Form D1b: Biomarkers used to support Etiological Diagnosis

ADRC: _____ PTID: _____ Form date: __ __ / __ __ / __ __ __ __ Visit #: _____ Examiner's initials: _____

Language:	Mode:	Key (remote reason):
☐1 English ☐2 Spanish	☐1 In-person ☐2 Remote *(reason):* ___ ☐1 Telephone ☐2 Video	*1=Too cognitively impaired* *2=Too physically impaired* *3=Homebound or nursing home* *4=Refused in-person visit* *5=Other*

***INSTRUCTIONS**: This form is to be completed by the clinician for all participants, including cognitively unimpaired. For additional clarification and examples, see* **UDS Coding Guidebook** *for* **Form D1b**. *Check only <u>one</u> box per question.*

1. Were any biomarker results used to support the current etiological diagnosis? *(Consider any biomarker results from any time that may be clinically relevant)*
☐0 No **(SKIP TO QUESTION 12)**
☐1 Yes **(CONTINUE TO QUESTION 2)**

Section 1 – Biomarkers and imaging

Complete this section if any of the following biomarker measures were used to **<u>support or exclude</u>** a presumed etiological diagnosis, including unimpaired individuals who have biomarker characterization. Please complete the checklist below for each data source available and the related questions for each supporting data. Then complete **Section 2: Etiological Diagnosis**. This section is not intended to capture actual data values or register sample availability; instead this section's purpose is to record what information was used by the clinician (or at consensus) to inform an etiological diagnosis.

Fluids

2. **Fluid Biomarkers** – Were fluid biomarkers used for assessing the etiological diagnosis?
☐0 No **(SKIP TO QUESTION 5)**
☐1 Yes, only blood-based biomarkers were used **(CONTINUE TO QUESTION 3, and SKIP QUESTIONS 4 – 4d)**
☐2 Yes, only CSF-based biomarkers were used **(SKIP TO QUESTION 4)**
☐3 Yes, blood- and CSF-based biomarkers were used

Please use the following questions to indicate the results of the fluid biomarker test(s) used by the clinican (or at consensus) to determine the etiological diagnosis at this visit.

If a fluid biomarker was used to exclude an etiological diagnosis, select **0=No**. If a fluid biomarker was found to be consistent with a diagnosis, select **1=Yes**. If a fluid biomarker was found to be indeterminate, select **9**. In cases where one or more of the etiologies listed were not assessed using fluid biomarkers, leave the row blank and this will default to **Not Applicable** in the NACC database.

3. Blood-based biomarkers		No	Yes	Indeterminate
3a.	Consistent with AD	☐0	☐1	☐9
3b.	Consistent with FTLD	☐0	☐1	☐9
3c.	Consistent with LBD	☐0	☐1	☐9
3d.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

4. CSF-based biomarkers		No	Yes	Indeterminate
4a.	Consistent with AD	☐0	☐1	☐9
4b.	Consistent with FTLD	☐0	☐1	☐9
4c.	Consistent with LBD	☐0	☐1	☐9
4d.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

Section 1 – Biomarkers and imaging *continued...*

Imaging

5.	**Imaging** – Was imaging used for assessing etiological diagnosis?	☐0 No **(SKIP TO QUESTION 8)** ☐1 Yes, only PET/SPECT imaging was used **(CONTINUE TO QUESTION 6, and SKIP QUESTIONS 7 – 7a3f)** ☐2 Yes, only MR imaging was used **(SKIP TO QUESTION 7)** ☐3 Yes, PET/SPECT and MR imaging were used

Please use the following questions to indicate the results of the imaging used by the clinican (or at consensus) to determine the etiological diagnosis at this visit.

If imaging was used to exclude an etiological diagnosis, select **0=No**. If imaging was found to be consistent with a diagnosis, select **1=Yes**. If imaging was found to be indeterminate, select **9**. In cases where one or more of the etiologies listed were not assessed using imaging, leave the row blank and this will default to **Not Applicable** in the NACC database.

6. PET/SPECT

6a. Tracer-based PET - Were tracer-based PET measures used in assessing an etiological diagnosis?
☐0 No **(SKIP TO QUESTION 6b)**
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

If used in diagnosis, indicate the results:

		No	Yes	Indeterminate
6a1.	Elevated Amyloid	☐0	☐1	☐9
6a2.	Elevated tau pathology	☐0	☐1	☐9

6b. FDG PET - Was FDG PET data or information used to support an etiological diagnosis?
☐0 No **(SKIP TO QUESTION 6c)**
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

		No	Yes	Indeterminate
6b1.	Consistent with AD	☐0	☐1	☐9
6b2.	Consistent with FTLD	☐0	☐1	☐9
6b3.	Consistent with LBD	☐0	☐1	☐9
6b4.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

6c. Dopamine Transporter (DAT) Scan - Was DAT Scan data or information used to support an etiological diagnosis?
☐0 No
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

6d. Other tracer-based imaging - Were other tracer-based imaging used to support an etiological diagnosis?
(SPECIFY): _____
☐0 No **(SKIP TO QUESTION 7a)**
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

		No	Yes	Indeterminate
6d1.	Consistent with AD	☐0	☐1	☐9
6d2.	Consistent with FTLD	☐0	☐1	☐9
6d3.	Consistent with LBD	☐0	☐1	☐9
6d4.	Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

Section 1 – Biomarkers and imaging *continued...*

7. Structural Imaging

If structural imaging was used in the diagnosis, specify the scan results below:

7a. **Structural Imaging (i.e., MRI or CT)** – Was structural imaging data or information used to support an etiological diagnosis?

☐0 No **(SKIP TO QUESTION 8)**
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

		No	Yes	Indeterminate
7a1.	Atrophy pattern consistent with AD	☐0	☐1	☐9
7a2.	Atrophy pattern consistent with FTLD	☐0	☐1	☐9
7a3.	Consistent with Cerebrovascular disease (CVD)	☐0	☐1	☐9
	If there is evidence for CVD on imaging, indicate the findings (*check all that apply*)**:**			
7a3a.	Large vessel infarct(s)	☐0	☐1	☐9
7a3b.	Lacunar infarct(s)	☐0	☐1	☐9
7a3c.	Macrohemorrhage(s)	☐0	☐1	☐9
7a3d.	Microhemorrhage(s)	☐0	☐1	☐9
7a3e.	Moderate white–matter hyperintensity (CHS score 5–6)	☐0	☐1	☐9
7a3f.	Extensive white–matter hyperintensity (CHS score 7–8+)	☐0	☐1	☐9

Other biomarker modalities *(e.g., tissues, skin, retinal imaging, etc.)*

Please use the following questions to indicate the results of any additional biomarker modalities used by the clinician (or at consensus) to support the etiological diagnosis at this visit.

If a biomarker modality was used to exclude an etiological diagnosis, select **0=No.** If a biomarker modality was found to be consistent with a diagnosis, select **1=Yes**. If a biomarker modality was found to be indeterminate, select **9**. In cases where one or more of the etiologies listed were not assessed using a biomarker modality, leave the row blank and this will default to **Not Applicable** in the NACC database.

8. **Other biomarker modality** - Was another biomarker modality used to support an etiological diagnosis?
(SPECIFY): _____

☐0 No **(SKIP TO QUESTION 11)**
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

		No	Yes	Indeterminate
8a.	☐1 Consistent with AD	☐0	☐1	☐9
8b.	☐1 Consistent with FTLD	☐0	☐1	☐9
8c.	☐1 Consistent with LBD	☐0	☐1	☐9
8d.	☐1 Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

9. **Other biomarker modality** - Was another biomarker modality used to support an etiological diagnosis?
(SPECIFY): _____

☐0 No **(SKIP TO QUESTION 11)**
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

		No	Yes	Indeterminate
9a.	☐1 Consistent with AD	☐0	☐1	☐9
9b.	☐1 Consistent with FTLD	☐0	☐1	☐9
9c.	☐1 Consistent with LBD	☐0	☐1	☐9
9d.	☐1 Consistent with other etiology (**SPECIFY**): _____	☐0	☐1	☐9

Section 1 – Biomarkers and imaging *continued...*

10. Other biomarker modality - Was another biomarker modality used to support an etiological diagnosis?
(SPECIFY): _____

☐0 No **(SKIP TO QUESTION 11)**
☐1 Yes, results were normal or abnormal
☐2 Yes, results were indeterminate

		No	Yes	Indeterminate
10a.	☐1 Consistent with AD	☐0	☐1	☐9
10b.	☐1 Consistent with FTLD	☐0	☐1	☐9
10c.	☐1 Consistent with LBD	☐0	☐1	☐9
10d.	☐1 Consistent with other etiology **(SPECIFY):** _____	☐0	☐1	☐9

Supportive genetics

11. Is there an Autosomal Dominant pathogenic variant to support an etiological diagnosis?

☐0 No
☐1 Yes
☐9 Unknown/Not disclosed

Section 2 – Etiological diagnoses

*Using all the available data (i.e. clincial, cognitive, biomarker, etc) please provide an etiological diagnosis. For those with no biomarker data, enter a **presumed** etiological diagnosis.*

Must be filled out for all participants. Indicate whether a given condition is a primary, contributing, or non-contributing cause of the observed impairment, based on the clinician's best judgment. Select one or more etiological diagnoses from questions *(below)* as **Present**; all others will default to **Absent** in the NACC database >> *only one diagnosis should be selected as* **1 = Primary.**

For unimpaired participants: Indicate the presence of any etiological diagnoses by selecting **1 = Present**, and leave the questions on whether the diagnosis was primary, contributing, or non-contributing blank.

	Etiological Diagnoses	Present		Primary	Contributing	Non-contributing
12.	Alzheimer's disease	☐1	**12a.**	☐1	☐2	☐3
13.	Lewy body disease	☐1	**13a.**	☐1	☐2	☐3
14.	Frontotemporal lobar degeneration	☐1	**14a.**	☐1	☐2	☐3
	If **present**, select one:					
14b1.	Progressive supranuclear palsy (PSP)	☐1	**14b1a.**	☐1	☐2	☐3
14b2.	Corticobasal degeneration (CBD)	☐1	**14b2a.**	☐1	☐2	☐3
14b3.	FTLD with motor neuron disease	☐1	**14b3a.**	☐1	☐2	☐3
14b4.	FTLD NOS	☐1	**14b4a.**	☐1	☐2	☐3
14c.	If FTLD **(QUESTION 13)** is **present**, specify FTLD subtype: ☐1 Tauopathy ☐2 TDP-43 proteinopathy ☐3 Other **(SPECIFY):** _____ ☐9 Unknown					
15.	Vascular brain injury (based on clinical and imaging evidence according to your Center's standards)	☐1	**15a.**	☐1	☐2	☐3
16.	Multiple system atrophy	☐1	**16a.**	☐1	☐2	☐3
17.	Chronic traumatic encephalopathy	☐1	**17a.**	☐1	☐2	☐3
18.	Down syndrome	☐1	**18a.**	☐1	☐2	☐3
19.	Huntington's disease	☐1	**19a.**	☐1	☐2	☐3
20.	Prion disease (CJD, other)	☐1	**20a.**	☐1	☐2	☐3
21.	Cerebral amyloid angiopathy	☐1	**21a.**	☐1	☐2	☐3
22.	LATE: Limbic-predominant age-related TDP-43 encephalopathy	☐1	**22a.**	☐1	☐2	☐3
23.	Other **(SPECIFY):** _____	☐1	**23a.**	☐1	☐2	☐3