuum**

Use the information above to select the biological stage of the participant:

	Initial-stage biomarkers	Early-stage biomarkers	Intermediate- to advanced-stage biomarkers	
	Amyloid PET	Tau PET medial temporal region	Tau PET neocortical uptake	
PET	A+T ₂₋	A+T _{2MTL+}	A+T _{2MOD+2HIGH+}	
9. Select the biological stage of the participant:	☐ 1 (A)	☐ 2 (B)	☐ 3 (C-D)	☐ 9 Unable to determine stage (e.g., missing necessary biomarkers like tau PET)

Section 3 – Clinical staging for individuals on the Alzheimer’s disease continuum

Stage 0 Asymptomatic, deterministic gene

- No evidence of clinical change. Biomarkers in normal range.
**Participants with Down Syndrome may not be fully independent even in stage 0 because of underlying intellectual disability. In these participants, decline in functional independence from baseline may be a more appropriate indicator of stage.*

Stage 1 Asymptomatic, biomarker evidence only

- Performance within expected range on objective cognitive tests.
- No evidence of recent cognitive decline or new symptoms.

Stage 2 Transitional decline: Mild detectable change, but minimal impact on daily function

- Normal performance within expected range on objective cognitive tests.
- Decline from previous level of cognitive or neurobehavioral function that represents a change from individual baseline within the past 1 to 3 years, and has been persistent for at least 6 months.
- May be documented by evidence of subtle decline on longitudinal cognitive testing, which may involve memory or other cognitive domains but performance still within normal range.
- May be documented through subjective report of cognitive decline (SCD).
- May be documented with recent-onset change in mood, anxiety, motivation not explained by life events.
- Remains fully independent with no or minimal functional impact on activities of daily living (ADLs).

Stage 3 Cognitive impairment with early functional impact

- Performance in the impaired/abnormal range on objectives cognitive tests.
- Evidence of decline from baseline, documented by the individual’s report or by an observer’s (e.g., study partner) report or by change on longitudinal cognitive testing or neurobehavioral assessments.
- Performs daily life activities independently but cognitive difficulty may result in detectable functional impact on complex ADLs (i.e., may take more time or be less efficient but still can complete — either self-reported or corroborated by an observer).

Stage 4 Dementia with mild functional impairment

- Progressive cognitive and mild functional impairment on instrumental ADLs, with independence in basic ADLs.

Stage 5 Dementia with moderate functional impairment

- Progressive cognitive and moderate functional impairment on basic ADLs requiring assistance.

Stage 6 Dementia with severe functional impairment

- Progressive cognitive and functional impairment, and complete dependence for basic ADLs.

10. Clinical AD stage

- ☐ 0 Stage 0
☐ 1 Stage 1
☐ 2 Stage 2
☐ 3 Stage 3
☐ 4 Stage 4
☐ 5 Stage 5
☐ 6 Stage 6
☐ 9 Unable to determine stage