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NACC Neuropathology Data Submission Manual

Version 7
(July 2006 Data Freeze)

NOTE: Version 7 is NOT the most current version of the NP form and is no longer used for data submission. For the most current version, please visit http://www.alz.washington.edu.

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(In order by variable NUMBER)

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ALPHABETICAL INDEX OF VARIABLES

(In order by variable NAME)

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General Instructions

A. The NP Data Submission System

The NP data submission system implemented by NACC is to be used for your data submission. This system is available through the NACC website at https://www.alz.washington.edu. Access to the system is under your particular Center's data management menu. Use the following steps to access it.

1. Point browser at https://www.alz.washington.edu
2. Click on "Member Login"
3. Fill in the user name and password then click "OK" (If you do not have an account contact NACC)
4. Click on "The NACC Database"
5. Click on "I accept the terms of this agreement"
6. Click on "The Neuropathology Data Set"
7. Click on the name of your Center
8. Click on "Data Manager Menu"
9. Click on "Neuropathology Data Submission System"

The system is designed to allow an easy way to submit, error-check, verify and process your Center's data into the NACC database.

Data files may be uploaded from your local computer, or data entry can be done on the web. Most Centers will want to submit just new NP IDs and modifications to some previously submitted NP IDs, rather than submitting replacement datasets. However, replacement datasets are also acceptable. Once a final submission has been created, primary and secondary error checks may be run from the website. Alerts and other discrepancies must be verified through the website programs. Once this has been accomplished, the data is processed into the NACC database and certification reports can be created. **NACC must be contacted once you have completed your data submission by clicking on the "Notify NACC" link on the website.**

This system allows the Center's Data Manager to control their data submission to NACC completely through the NACC website.

B. Data Submission Date and Transmission Options

There is no deadline for submitting NP data, and data may be submitted continuously. NACC will freeze the submitted data twice per year, tentatively planned for January 1st and July 1st, and prepare reports.

Be sure to notify NACC once you have finished submitting, error-checking and processing your data using the NP data submission system.

Data may be transmitted in one of three modes.

1. Upload a data file (See above);

2. Web data entry. Use the NP web data entry to enter data directly through NACC's website, https://www.alz.washington.edu (see the section elsewhere in this manual entitled "NACC Neuropathology Web Data Management");

3. Send the paper forms (Neuropathology Data Form) filled out for each NP ID, and let NACC do the data entry. This might be appropriate at sites that have enrolled relatively few subjects.

Data files should be submitted via NACC's website. The website is now using SSL encryption software, so it is not necessary to password protect or zip your file. The data will be protected automatically while it is being uploaded.

C. File Types (if submitting data by file)

NACC will accept three types of files for the Neuropathology Data Submission:

- Fixed-format ASCII files ("flat files")
- SAS files
- SPSS files

These file types are described in more detail below.

Fixed-format ASCII files ("flat files"):

Each variable has a designated column assignment. One blank space has been allotted to separate each item from the next item. If there is no date for a particular item, its position must be filled with the correct number of blanks for that item.

SAS Files:

Two kinds of SAS files may be accepted by NACC:

1. PC SAS Version 7.0 – 9.0 files: These files have an extension of .sas7bdat.
2. SAS transport files – These files can be created on any system that runs SAS. A SAS program must be written to create transport files. If you need help writing the transport program, contact NACC.

SAS files must have all neuropath variables, with each variable having the correct type and length. Extra variables and formatted variables are not allowed.

SPSS Files:

SPSS files must have all neuropathology variables, with each variable of the correct type and length. Extra variables and formatted variables are not allowed. SPSS files must be saved and submitted in the portable file format (with an extension of **.por**).

D. General Coding Instructions

1. Required Items: All data elements in the neuropathology data submission are required, except for NPID.

2. Leading Zeroes and Justification: While entries should be right-justified and leading zeroes avoided, the error-check program accepts leading zeroes as long as the item is right-justified.

3. Missing Codes: Missing codes should be used for missing values from all sources, including "not recorded," "not applicable," "patient refusals," and "unknown" for any reason.

   Data that are missing should be indicated by 9's. *Please fill the entire field with 9's.* For example, if the missing item has one column, enter one 9 in that item's field; if the missing item has two columns, enter two 9's; and so on.

   Missing data, signified by missing codes, may be used in most elements except as noted in the Data Element Dictionary. It is expected that some Centers will not have data for all the items. Please provide as complete a record as possible.

4. Skips and Blanks: Skip patterns occur when you are directed by an item's response to a subsequent item that does not immediately follow the item you are completing. For fixed-format files, the items that are skipped should remain blank and are the only items that should be blank. For SAS files, use a " . " instead of a blank for numeric fields. For character fields, use " ". NOTE: Skip patterns have been removed from NPGROSS and NPVASC.

5. Definition of Valid Date:

   If MONTH = 2, (February), then DAY cannot be greater than 28 except in years that are divisible by 4, in which DAY cannot be greater than 29. If MONTH = 4, 6, 9, or 11, then DAY cannot be greater than 30.

   A year of death (NPDODYR) that precedes 1970 will generate an error. A year of death between 1970 and 1983 will generate an alert, because the earliest funding date for any Center was 1984.

   Dates must occur in the following order (earliest to latest):

   Date of death
   Date neuropath form was completed

E. Error-Check Program

The error-check program is designed to check for and detect unallowable and unlikely values. See the “Error Checking” section for more details about types of errors generated.

We have tried to minimize the contingency checks with this program. We may be contacting individual centers at a later time to discuss specific data contingency problems not included in this program.

Summary of Changes

Changes will be highlighted in **red** in the Data Element Dictionary and on the NP Data Form. In this current version, the following applies:

1. There are no new variables.

2. There are no changes.

Files should be submitted via the NP data submission system on NACC's website, https://www.alz.washington.edu.

NP Data Template

Columns	Variable	Form
1-2	ADCID	0. Center ID (1-2) __ __
4-13	PTID	1. MDS Patient ID (4-13) __ __ __ __ __ __ __ __ __ __
		2. Date form completed:
15-16	NPFORMMO	2a. Month (15-16) __ __
18-19	NPFORMDY	2b. Day (18-19) __ __
21-24	NPFORMYR	2c. Year (21-24) __ __ __ __
26-35	NPID	3. Neuropath ID (26-35) __ __ __ __ __ __ __ __ __ __
37	NPSEX	4. Gender (37) __ 1 Male 2 Female
39-41	NPDAGE	5. Age at Death (39-41) __ __ __
		6. Date of death:
43-44	NPDODMO	6a. Month (43-44) __ __
46-47	NPDODDY	6b. Day (46-47) __ __
49-52	NPDODYR	6c. Year (49-52) __ __ __ __
54	NPGROSS	7. Does the brain have any gross or microscopic pathology (including any Alzheimer type pathology such as senile plaques and neurofibrillary tangles?) (54) 1 Yes 2 No
56	NPNIT	8A. NIA/Reagan Institute neuropathological criteria used: (56) 1 High likelihood of dementia being due to Alzheimer's disease 2 Intermediate likelihood of dementia being due to Alzheimer's disease 3 Low likelihood of dementia being due to Alzheimer's disease 4 Criteria not met 5 Not done 9 Missing/unknown

Columns	Variable	Form
58	NPCERAD	8B. CERAD neuropathological criteria used: (58) 1 Definite Alzheimer's disease 2 Probable Alzheimer's disease 3 Possible Alzheimer's disease 4 Criteria not met 5 Not done 9 Missing/unknown
60	NPADRDA	8C. ADRDA/Khachaturian neuropathological criteria used: (60) 1 Alzheimer's disease 2 Criteria not met 3 Not done 9 Missing/unknown
62	NPOCRIT	8D. Other or unspecified neuropathological criteria used (e.g., Tierney, etc.): (62) 1 Alzheimer's disease, unspecified 2 Criteria not met 3 Not done 9 Missing/unknown
64	NPBRAAK	9. Braak & Braak Neurofibrillary Stage: (64) 1 Stage I 2 Stage II 3 Stage III 4 Stage IV 5 Stage V 6 Stage VI 7 Neurofibrillary degeneration not present 8 Not assessed 9 Missing/unknown
66	NPNEUR	10. Neuritic plaques (plaques with argyrophilic dystrophic neurites with or without dense amyloid cores): (66) 1 Frequent neuritic plaques 2 Moderate neuritic plaques 3 Sparse neuritic plaques 4 No neuritic plaques 5 Not assessed 9 Missing/unknown

Columns	Variable	Form
68	NPDIFF	11. Diffuse plaques (plaques with non-compact amyloid and no apparent dystrophic neurites): (68) 1 Frequent neuritic plaques 2 Moderate neuritic plaques 3 Sparse neuritic plaques 4 No neuritic plaques 5 Not assessed 9 Missing/unknown
70	NPVASC	12. Is ischemic, hemorrhagic or vascular pathology present? (70) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
72	NPLINF	12A. Are one or more large artery cerebral infarcts present? (72) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
74	NPMICRO	12B. Are one or more cortical, microinfarcts (including “granular atrophy”) present? (74) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
76	NPLAC	12C. Are one or more lacunes, (small artery infarcts and/or hemorrhages) present? (76) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
78	NPHEM	12D. Are single or multiple hemorrhages present? (78) 1 Yes 2 No 3 Not assessed 9 Missing/unknown

Columns	Variable	Form
80	NPART	12E. Is subcortical arteriosclerotic leukoencephalopathy present? (80) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
82	NPNEC	12F. Is cortical laminar necrosis present? (82) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
84	NPSCL	12G. Is medial temporal lobe sclerosis (including hippocampal sclerosis) present? (84) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
86	NPAVAS	12H. Is atherosclerotic vascular pathology (of the circle of Willis) present? (86) 1 None 2 Mild 3 Moderate 4 Severe 5 Not assessed 9 Missing/unknown
88	NPARTER	12I. Is arteriosclerosis (small parenchymal arteriolar disease) present? (88) 1 None 2 Mild 3 Moderate 4 Severe 5 Not assessed 9 Missing/unknown

Columns	Variable	Form
90	NPAMY	12J. Is amyloid angiopathy present? (90) 1 None 2 Mild 3 Moderate 4 Severe 5 Not assessed 9 Missing/unknown
92	NPOANG	12K. Is there another type of angiopathy (e.g., CADASIL or arteritis) present? (92) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
94	NPVOTH	12L. Is there other pathology related to ischemic or vascular disease not previously specified present? (94) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
96	NPLEWY	13. Pathology is consistent with criteria of Consortium on Dementia with Lewy Bodies for: (96) 1 Lewy body pathology, brainstem predominant type 2 Lewy body pathology, intermediate or transitional (limbic) type 3 Lewy body pathology, diffuse (neocortical) type 4 Lewy body pathology, unspecified or not further assessed 5 No Lewy bodies 6 Not assessed 9 Missing/unknown
98	NPPICK	14A. Pick's disease: (98) 1 Yes 2 No 3 Not assessed 9 Missing/unknown

Columns	Variable	Form
100	NPCORT	14B. Corticobasal degeneration: (100) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
102	NPPROG	14C. Progressive supranuclear palsy: (102) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
104	NPFRONT	14D. Frontotemporal dementia and Parkinsonism with tau-positive or argyrophilic inclusions: (104) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
106	NPTAU	14E. Tauopathy, other (e.g., tangle-only dementia and argyrophilic grain dementia): (106) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
108	NPFTD	14F. FTD with ubiquitin-positive (tau-negative) inclusions: (108) 1 FTD with motor neuron disease 2 FTD without motor neuron disease 3 None present 4 Not assessed 9 Missing/unknown
110	NPFTDNO	14G. Is there FTD with no distinctive histopathology (tau-negative, ubiquitin-negative, and no argyrophilic inclusions)? (110) 1 Yes 2 No 3 Not assessed 9 Missing/unknown

Columns	Variable	Form
112	NPFTDSPC	14H. Was FTD "not otherwise specified" present (e.g., "immunostaining for ubiquitin and tau not done")? (112) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
114	NPCJ	15A. Is Creutzfeldt-Jakob disease or variant CJD present? (114) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
116	NPPRION	15B. Are other prion diseases present (e.g., Gerstmann-Straussler syndrome)? (116) 1 Yes 2 No 3 Not assessed 9 Missing/unknown
118	NPMAJOR	16A. Are other major pathological disorders present (not addressed by questions 8-15)? (118) 1 Yes 2 No 3 Not assessed 9 Missing/unknown SKIP: If 2, 3, or 9, go to #17A. 16B. If 16A is yes, specify below (one disorder per line):
120-149	NPMPATH1	1. _____
151-180	NPMPATH2	2. _____
182-211	NPMPATH3	3. _____

Columns	Variable	Form
213	NPGENE	17A. **Family history information relevant to neuropathologic diagnosis:** (213) 1 Family history of similar neurodegenerative disorder 2 Family history of other (dissimilar) neurodegenerative disorder 3 No family history of similar or dissimilar neurodegenerative disorder 4 Family history of both similar and dissimilar neurodegenerative disorder 9 Family history unknown/not available/missing SKIP: If 1, 3, or 9, go to #18A.
215-244	NPFHSPEC	17B. If 17A is 2 or 4, then specify: _____
246	NPAPOE	18A. Apolipoprotein-E: (246) 1 e3, e3 2 e3, e4 3 e3, e2 4 e4, e4 5 e4, e2 6 e2, e2 9 Missing/unknown/not assessed
248	NPTAUHAP	18B. Tau haplotype: (248) 1 H1, H1 2 H1, H2 3 H2, H2 4 Other polymorphism (e.g., A0) 9 Missing/unknown/not assessed
250	NPPRNP	18C. PRNP codon 129: (250) 1 M, M 2 M, V 3 V, V 9 Missing/unknown/not assessed

Columns	Variable	Form
252-253	NPCHROM	19. Genetic or chromosomal abnormalities. (252-253) 1 APP mutation 2 PS1 mutation 3 PS2 mutation 4 Tau mutation 5 α- Synuclein mutation 6 Parkin mutation 7 PRNP mutation 8 Huntingtin mutation 9 Notch 3 mutation (CADASIL) 10 Other known genetic mutation (e.g., ABri, neuroserpin) 11 Down Syndrome 12 Other chromosomal abnormality 13 No known genetic or chromosomal abnormality 50 Not assessed 99 Missing/unknown

NACC Neuropathology
Data Element Dictionary

The data element dictionary is formatted the same as the one in the MDS manual, due to favorable feedback. **Variable names** are indicated in **Blue**. Each variable has its own **Green** box. Each box includes the following information:

Variable Number – Indicates order of appearance on the Neuropathology form.

Variable Name – For non-fixed-format files, variable name must match exactly.

Short Descriptor – Used on the web page to indicate variable.

Neuropathology (NP) Question – The question as it appears on the Neuropathology Data Form.

Length of Field – For fixed field formats, number of columns for this variable.

Column Positions – For fixed field formats, the column numbers for this variable.

SAS Variable Type – For non-fixed field formats, variable type as numerical or character.

SAS Variable Length – For non-fixed field formats, variable length.

Allowable Codes and Missing Codes – List of codes with mapping instructions.

Skips and Blanks – Instructions for skip patterns.

Comments – Other instructions as needed.

NOTE: All data elements are required except NPID.

Variable Number	**0**
Variable Name	**ADCID**
Short Descriptor	**Center**
NP Question	**Center ID**
Length of Field	**2**
Column Positions	**1–2**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–36, Use code below as your Center ID:** 1 = BAYLOR 2 = BOSTON U 3 = CASE WESTERN 4 = COLUMBIA 5 = DUKE 6 = EMORY 7 = MASSACHUSETTS GENERAL 8 = INDIANA U 9 = JOHNS HOPKINS 10 = MAYO 11 = MOUNT SINAI 12 = NEW YORK U 13 = NORTHWESTERN 14 = OREGON HEALTH SCIENCES 15 = RUSH U 16 = U CALIFORNIA, DAVIS 17 = U CALIFORNIA, LOS ANGELES 18 = U CALIFORNIA, SAN DIEGO 19 = U KENTUCKY 20 = U MICHIGAN 21 = U PENNSYLVANIA 22 = U PITTSBURGH 23 = U ROCHESTER 25 = U TEXAS SOUTHWESTERN 26 = U WASHINGTON 27 = WASHINGTON U, SAINT LOUIS 28 = U ALABAMA 30 = U SOUTHERN CALIFORNIA 31 = U CALIFORNIA, IRVINE 32 = STANFORD 33 = U ARIZONA 34 = U ARKANSAS 35 = U CALIFORNIA, SAN FRANCISCO 36 = FLORIDA
Comment	**NOTE: ADCID will be a randomly generated Center ID in the Public Use Data Set.**

Variable Number	**1**
Variable Name	**PTID**
Short Descriptor	**MDS ID**
NP Question	**MDS Patient ID**
Length of Field	**10**
Column Positions	**4–13**
SAS Variable Type	**Character**
SAS Variable Length	**10**
Allowable Codes	**Follow your center's MDS Patient ID scheme**
Comment	MDS Patient ID must be unique within data set from your center (no duplicates). MDS PTID for each subject must be the same at each data submission; MDS PTID cannot change once it has been assigned by your Center. PTID is the same for a given subject at both the MDS Data Call and the Neuropathology Data Submission. **NOTE: PTID is not available to researchers or the public. It is replaced in the accessible MDS database by a randomly generated NACCID**

Variable Number	**2a**
Variable Name	**NPFORMMO**
Short Descriptor	**Date Form Completed**
NP Question	**Date Form Completed: Month**
Length of Field	**2**
Column Positions	**15–16**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–12**
Comment	Must meet criteria for valid date.

Variable Number	**2b**
Variable Name	**NPFORMDY**
Short Descriptor	**Date Form Completed**
NP Question	**Date form completed: Day**
Length of Field	**2**
Column Positions	**18–19**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–31**
Comment	Must meet criteria for valid date.

Variable Number	**2c**
Variable Name	**NPFORMYR**
Short Descriptor	**Date Form Completed**
NP Question	**Date form completed: Year**
Length of Field	**4**
Column Positions	**21–24**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**2001 – current year**
Comment	Must meet criteria for valid date.

Variable Number	**3**
Variable Name	**NPID**
Short Descriptor	**Neuropath ID**
NP Question	**Neuropath ID**
Length of Field	**10**
Column Positions	**26–35**
SAS Variable Type	**Character**
SAS Variable Length	**10**
Allowable Codes	**Follow your center's Neuropathology Patient ID scheme**
Comment	Neuropath ID number must be unique within data set from your center (no duplicates). NPID for each subject must be the same each time data are submitted or received; NPID cannot change once it has been assigned by your Center. **NOTE: NPID will not be available in the Public Use Data Set.**

Variable Number	**4**
Variable Name	**NPSEX**
Short Descriptor	**Gender**
NP Question	**Subject's sex**
Length of Field	**1**
Column Positions	**37**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1 or 2** 1 = Male 2 = Female
Comment	***Missing (9s) not allowed.*** Must be same as MDS data element SEX.

Variable Number	**5**
Variable Name	**NPDAGE**
Short Descriptor	**Age at Death**
NP Question	**Age at Death**
Length of Field	**3**
Column Positions	**39–41**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**0–130**
Comment	**NPDAGE must be rounded down (not up)** **Calculate the death age, then drop any decimal portion. For Example, if the death age is 81.9 then NPDAGE = 81.**

Variable Number	**6a**
Variable Name	**NPDODMO**
Short Descriptor	**Date of Death**
NP Question	**Subject's date of death: Month**
Length of Field	**2**
Column Positions	**43–44**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–12**
Missing Code	**99**
Comment	Must be same date as in MDS. Must meet criteria for valid date. Must be before the NP data form completed (2).

Variable Number	**6b**
Variable Name	**NPDODDY**
Short Descriptor	**Date of Death**
NP Question	**Subject's date of death: Day**
Length of Field	**2**
Column Positions	**46–47**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Missing Code	**99**
Allowable Codes	**1–31**
Comment	Must be same date as in MDS. Must meet criteria for valid date. Must be before the NP data form completed (2).

Variable Number	**6c**
Variable Name	**NPDODYR**
Short Descriptor	**Date of Death**
NP Question	**Subject's date of death: Year**
Length of Field	**4**
Column Positions	**49–52**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**Cannot precede 1970; in most cases, should not precede 1984.**
Comment	Must be same date as in MDS. Must meet criteria for valid date. Must be before the NP data form completed (2).

Variable Number	**7**
Variable Name	**NPGROSS**
Short Descriptor	**Brain have G/M Path**
NP Question	**Does the brain have any gross or microscopic pathology (including any Alzheimer type pathology such as senile plaques and neurofibrillary tangles)?**
Length of Field	**1**
Column Positions	**54**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1, 2** 1 = Yes 2 = No
Comment	Code 9 (no neuropathology diagnosis available) not allowed. SKIP PATTERN REMOVED

Variable Number	**8A**
Variable Name	**NPNIT**
Short Descriptor	**NIA/Reagan Ins Crit**
NP Question	**NIA/Reagan Institute neuropathological criteria used:**
Length of Field	**1**
Column Positions	**56**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–5** 1 = High likelihood of dementia being due to Alzheimer's disease 2 = Intermediate likelihood of dementia being due to Alzheimer's disease 3 = Low likelihood of dementia being due to Alzheimer's disease 4 = Criteria not met 5 = Not Done
Missing Code	9 = Missing/unknown

Variable Number	**8B**
Variable Name	**NPCERAD**
Short Descriptor	**CERAD Criteria**
NP Question	**CERAD neuropathological criteria used:**
Length of Field	**1**
Column Positions	**58**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–5** 1 = Definite Alzheimer's disease 2 = Probable Alzheimer's disease 3 = Possible Alzheimer's disease 4 = Criteria not met 5 = Not done
Missing Code	9 = Missing/Unknown

Variable Number	**8C**
Variable Name	**NPADRDA**
Short Descriptor	**ADRDA/Khach Criteria**
NP Question	**ADRDA/Khachaturian neuropathological criteria used:**
Length of Field	**1**
Column Positions	**60**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Alzheimer's disease 2 = Criteria not met 3 = Not done
Missing Code	9 = Missing/Unknown

Variable Number	**8D**
Variable Name	**NPOCRIT**
Short Descriptor	**Other Criteria**
NP Question	**Other or unspecified neuropathological criteria used (e.g., Tierney, etc.):**
Length of Field	**1**
Column Positions	**62**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Alzheimer's disease, unspecified 2 = Criteria not met 3 = Not done
Missing Code	9 = Missing/Unknown

Variable Number	**9**
Variable Name	**NPBRAAK**
Short Descriptor	**Braak & Braak Stage**
NP Question	**Braak & Braak Neurofibrillary Stage.**
Length of Field	**1**
Column Positions	**64**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–8** 1 = Stage I 2 = Stage II 3 = Stage III 4 = Stage IV 5 = Stage V 6 = Stage VI 7 = Neurofibrillary degeneration not present 8 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**10**
Variable Name	**NPNEUR**
Short Descriptor	**Neuritic Plaques**
NP Question	**Neuritic plaques (plaques with argyrophilic dystrophic neurites with or without dense amyloid cores).**
Length of Field	**1**
Column Positions	**66**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–5** 1 = Frequent neuritic plaques 2 = Moderate neuritic plaques 3 = Sparse neuritic plaques 4 = No neuritic plaques 5 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**11**
Variable Name	**NPDIFF**
Short Descriptor	**Diffuse Plaques**
NP Question	**Diffuse plaques (plaques with non-compact amyloid and no apparent dystrophic neurites).**
Length of Field	**1**
Column Positions	**68**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–5** 1 = Frequent diffuse plaques 2 = Moderate diffuse plaques 3 = Sparse diffuse plaques 4 = No diffuse plaques 5 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12**
Variable Name	**NPVASC**
Short Descriptor	**Isch, Hemor, or Vasc**
NP Question	**Is ischemic, hemorrhagic or vascular pathology present?**
Length of Field	**1**
Column Positions	**70**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown
Comment	SKIP PATTERN REMOVED

Variable Number	**12A**
Variable Name	**NPLINF**
Short Descriptor	**Large Art Infarcts**
NP Question	**Are one or more large artery cerebral infarcts present?**
Length of Field	**1**
Column Positions	**72**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12B**
Variable Name	**NPMICRO**
Short Descriptor	**Mult Microinfarcts**
NP Question	**Are one or more cortical microinfarcts (including "granular atrophy") present?**
Length of Field	**1**
Column Positions	**74**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12C**
Variable Name	**NPLAC**
Short Descriptor	**One or More Lacunes**
NP Question	**Are one or more lacunes (small artery infarcts and/or hemorrhages) present?**
Length of Field	**1**
Column Positions	**76**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12D**
Variable Name	**NPHEM**
Short Descriptor	**Hemorrhages**
NP Question	**Are single or multiple hemorrhages present?**
Length of Field	**1**
Column Positions	**78**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12E**
Variable Name	**NPART**
Short Descriptor	**Arteriosclerotic**
NP Question	**Is subcortical arteriosclerotic leukoencephalopathy present?**
Length of Field	**1**
Column Positions	**80**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12F**
Variable Name	**NPNEC**
Short Descriptor	**Laminar Necrosis**
NP Question	**Is cortical laminar necrosis present?**
Length of Field	**1**
Column Positions	**82**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12G**
Variable Name	**NPSCL**
Short Descriptor	**Sclerosis**
NP Question	**Is medial temporal lobe sclerosis (including hippocampal sclerosis) present?**
Length of Field	**1**
Column Positions	**84**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12H**
Variable Name	**NPAVAS**
Short Descriptor	**Ather Vascular**
NP Question	**Is atherosclerotic vascular pathology (of the circle of Willis) present?**
Length of Field	**1**
Column Positions	**86**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–5** 1 = None 2 = Mild 3 = Moderate 4 = Severe 5 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12I**
Variable Name	**NPARTER**
Short Descriptor	**Arteriosclerosis**
NP Question	**Is arteriosclerosis (small parenchymal arteriolar disease) present?**
Length of Field	**1**
Column Positions	**88**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–5** 1 = None 2 = Mild 3 = Moderate 4 = Severe 5 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12J**
Variable Name	**NPAMY**
Short Descriptor	**Amyloid Angiopathy**
NP Question	**Is amyloid angiopathy present?**
Length of Field	**1**
Column Positions	**90**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–5** 1 = None 2 = Mild 3 = Moderate 4 = Severe 5 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**12K**
Variable Name	**NPOANG**
Short Descriptor	**Another Angiopathy**
NP Question	**Is another type of angiopathy (e.g., CADASIL or arteritis) present?**
Length of Field	**1**
Column Positions	**92**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**12L**
Variable Name	**NPVOTH**
Short Descriptor	**Other Vascular**
NP Question	**Is there other pathology related to ischemic or vascular disease not previously specified present?**
Length of Field	**1**
Column Positions	**94**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/unknown

Variable Number	**13**
Variable Name	**NPLEWY**
Short Descriptor	**Lewy Bodies**
NP Question	**Pathology is consistent with criteria of Consortium on Dementia with Lewy Bodies for:**
Length of Field	**1**
Column Positions	**96**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–6** 1 = Lewy body pathology, brainstem predominant type 2 = Lewy body pathology, intermediate or transitional (limbic) type 3 = Lewy body pathology, diffuse (neocortical) type 4 = Lewy body pathology, unspecified or not further assessed 5 = No Lewy bodies 6 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14A**
Variable Name	**NPPICK**
Short Descriptor	**Picks Disease**
NP Question	**Pick's Disease:**
Length of Field	**1**
Column Positions	**98**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14B**
Variable Name	**NPCORT**
Short Descriptor	**Corticobasal Deg**
NP Question	**Corticobasal degeneration:**
Length of Field	**1**
Column Positions	**100**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14C**
Variable Name	**NPPROG**
Short Descriptor	**Prog Supra Palsy**
NP Question	**Progressive supranuclear palsy:**
Length of Field	**1**
Column Positions	**102**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14D**
Variable Name	**NPFRONT**
Short Descriptor	**Frontotemporal Dem**
NP Question	**Frontotemporal dementia and Parkinsonism with tau-positive or argyrophilic inclusions:**
Length of Field	**1**
Column Positions	**104**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14E**
Variable Name	**NPTAU**
Short Descriptor	**Tauopathy, Other**
NP Question	**Tauopathy, other (e.g., tangle-only dementia and argyrophilic grain dementia):**
Length of Field	**1**
Column Positions	**106**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14F**
Variable Name	**NPFTD**
Short Descriptor	**FTD with Ubiq**
NP Question	**FTD with ubiquitin-positive (tau-negative) inclusions:**
Length of Field	**1**
Column Positions	**108**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–4** 1 = FTD with motor neuron disease 2 = FTD without motor neuron disease 3 = None present 4 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14G**
Variable Name	**NPFTDNO**
Short Descriptor	**FTD with No Hist**
NP Question	**Is there FTD with no distinctive histopathology (tau-negative, ubiquitin-negative, and no argyrophilic inclusions)?**
Length of Field	**1**
Column Positions	**110**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**14H**
Variable Name	**NPFTDSPC**
Short Descriptor	**FTD Not Specified**
NP Question	**Was FTD "not otherwise specified" present (e.g., "immunostaining for ubiquitin and tau not done")?**
Length of Field	**1**
Column Positions	**112**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**15A**
Variable Name	**NPCJ**
Short Descriptor	**Creutz-Jak Disease**
NP Question	**Is Creutzfeldt-Jakob disease or variant CJD present?**
Length of Field	**1**
Column Positions	**114**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**15B**
Variable Name	**NPPRION**
Short Descriptor	**Other Prion**
NP Question	**Are other prion diseases present (e.g., Gerstmann-Straussler syndrome)?**
Length of Field	**1**
Column Positions	**116**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown

Variable Number	**16A**
Variable Name	**NPMAJOR**
Short Descriptor	**Other Maj Path**
NP Question	**Are other major pathological disorders present (not addressed by questions 8–15)?**
Length of Field	**1**
Column Positions	**118**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = Yes 2 = No 3 = Not assessed
Missing Code	9 = Missing/Unknown
Skips	If NPMAJOR = 2, 3 or 9, then go to #17A, NPGENE

Variable Number	**16B1**
Variable Name	**NPMPATH1**
Short Descriptor	**Specify 1**
NP Question	**If 16A is yes, then specify below:**
Length of Field	**30**
Column Positions	**120–149**
SAS Variable Type	**Character**
SAS Variable Length	**30**
Blanks	Blank if #16A NPMAJOR = 2, 3 or 9
Comment	For 16B1, 16B2, and 16B3 provide most prominent three disorders

Variable Number	**16B2**
Variable Name	**NPMPATH2**
Short Descriptor	**Specify 2**
NP Question	**If 16A is yes, then specify below:**
Length of Field	**30**
Column Positions	**151–180**
SAS Variable Type	**Character**
SAS Variable Length	**30**
Blanks	Blank if #16A NPMAJOR = 2, 3 or 9
Comment	For 16B1, 16B2, and 16B3 provide most prominent three disorders

Variable Number	**16B3**
Variable Name	**NPMPATH3**
Short Descriptor	**Specify 3**
NP Question	**If 16A is yes, then specify below:**
Length of Field	**30**
Column Positions	**182–211**
SAS Variable Type	**Character**
SAS Variable Length	**30**
Blanks	Blank if #16A NPMAJOR = 2, 3 or 9
Comment	For 16B1, 16B2, and 16B3 provide most prominent three disorders

Variable Number	**17A**
Variable Name	**NPGENE**
Short Descriptor	**Family history**
NP Question	**Family history information relevant to neuropathologic diagnosis.**
Length of Field	**1**
Column Positions	**213**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1**–4 1 = Family history of similar neurodegenerative disorder 2 = Family history of other (dissimilar) neurodegenerative disorder 3 = No family history of similar or dissimilar neurodegenerative disorder 4 = Family history of both similar and dissimilar neurodegenerative disorder
Missing Code	9 = Family history unknown/not available/missing
Skips	If NPGENE = 1, 3 or 9, then go to #18A, NPAPOE If NPGENE = 2 or 4, then continue.

Variable Number	**17B**
Variable Name	**NPFHSPEC**
Short Descriptor	**Specify**
NP Question	**If 17A is 2 or 4, then specify:**
Length of Field	**30**
Column Positions	**215–244**
SAS Variable Type	**Character**
SAS Variable Length	**30**
Blanks	**Blank if #17A, NPGENE = 1, 3 or 9**
Comment	Provide the one most prominent disorder

Variable Number	**18A**
Variable Name	**NPAPOE**
Short Descriptor	**APOE**
NP Question	**Apolipoprotein-E:**
Length of Field	**1**
Column Positions	**246**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–6** 1 = e3, e3 2 = e3, e4 3 = e3, e2 4 = e4, e4 5 = e4, e2 6 = e2, e2
Missing Code	9 = Missing/unknown/not assessed

Variable Number	**18B**
Variable Name	**NPTAUHAP**
Short Descriptor	**Tau Haplotype**
NP Question	**Tau Haplotype:**
Length of Field	**1**
Column Positions	**248**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–4** 1 = H1, H1 2 = H1, H2 3 = H2, H2 4 = Other polymorphism (e.g., A0)
Missing Code	9 = Missing/unknown/not assessed

Variable Number	**18C**
Variable Name	**NPPRNP**
Short Descriptor	**PRNP codon 129**
NP Question	**PRNP codon 129:**
Length of Field	**1**
Column Positions	**250**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–3** 1 = M, M 2 = M, V 3 = V, V
Missing Code	9 = Missing/unknown/not assessed

Variable Number	**19**
Variable Name	**NPCHROM**
Short Descriptor	**Gen or Chrom Abnorm**
NP Question	**Genetic or Chromosomal abnormalities.**
Length of Field	**2**
Column Positions	**252–253**
SAS Variable Type	**Numeric**
SAS Variable Length	**8**
Allowable Codes	**1–13, 50** 1 = APP mutation 2 = PS1 mutation 3 = PS2 mutation 4 = Tau mutation 5 = α- Synuclein mutation 6 = Parkin mutation 7 = PRNP mutation 8 = Huntingtin mutation 9 = Notch 3 mutation (CADASIL) 10 = Other known genetic mutation (e.g., ABri, neuroserpin) 11 = Down Syndrome 12 = Other chromosomal abnormality 13 = No known genetic or chromosomal abnormality 50 = Not assessed 99 = Missing/unknown

Primary Error-Checking

NACC NP Error Messages

Several types of error messages may be generated by the NP primary error checking program**:** range errors, contingency errors, and errors related to type of file being checked (i.e., alignment or variable type).

Files with errors are not accepted for submission. Errors must be corrected before the NP submission system will allow you to proceed. Alerts are accepted if verified. Alerts are verified by going to Step 3 at the NP submission system's main menu (after any errors have been corrected).

Examples of types of Error Messages are as follows:

1. **Range** – Alpha item in numeric field (only for ASCII Files)

Line # in file:	1
MDS Patient ID #:	21
Variable Number:	4
Variable Name:	NPSEX
Type of Check:	Range
Action Required:	ERROR: Correct unallowable value.
Incorrect Value:	a
	Non-digits not allowed in this item.
(New Value):	

2. **Range** – Value not within defined limits

Line # in file:	1
MDS Patient ID #:	21
Variable Number:	4
Variable Name:	NPSEX
Type of Check:	Range
Action Required:	ERROR: Correct unallowable value.
Incorrect Value:	3
(New Value):	

3. **Contingency –** Data element should have been skipped

Line # in file:	1
MDS Patient ID #:	0000000001
Variable Number:	16a, 16b1
Variable Name:	NPMAJOR, NPMPATH1
Type of Check:	Contingency
Action Required:	ERROR: Correct by making values consistent.
Incorrect Value:	NPMPATH1=Smiths disorder The NPMPATH1 item should have been skipped (i.e. [BLANK]) because NPMAJOR=2.
(New Value):	

4. **Contingency** – Data element probably incorrect because of value of another data element

Line # in file:	1
MDS Patient ID #:	0000000001
Variable Number:	6a, 6b, 6c
Variable Name:	NPFORMMO, NPFORMDY, NPFORMYR NPDODMO, NPDODDY, NPDODYR
Type of Check:	Contingency
Action Required:	ERROR: Correct by making values consistent.
Incorrect Value:	Death date 11,22,2001 must precede or equal date form was completed 11, 9,2001.
(New Value):	

5. **Range Alert** – Data element incorrect because of unlikely year.

Line # in file:	1
MDS Patient ID #:	0000000001
Variable Number:	6c
Variable Name:	NPDODYR
Type of Check:	Range
Action Required:	ALERT: Check unlikely value. NPDODYR (death year) was Verified/Corrected (Circle one)
Incorrect Value:	1970
(New Value):	

6. **Range** – Duplicate ADCID and PTID with another record.
   First record is checked for errors. Second is not checked any further for errors, beyond being a duplicate record.

Line # in file:	8
MDS Patient ID #:	0000000003
Variable Number:	
Variable Name:	ADCID, PTID
Type of Check:	Range
Action Required:	ERROR: Correct unallowable value.
Incorrect Value:	ADCID=4 PTID=0000000003 Same (ADCID, PTID)-value as Line #7. NB: No further checking of this UNALLOWABLE RECORD.
(New Value):	

7. **Alignment** – Spaces following data elements must be left blank (for ASCII files only). All error checking for this record is stopped if this happens.

Line # in file:	1
MDS Patient ID #:	0000000001
Variable Number:	3
Variable Name:	NPID
Type of Check:	Alignment
Action Required:	ERROR: Correct unallowable value.
Incorrect Value:	The space following this item was not left blank: Column 36 is filled in. NB: No further checking of this UNALLOWABLE RECORD.
(New Value):	

8. **Variable Length** – Variable must be of the correct length (SAS and SPSS files only).

NPGROSS has the wrong length. Length = 4 Should be 8
SAS Input File Invalid! No further Error Checking.

9. **Variable Existence** – Variable must exist on the input data set (SAS and SPSS files only).

NPID is not on the Input File SAS Input File Invalid! No further Error Checking.

10. **Extra Variable**– Variable must be appropriate for the Input Data Set (SAS and SPSS files only).

LASTNAME is not a variable needed for the minimum dataset. SAS Input File Invalid! No further Error Checking.

11. **Variable Type** – Variable must be of the correct type (SAS and SPSS files only).

NPDAGE has the wrong type. Type = Character. Should be Numeric SAS Input File Invalid! No further Error Checking

Submitting Data

A. Preparing your Data Submission

NP data submissions may be prepared locally and the files uploaded through the NACC website, or prepared using web data entry. Either a total replacement submission may be created or a submission which updates previously submitted data.

All submissions are managed through the NP data submission system (see General Instructions). The Center Data Manager is able to manage his/her submission completely using the NACC website.

Once the local file(s) have been prepared or the web data entry completed, access the NACC website as detailed under General Instructions. Refer to step 1 of the submission menu. Select either 1A or 1B. For 1B, uploading data file(s) for your submission, note that **you should not encrypt or password protect your files as this is automatically done by the website**.

When your file(s) have been uploaded or the web entry is complete, use option 1D - create your final submission. This allows creation of a final file of all IDs for error checking, verifying and processing into the NACC database. You may skip this step if you have uploaded one replacement data file and are using it as your submission.

B. Error-checking your Submission

Once your final submission has been prepared then it must be error-checked. See option 2 on the NP data submission menu. First, execute the primary error checks. If there are errors a new file will have to be uploaded, or if using web data entry, appropriate changes will have to be made. Another final submission will have to be created. Once all errors have been fixed then any alerts will have to be verified. Use option 3 – verifying alerts and other discrepancies. The secondary error-checks can now be executed. Carefully examine the secondary error-check report for discrepancies that may be fixed. Again any fixes must be accomplished by uploading another file, or if using web data entry, modifying over the web. Another final file will have to be created, then the primary error-checks run, followed by the secondary.

C. Verifying Alerts and Other Discrepancies

Once the secondary error-checks have been successfully executed, all discrepancies must be verified. Choose options from the NP data submission menu. For each item on the list the discrepancy must be verified. Some verifications are for the whole submission and some must be done for each individual patient ID.

D. Processing Data into the NP database

If all discrepancies have been verified your submission may be processed into the NACC database. Choose option 4 from the NP data submission menu.

E. Creating Certification Reports

The final step is to create your certification reports; choose options from the NP data submission menu. Once completed examine the reports carefully. If you are satisfied with the reports, click the “NOTIFY NACC” link in the NP data submission menu. NACC will then review your submission and issue the certification reports and certification form for your Director to sign.

NACC Neuropathology Web Data Management

A. Introduction

The NACC Neuropathology Web Data Management System was designed to allow ADCs/ADRCs to access their Center's NACC NP data through the NACC website. All autopsied IDs from the last Minimum Data Set (MDS) and Neuropathology Data Submissions are included in a Center's Neuropathology Data Set. Data entry may be done for new IDs, and modifications or updates may be done for previously submitted IDs.

New MDS IDs may be added, but they must be included in the next MDS Data Call and indicated as autopsied. **Newly-entered MDS IDs which are not submitted in the next MDS Data Call will be deleted from your Center's Neuropathology Data Set**.

IDs entered in the MDS as having been autopsied may **not** be deleted from the Neuropathology Web Data Management System.

1. Minimum System Requirements

Internet connection: A hard-wired connection is recommended; a modem can be used instead, but this may make data entry a slow, tedious process and cause possible data errors to occur.

Browser: Recommended minimum versions are Netscape Communicator 4.7 or Microsoft Internet Explorer 5.0.

Screen size: Recommended minimum is 17 inches (smaller sizes will work, but will be more difficult to use).

2. NACC Contacts

If a problem occurs with the system, please notify the NACC office via e-mail at naccmail@u.washington.edu or call us at 206-543-8637.

3. Future Submissions

NACC is always looking for ways to improve its software. Please feel free to contact us with comments/suggestions. We are interested in talking to you!

4. Advantages

There are many advantages to performing web-based data entry rather than submitting files or paper forms, including:

a. Immediate access to your data.

b. Frequent data submissions, at your convenience, instead of only once or twice a year.

c. The convenience of a web-based interface for access to this information by Center personnel.

5. Limitations

If you have a low-speed web connection or web traffic is high, entering data may be slow and possible errors could occur. Verifying data will minimize errors. Always check your data entry and submissions.

6. Security

The Neuropathology Web Data Management System is accessed through the NACC website. Only authorized neuropathology data managers may use the system, and these managers will have access to only the data from their own Center. To access the system, a manager must have an appropriate user name and password.

7. General Data Management

All MDS IDs which have been autopsied must have a corresponding Neuropathology Data Form. Each Center has a secured data file, and only that Center's data manager and other designated Center personnel have access to this data file. All MDS IDs which were autopsied have a form (record) in this data file. The MDS IDs for which data was submitted during the initial NP Data Submission will have a completed form (record) in this data file. MDS IDs for which neuropathology data was not submitted will have a form (record) in this data file, but all of the data elements will be blank.

It is very important that the MDS ID is correct. Please check all pertinent information before updating an MDS ID. The MDS ID *must* correspond to the MDS ID submitted by your Center's Data Manager during the last MDS Data Call.

Instructions for accessing the Neuropathology Web Data Management System are provided in section B.1, *Accessing the System*. To enter data for an existing MDS ID, see section C.3, *"Edit" Function*. To enter data for newly-autopsied IDs not currently in the MDS, first add the MDS ID (see section C.2, *"Add" Function*), and then enter the data using the "Edit" function.

In general, the steps for neuropathology data management are as follows:

<u>Current MDS IDs</u>:

a. Choose the "Edit" function.
b. Scroll down to find the desired MDS ID in the list displayed.
c. Choose the MDS ID.
d. Edit fields as appropriate.
e. Click on the "Submission" button.
f. If errors are indicated, make corrections and then click on "Submission" again.
g. The system will indicate "ID Submitted" when the edit is accepted.

h. Choose the “Verify” function.

i. Choose the MDS ID.

j. Enter the data elements as appropriate.

k. Click on the “Verify” button.

l. If errors or verification issues are indicated, make corrections and then click on the “Verify” button again.

m. The system will indicate “ID Verified” if successful.

New MDS IDs:

a. Choose the “Add” function.

b. Type in the MDS ID as requested; if no errors are encountered, the system will indicate that the MDS ID has been added.

c. To enter data for the new MDS ID, follow the steps listed previously for current MDS IDs.

8. Disclaimer

As all websites are dynamic by nature, the sample screens provided in this manual may not be an exact representation of the most current page on the website itself. Though details may change, the sample screens still provide the user with a visual companion to the written instructions, as well as navigational orientation.

B. System Operation

1. Accessing the System

The NP Web Data Management System is at NACC's website (https://www.alz.washington.edu). To access your NP data:

1) Choose "Member Login" and enter your username and password.
2) Choose "The NACC Database".
3) Read and accept the Disclaimer and Confidentiality Agreement.
4) Choose "The Neuropathology Data Set".
5) Choose your Center's name (Figure 1); if you do not have authorized access for the Center selected, the system will deny access.

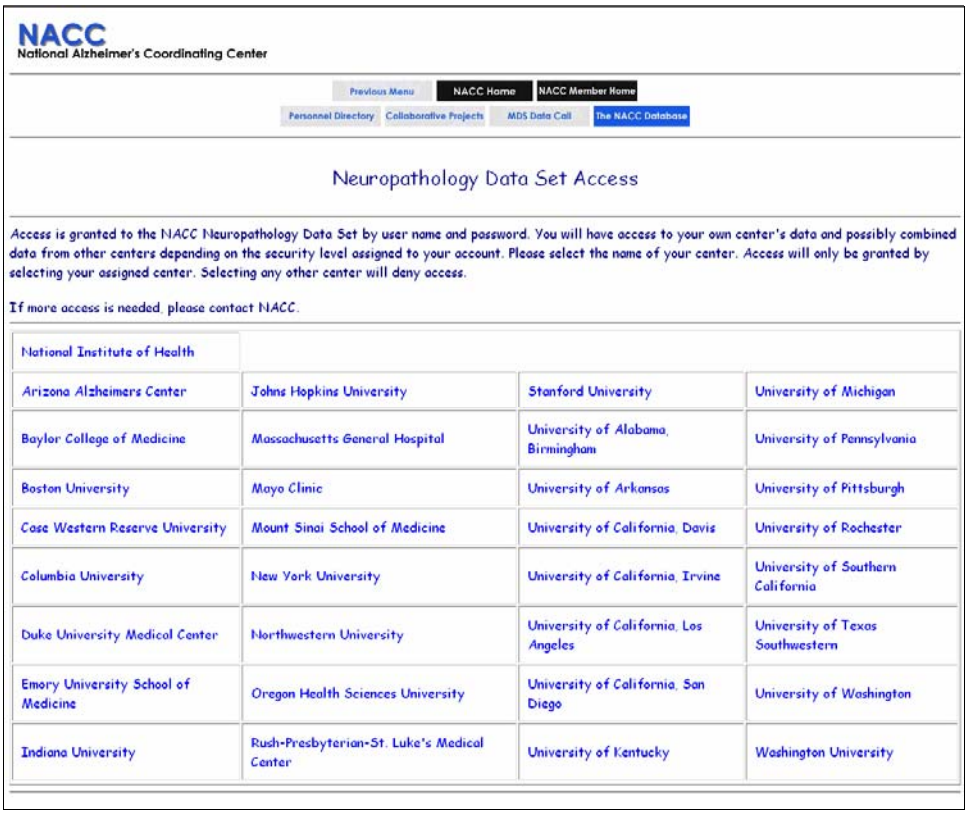

Figure 1.

6) Choose "Data Manager Menu".
7) Choose "Neuropathology Data Submission System". Your account must be specially authorized to access this area.
8) Choose Step 1A, "Web data entry and modification".

2. Navigating the System

On each NACC web page is a group of buttons which allow the user to navigate easily through the NACC website (see below). Clicking on one of these buttons will display the corresponding web page:

Figure 2.

Previous Menu	Displays the previous menu in the Web Data Management System (unlike the browser's "Back" button, which will display the previously viewed page).
NACC Home	Displays the NACC home page.
NACC Member Home	Displays the home page for NACC members only.
Personnel Directory	Displays the ADC Directory page.
Collaborative Projects	Displays information regarding NACC projects.
MDS Data Call	Displays information on the MDS Data Call.
The NACC Database	Displays the Data and Studies page. (On sample screens in subsequent pages, this button is still labeled as "Data and Studies", although it has since been changed to "The NACC Database" on the website.)

C. Data Management Functions

Log-in to the Neuropathology Data Management system for your Center (see previous instructions in section B.1) and the *Neuropathology Data Management* page will be displayed (Figure 3). Click on a function name (Display, Add, Edit, Verify, Delete) to display the corresponding web page.

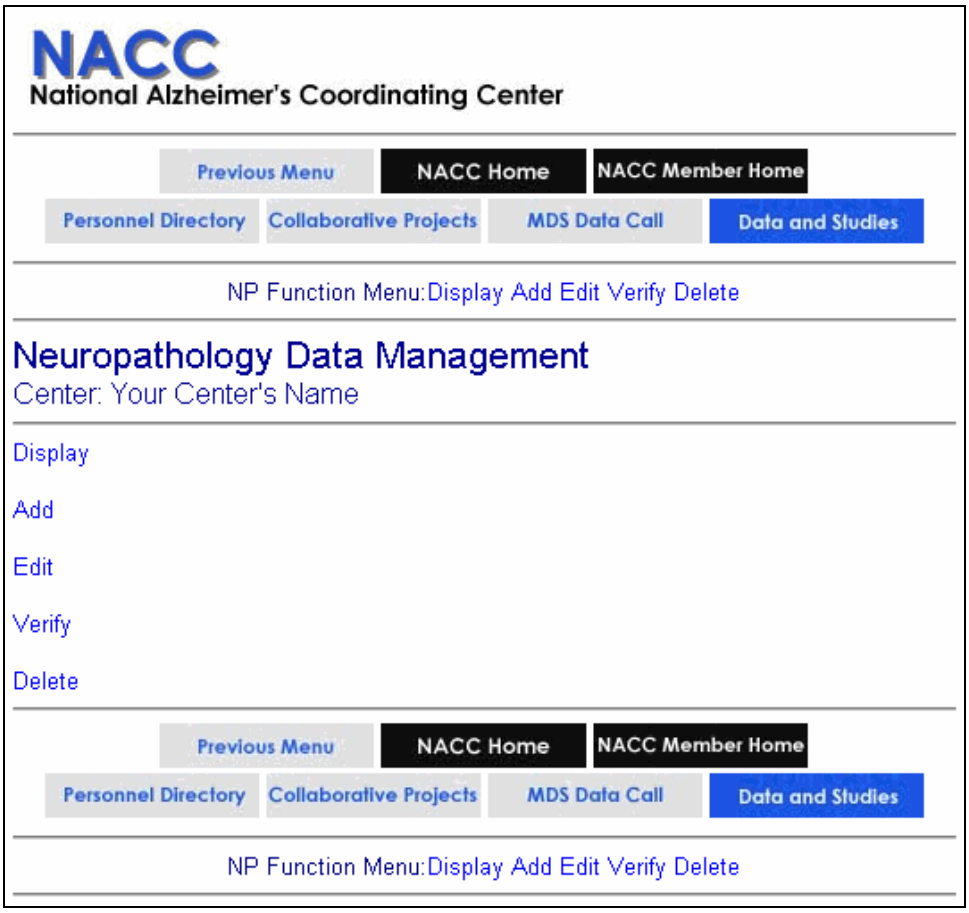

Figure 3.

1. "Display" Function

This function allows the display of neuropathology data for a selected MDS ID. Selecting this function will open the *NACC Neuropathology Display Data (Select ID)* page (Figure 4).

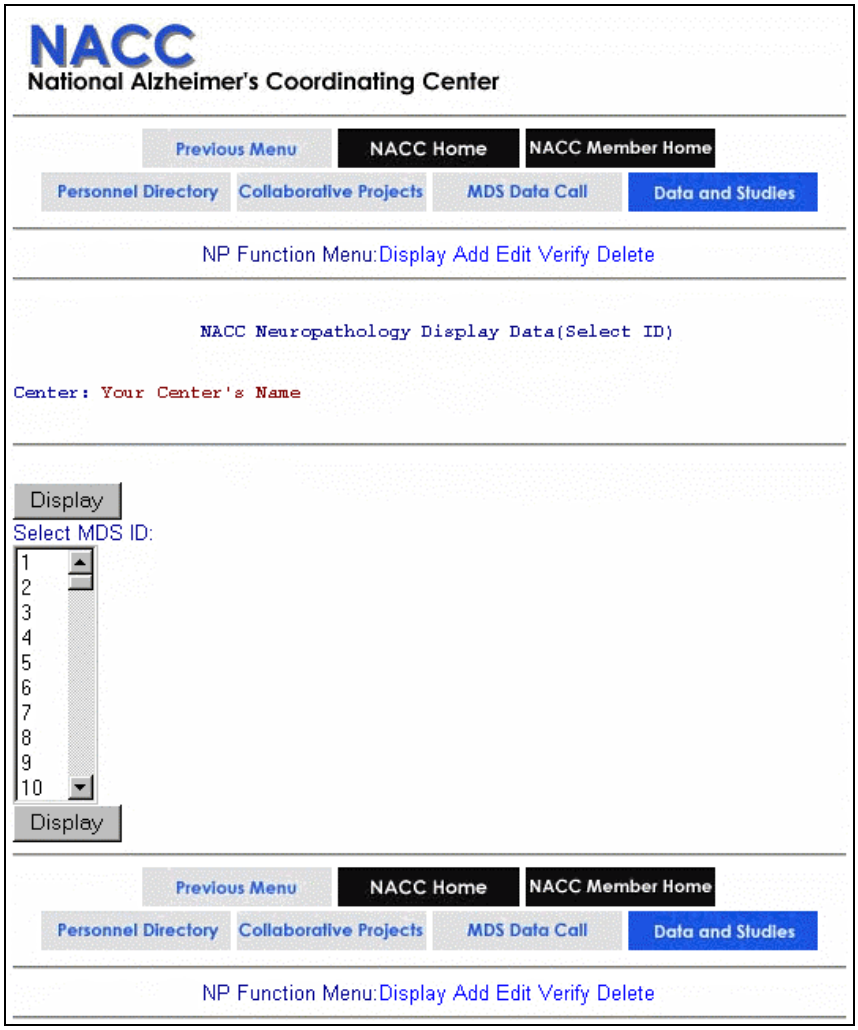

Figure 4.

The MDS IDs displayed are those submitted by your Center during the last MDS Data Call and any new MDS IDs added through the Neuropathology Web Data Management System since the last Data Call. The IDs are usually in sequential order, but newly-added MDS IDs may be displayed at the end of the list. IDs are shown exactly as entered into the MDS, except leading blanks are ignored.

To display data for an MDS ID:

- Scroll down to find the desired MDS ID.
- Choose the MDS ID.
- Click on the "Display" button.

The *NACC Neuropathology Display Data (Display)* page will show the current data for the MDS ID selected (Figure 5).

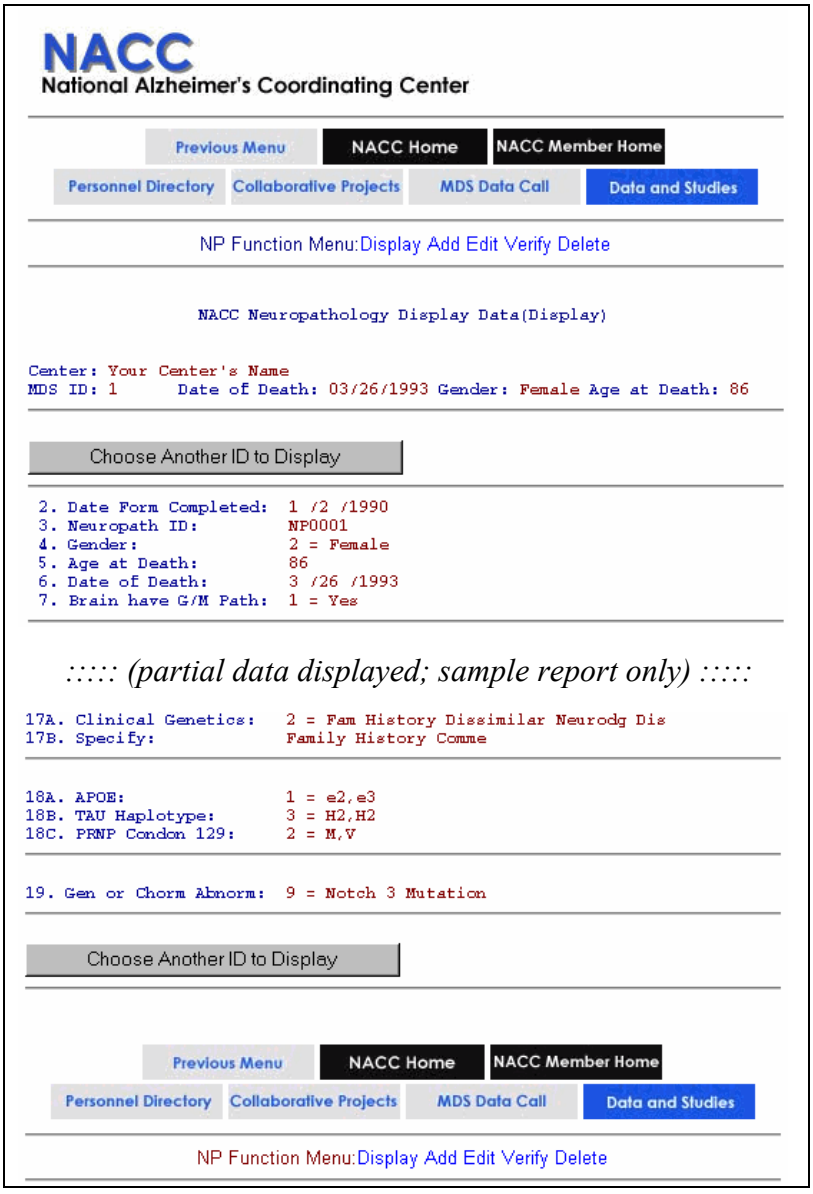

Figure 5.

Click on the "Choose Another ID to Display" button to return to the *NACC Neuropathology Display Data (Select ID)* page. (The "Previous Menu" button will also open this page.)

2. "Add" Function

This function will allow the addition of new MDS IDs to the Neuropathology Web Data Management System. New MDS IDs entered must be included in the next NACC Data Call, and have the data element "Autopsy=Yes". **If a newly-added MDS ID is not submitted in the next MDS Data Call, it will be deleted from the Neuropathology Web Data Management System**.

Click on the “Add” function to open the *NACC Neuropathology Add ID (Request ID)* page (Figure 6).

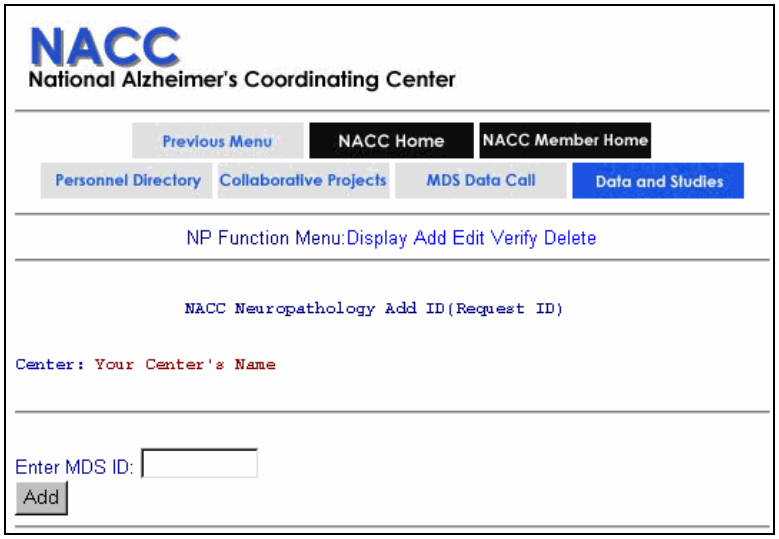

Figure 6.

To add a new MDS ID:

- Click on the box after “Enter MDS ID”.
- Type the new MDS ID.
- Click on the “Add” button.

  Take care when adding new MDS IDs to ensure that they are entered in the same format as IDs already in your MDS. For example, if all your current MDS IDs have leading zeros, then newly-added IDs should have leading zeros.

a. ID Added

If the MDS ID was successfully added, the *NACC Neuropathology Add ID (Request ID)* page will be displayed with the message "ID Added!" (Figure 7). You may continue to add additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

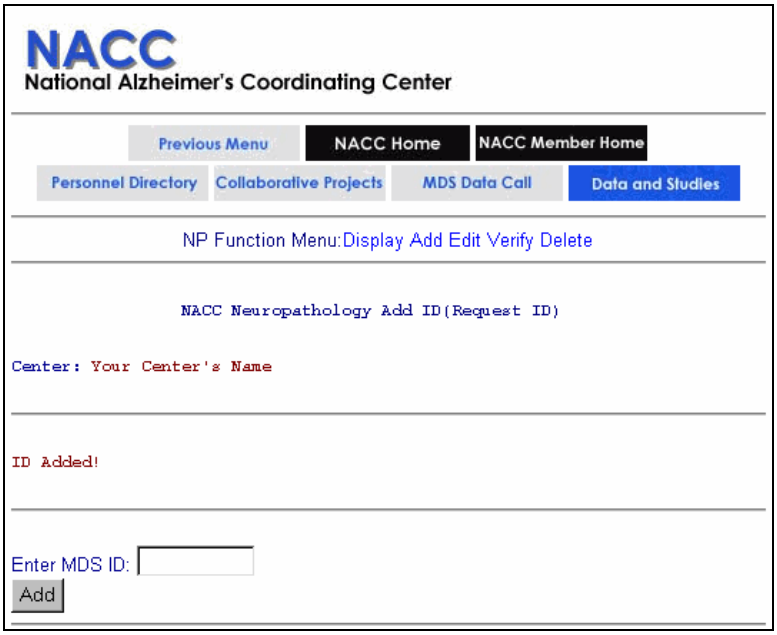

Figure 7.

b. Duplicate ID

If the ID already exists in the Neuropathology Data Set, a message will be displayed in the *NACC Neuropathology Add ID (ID Exists)* page (Figure 8). Duplicate MDS IDs are not allowed. When the system searches for duplicates, leading zeros and blanks are ignored.

Data for an existing MDS ID must be entered with the "Edit" function (see section C.3).

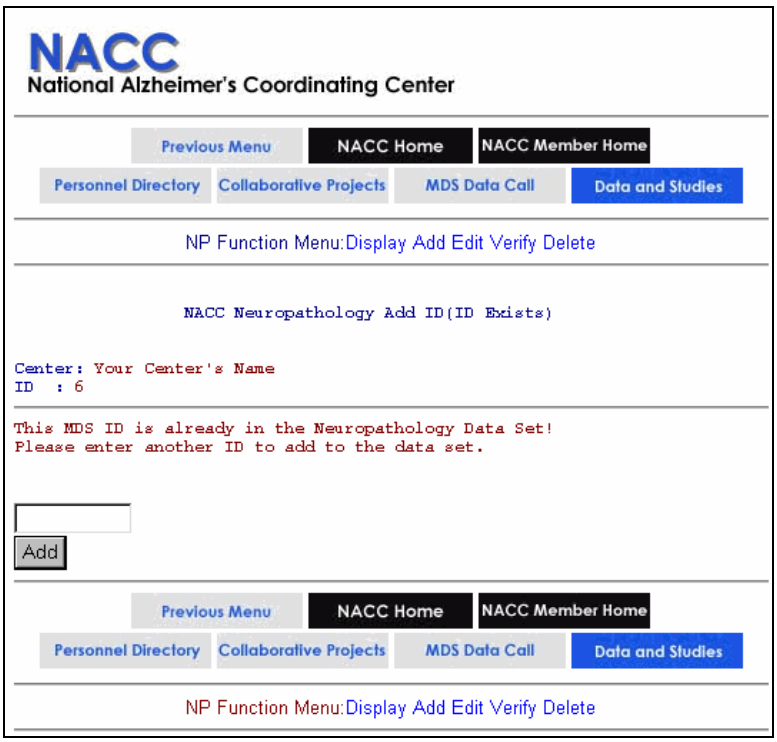

Figure 8.

You may continue to add additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

c. ID Not in MDS

If you type an ID that is not in the MDS, the *NACC Neuropathology Add ID (ID Not in MDS)* page will be displayed (Figure 9).

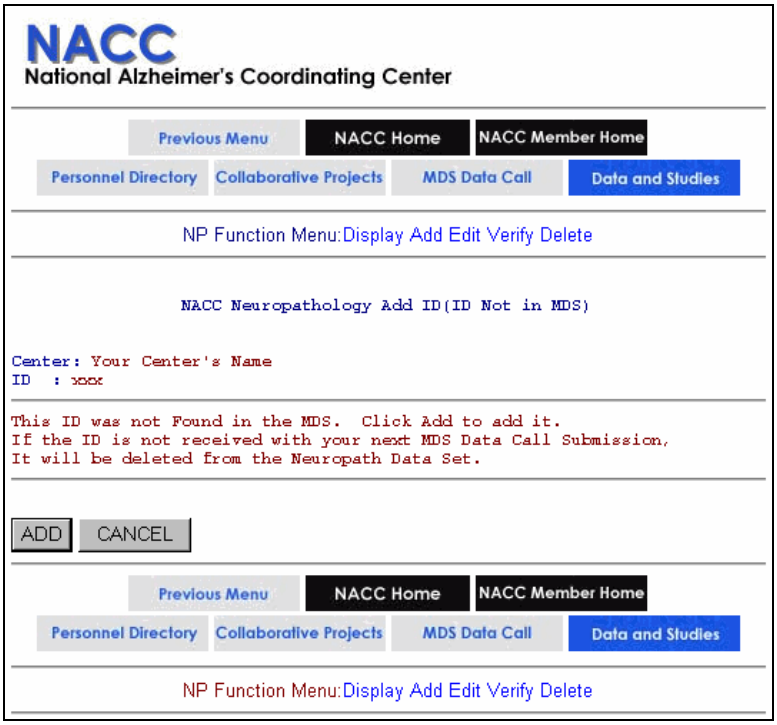

Figure 9.

Click the "Add" button and the MDS ID will be added to the Neuropathology Web Data Management System, even though it is not in the MDS. **If the MDS ID is not submitted during the next MDS Data Call, it will be deleted from the Neuropathology Web Data Management System**.

You may continue to add additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page. Click the "Cancel" button to return to the *NACC Neuropathology Add (Request ID)* page without adding the ID.

d. System Error

If the MDS ID could not be added, an error message will be displayed (Figure 10). This situation usually occurs when someone else at your Center is trying to submit the file at the same time. Try to enter the MDS ID again. If the problem persists, please contact NACC.

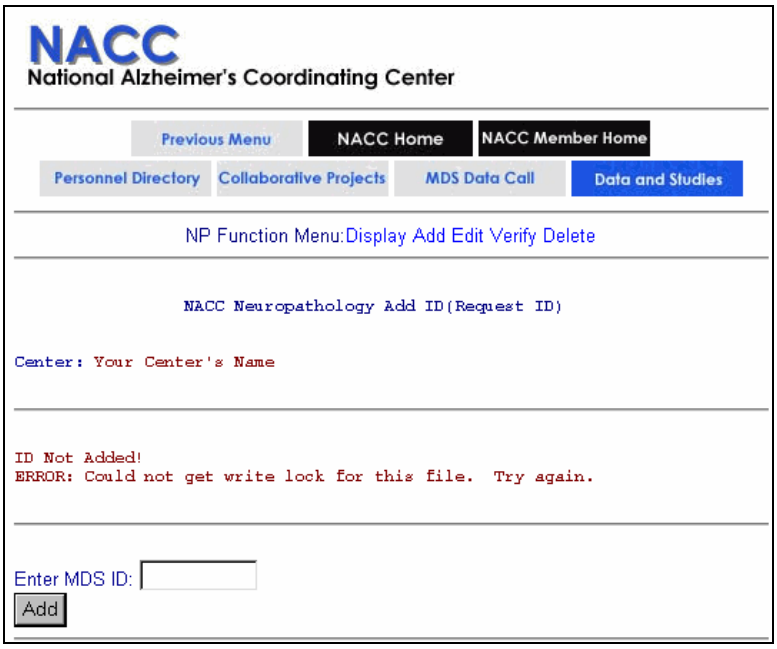

Figure 10.

You may continue to add additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

3. "Edit" Function

This function allows the entering or editing of neuropathology data for an MDS ID. Choose the "Edit" function to open the *NACC Neuropathology Edit (Select ID)* page (Figure 11).

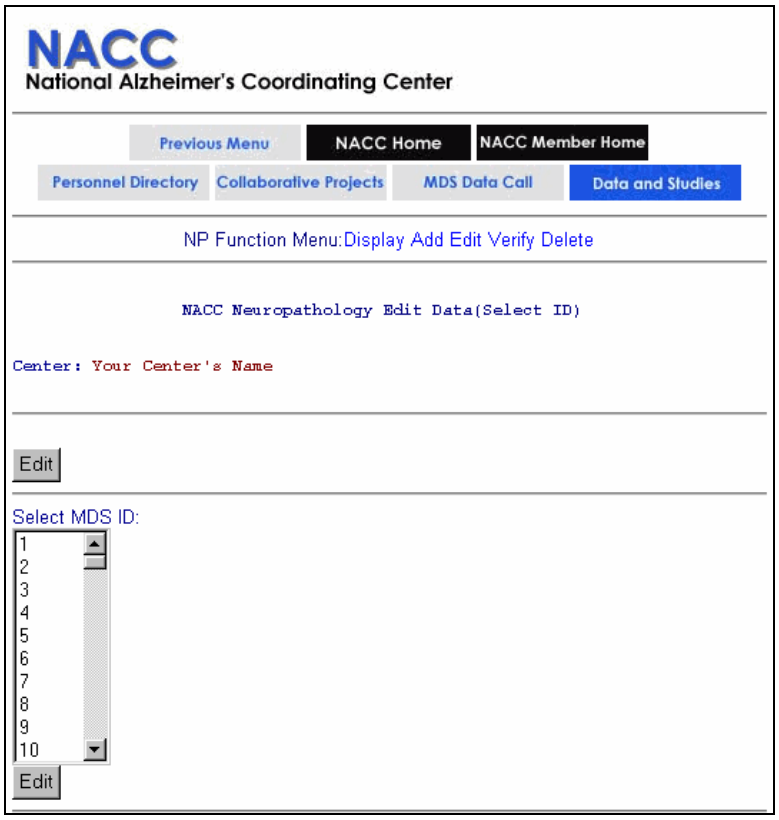

Figure 11.

The MDS IDs displayed are those submitted by your Center during the last MDS Data Call and any new MDS IDs added through the Neuropathology Web Data Management System since the last Data Call. The MDS IDs are usually in sequential order, but newly-added MDS IDs may be displayed at the end of the list. IDs are shown exactly as entered into the MDS, except leading blanks are ignored. Leading zeros are not ignored.

To edit or enter data:

- Scroll down to find the desired MDS ID.
- Choose the MDS ID.
- Click on the "Edit" button.

The *NACC Neuropathology Edit Data (Edit ID)* page will be displayed (Figure 12).

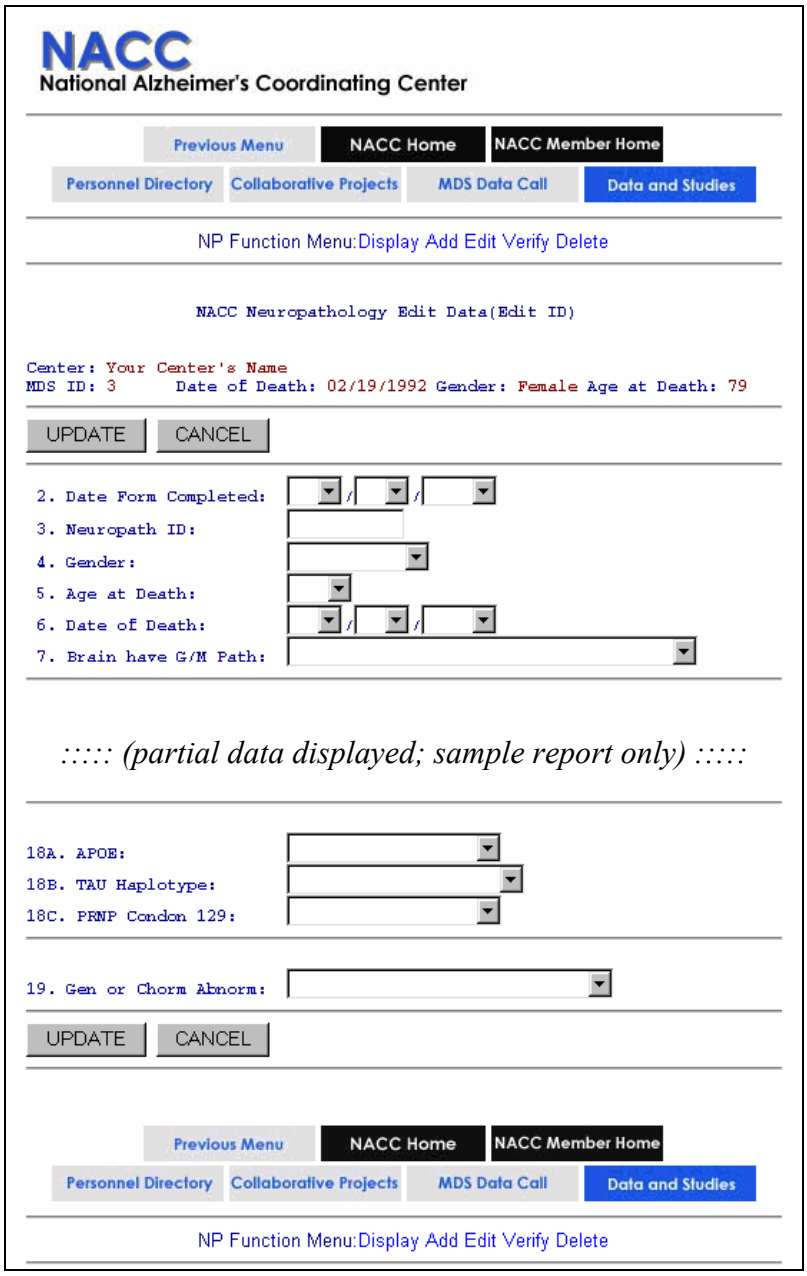

Figure 12.

Values initially displayed are the values currently in the database for this MDS ID. A blank value indicates a value has not yet been selected for this field or the data element is not applicable because of a value for a prior data element. Blank values are not acceptable for the final form submission to NACC unless they represent a 'not applicable' field.

The majority of the data elements have a pull-down list of values. Click on the arrow next to the element, use the scroll bar to display the values, and click on the appropriate value to select it. A few data elements are text boxes rather than pull-down lists. Type in the appropriate value for these elements.

Alternately, the tab key and the number keys may be used to enter data. Use the tab key to move to the desired data element and then type the number for the value of the data element. (Note: this method will **not** locate the second number of data elements with two-digit values).

Once all data elements have been entered for an MDS ID, click on the "Submit" button to execute the error check program. Data elements corresponding to MDS data elements are checked first (for example, date of death entered on this form must be the same as the date of death for this ID in the MDS). Each data element is then checked to determine that it is within the correct range. Logical checks are also performed on applicable data elements.

Click on the "Cancel" button to return to the *NACC Neuropathology Edit Data (Select ID)* page without updating the MDS ID.

a. ID Submitted

If the data elements entered for the MDS ID have no errors, the *NACC Neuropathology Edit Data (Select ID)* page will be displayed with the message "ID Submitted!" (Figure 13).

Figure 13.

You may continue to edit/enter additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

b. Data Entry Error

If data elements entered for the MDS ID have errors, the *NACC Neuropathology Edit Data (ID has Errors)* page will display a list describing all errors (Figure 14).

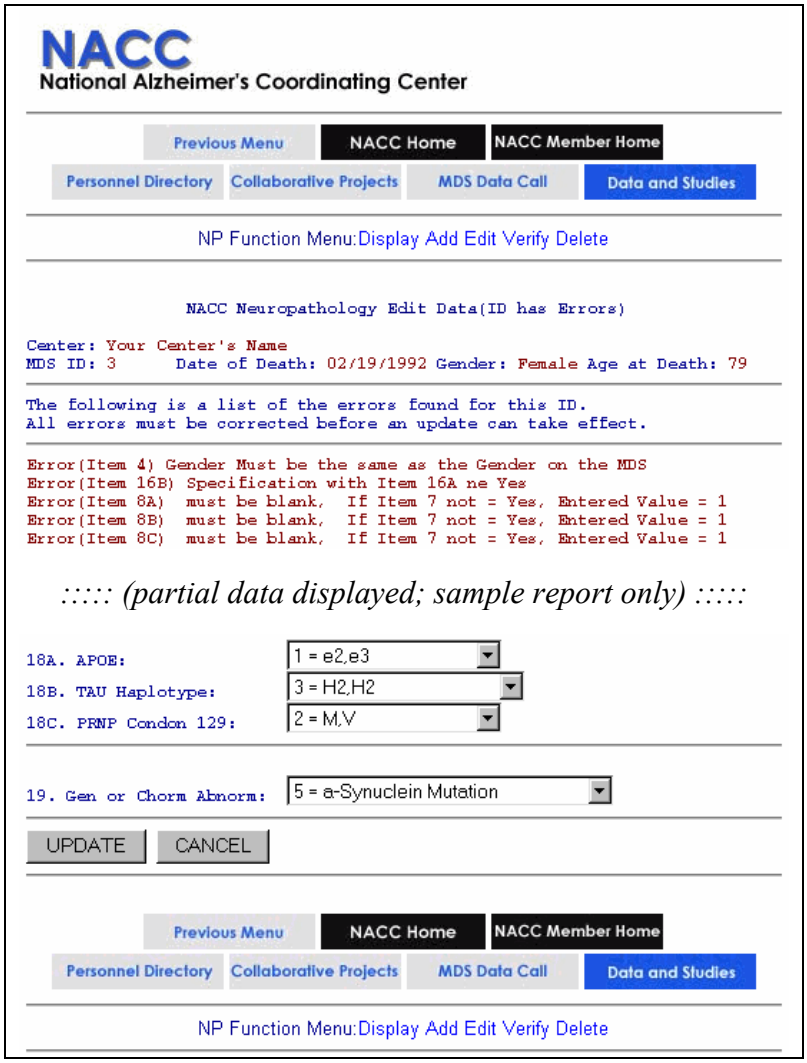

Figure 14.

To correct the errors:

- Edit the appropriate data elements (review the instructions above).
- Click on the "Submit" button to run the error check program again; repeat this process until all errors are corrected and the MDS ID is submitted.
- If the error is a contingency error, where a Neuropathology variable just entered does not match MDS data submitted, then:
  - Establish which data is correct. If you are not the Data Manager who submitted the MDS data to NACC, then contact the Data Manager. If you need help determining who your Data Manager is, contact NACC.
  - If the Neuropathology data was wrong, enter the correct value.

– If the MDS data was wrong, your Data Manager can go into the Web Data Management section for the MDS data and correct the variable. Once this is done, please contact NACC, and we will then run a program which allows the Neuropathology data management pages to recognize the newly-entered MDS data. We have plans to automate this process, but currently we must run the program manually.

Click on the "Cancel" button to return to the *NACC Neuropathology Edit Data (Select ID)* page without updating the MDS ID.

c. System Error

If the data elements entered for the MDS ID could not be submitted because of a system error, the *NACC Neuropathology Edit Data (Edit ID)* page will display an error message (Figure 15). This situation usually occurs when someone else at your Center is trying to submit the file at the same time. Try to submit the MDS ID again. If the problem persists, please contact NACC.

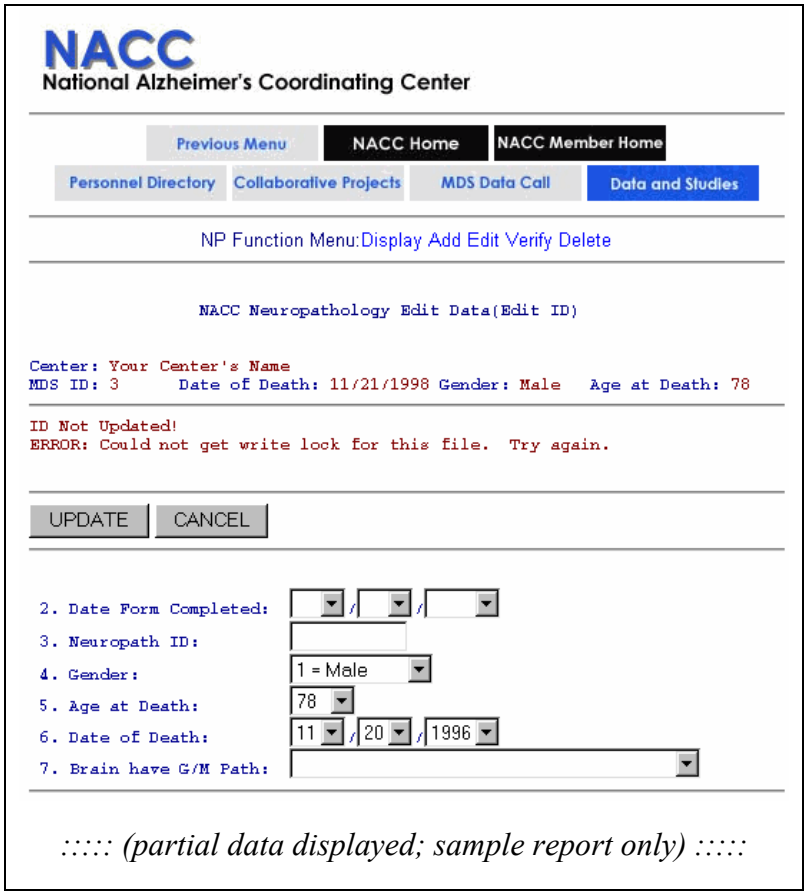

Figure 15.

Click on the "Cancel" button to return to the *NACC Neuropathology Edit Data (Select ID)* page without updating the MDS ID.

4. "Verify" Function

After the data elements for an MDS ID have been entered using the "Edit" function, the "Verify" function should be used to check that the data was entered correctly. ***It is recommended that all data be verified by someone other than the person who entered the data.*** This function does not submit or change data. Its purpose is to allow a second entry of the data, in order to verify accuracy and minimize data entry errors. Selecting this function opens the *NACC Neuropathology Verify Data (Select ID)* page (Figure 16).

Figure 16.

The MDS IDs displayed are those submitted by your Center during the last MDS Data Call and any new MDS IDs added through the Neuropathology Web Data Management System since the last Data Call. The MDS IDs are usually in sequential order, but newly-added MDS IDs may be displayed at the end of the list. IDs are shown exactly as entered into the MDS, except leading blanks are ignored. Leading zeros are not ignored.

To verify data:

- Scroll down to find the desired MDS ID.
- Choose the MDS ID.
- Click on the "Verify" button.

The *NACC Neuropathology Verify Data (Verify Data)* page will be displayed (Figure 17).

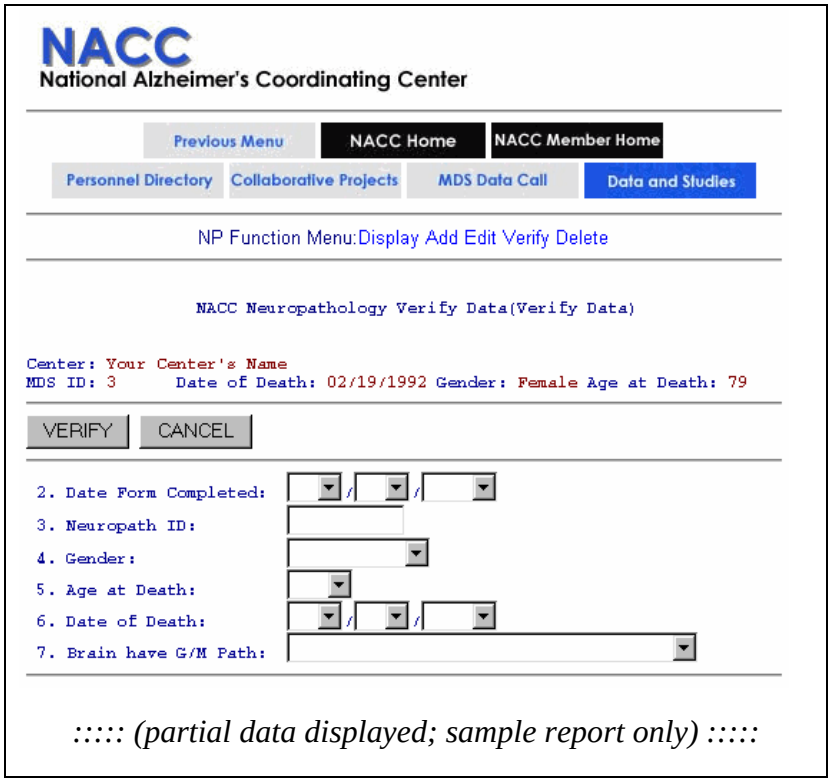

Figure 17.

Initially, all values are blank on the "Verify" page, and values must be entered for each data element. The majority of the data elements have a pull-down list of values. Click on the arrow next to the element, use the scroll bar to display the value wanted, and click on the desired value to select it. A few data elements are text boxes rather than pull-down lists. Type in the desired value for these elements.

Alternately, the tab key and the number keys may be used to enter data. Use the tab key to move to the desired data element and then type the number for the value of the data element. (Note: typing the value number will **not** locate the second number of data elements with two-digit values).

Once all data elements have been entered for an MDS ID, click on the "Verify" button to execute the error check program. Data elements corresponding to MDS data elements are checked first (for example, date of death entered on this form must be the same as the date of death for this ID in the MDS). Each data element is then checked to determine that it is within the correct range. Finally, the new

data is checked against the data already entered in the Neuropathology Web Data Management System to determine if the values are the same.

Click the “Cancel” button to return to the *NACC Neuropathology Verify Data (Select ID)* page without verifying the MDS ID.

a. ID Verified

If data elements for the MDS ID have no errors and match the values already in the data set, the *NACC Neuropathology Verify Data (Select ID)* page will be displayed with the message "ID Verified!" (Figure 18). When the MDS ID is successfully verified, you may continue to verify additional IDs, or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

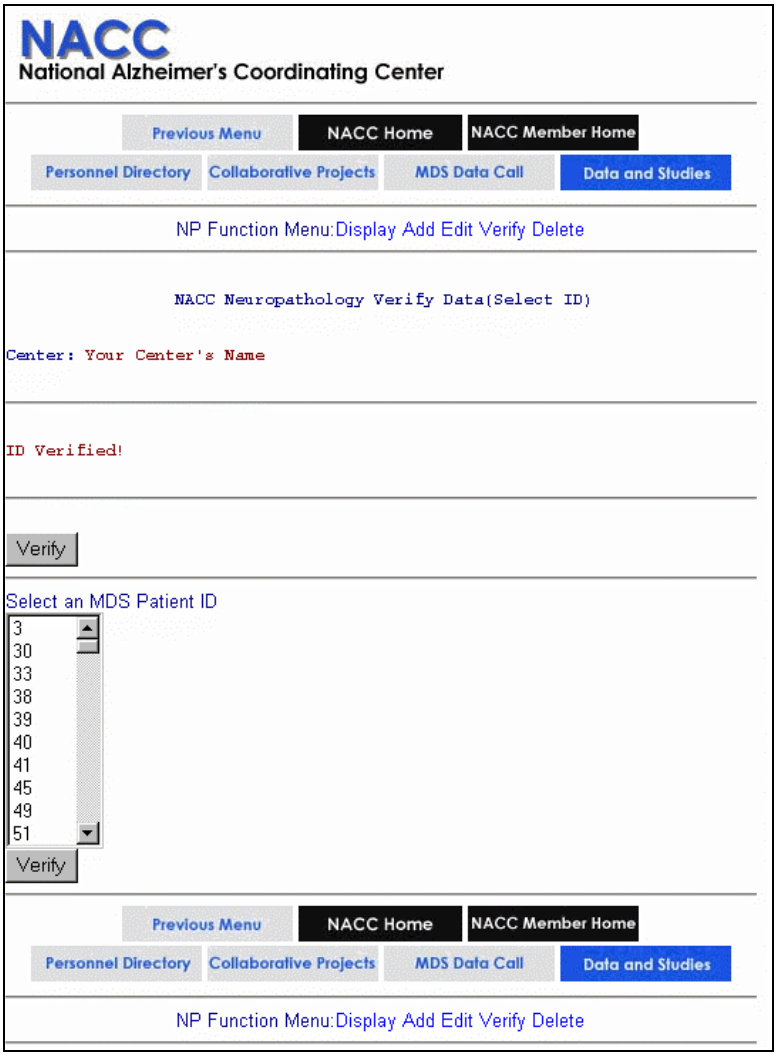

Figure 18.

b. Data Entry Error

If data elements entered for the MDS ID have errors or do not match the values already in the data set, the *NACC Neuropathology Verify Data (Verified Data has Errors)* page will display a list of all errors (Figure 19).

NACC
National Alzheimer's Coordinating Center

Previous Menu | NACC Home | NACC Member Home
Personnel Directory | Collaborative Projects | MDS Data Call | Data and Studies

NP Function Menu: Display Add Edit Verify Delete

NACC Neuropathology Verify Data(Verified Data has Errors)

Center: Your Center's Name
MDS ID: 3 Date of Death: 03/17/1993 Gender: Female Age at Death: 67

List of errors found for this ID using verification data.

Error(Item 4) Gender Must be the same as the Gender on the MDS
Error(Item 5) Age at Death Must be the same as the Age of Death on the MDS
Error(Item 6) Month of DOD Must be the same as the Month of DOD on the MDS
Error(Item 6) Day of DOD Must be the same as the Day of DOD on the MDS
Error(Item 6) Year of DOD Must be the same as the Year of DOD on the MDS

List of verification errors found for this ID.
Correct using edit or re-verify.

```
Item 1    not Verified.  New Month Value =    Old Value = 1
Item 1    not Verified.  New Day   Value =    Old Value = 2
Item 1    not Verified.  New Year  Value =    Old Value = 1990
Item 3    not Verified.  New Value =    Old Value = NP0001
Item 4    not Verified.  New Value =    Old Value = 2
Item 5    not Verified.  New Value =    Old Value = 76
Item 6    not Verified.  New Month Value =    Old Value = 3
Item 6    not Verified.  New Day   Value =    Old Value = 19
Item 6    not Verified.  New Year  Value =    Old Value = 1993
Item 7    not Verified.  New Value =    Old Value = 1
Item 8A   not Verified.  New Value =    Old Value = 2
Item 8B   not Verified.  New Value =    Old Value = 1
Item 8C   not Verified.  New Value =    Old Value = 3
Item 8D   not Verified.  New Value =    Old Value = 1
Item 9    not Verified.  New Value =    Old Value = 2
Item 10   not Verified.  New Value =    Old Value = 2
Item 11   not Verified.  New Value =    Old Value = 3
Item 12   not Verified.  New Value =    Old Value = 1
Item 12A  not Verified.  New Value =    Old Value = 2
Item 12B  not Verified.  New Value =    Old Value = 3
```

::::: *(partial data displayed; sample report only)* :::::

Figure 19.

To correct the data, select one of the following options:

1) Errors on the verification page–

   - Make corrections to the data elements as appropriate.
   - Click on the "Verify" button to run the error check program again; repeat this process until the MDS ID data is verified.

2) Errors in the data set and not on the verification page–

   - Click on "Edit" in the function menu.

- Locate and select the desired MDS ID.
- Change the data element values as appropriate and click on the "Submit" button.
- Use the browser's "Back" button to return to the verification page.
- Click on the "Verify" button to re-check the new values; repeat this process until all errors are corrected and the data is verified.

Click the "Cancel" button to return to the *NACC Neuropathology Verify Data (Select ID)* page without verifying the MDS ID.

c. System Error

If the data elements for the MDS ID could not be verified because of a system error, the *NACC Neuropathology Verify Data (Verify Data)* page will display an error message (Figure 20). This situation usually occurs when someone else at your Center is trying to submit the file at the same time. Try to verify the data again. If the problem persists, please contact NACC.

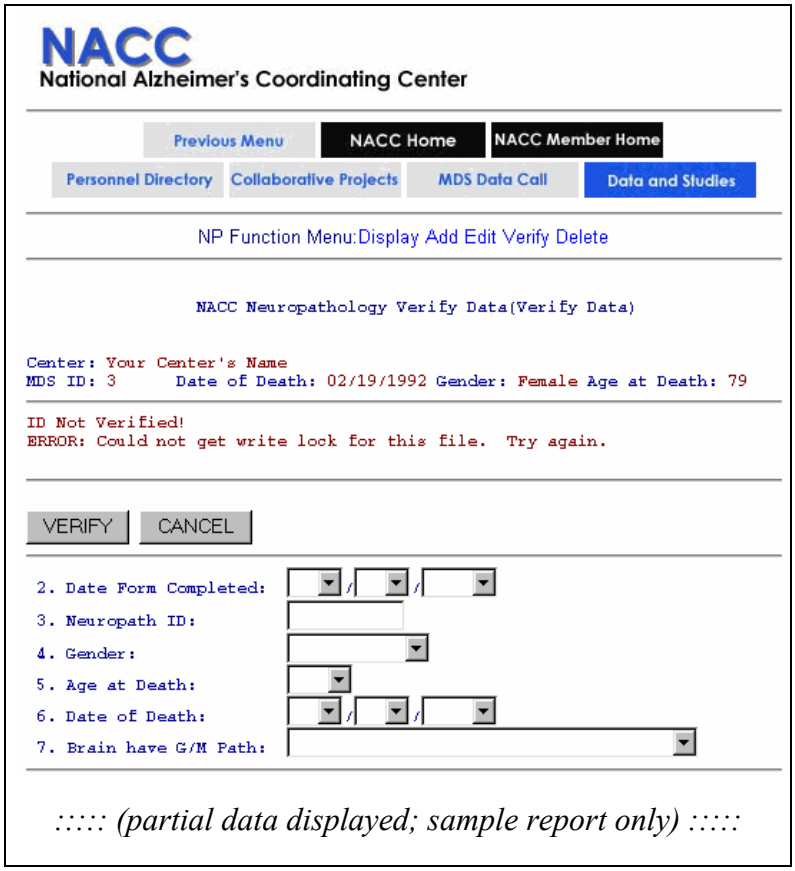

Figure 20.

Click the "Cancel" button to return to the *NACC Neuropathology Verify Data (Select ID)* page without verifying the MDS ID.

5. "Delete" Function

This function allows the deletion of MDS IDs which have been entered through the "Add" function of the Neuropathology Web Data Management System.

IDs identified in the MDS database as autopsied may not be deleted with this function. To delete these IDs from the MDS database, contact your Center's Data Manager prior to the next NACC Data Call.

To delete an MDS ID, click on "Delete" in the function menu to open the *Neuropathology Delete ID (Request ID)* page (Figure 21).

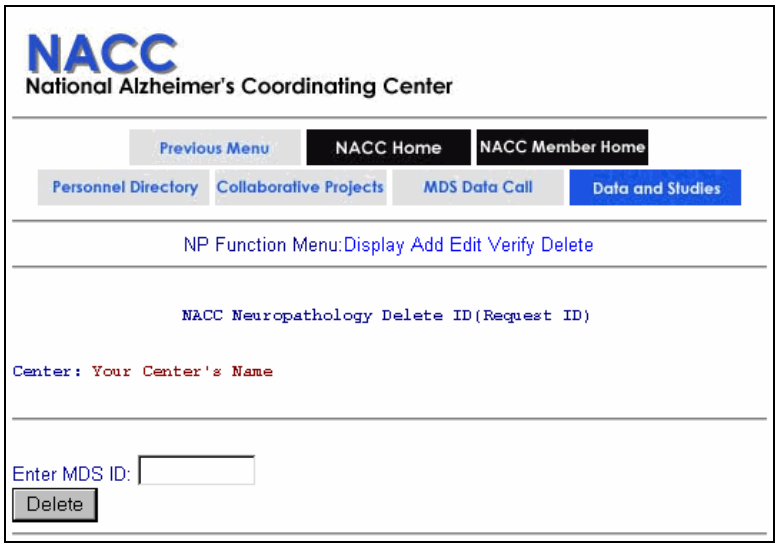

Figure 21.

Confirm that deletion is allowed:

- Click in the box after "Enter MDS ID".
- Type the MDS ID to be deleted, using the same format as IDs already in your MDS (for example, if your current MDS IDs have leading zeros, then type this ID with a leading zero).
- Click on the "Delete" button.

a. ID Found

If the MDS ID exists in the neuropathology data set and can be deleted, the *NACC Neuropathology Delete ID (ID Found)* page will be displayed (Figure 22).

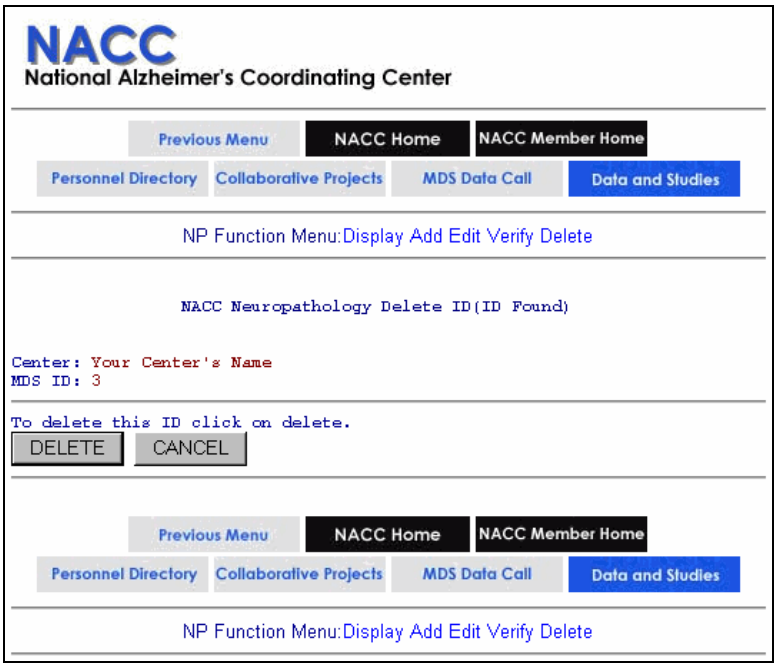

Figure 22.

- Click on the "Delete" button again to remove the MDS ID, or click on the "Cancel" button to return to the *NACC Neuropathology Delete ID (Request ID)* page.

If the MDS ID was successfully deleted, the *NACC Neuropathology Delete ID (Request ID)* page will be displayed with the message "ID Deleted!" (Figure 23). You may continue to delete additional MDS IDs or click on the "Previous Menu" button in the web page header to return to your Center's Neuropathology Data Management page.

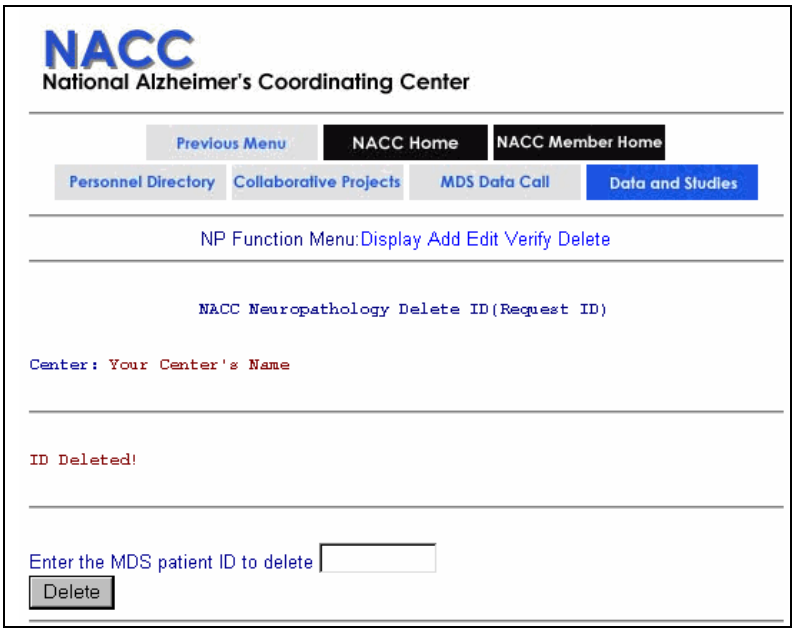

Figure 23.

b. System Error

If the MDS ID could not be deleted, an error message will be displayed (Figure 24). This situation usually occurs when someone else at your Center is trying to submit the file at the same time. Try to delete the MDS ID again. If the problem persists, please contact NACC.

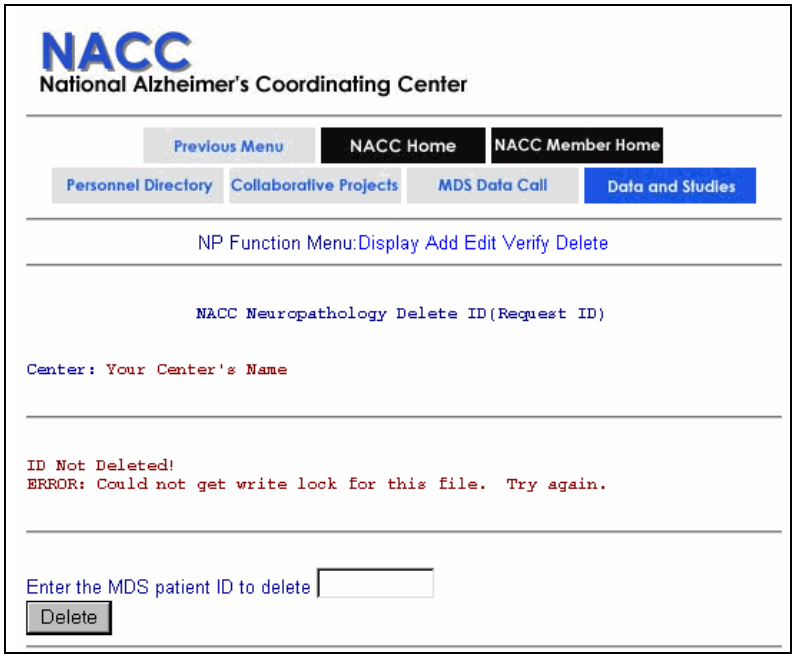

Figure 24.

You may continue to delete additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

c. ID Cannot be Located

If the MDS ID could not be deleted because it is not in the Neuropathology Web Data Management System, the *NACC Neuropathology Delete ID (ID Not Found)* page will be displayed (Figure 25). Check your MDS ID carefully using the "Display" function.

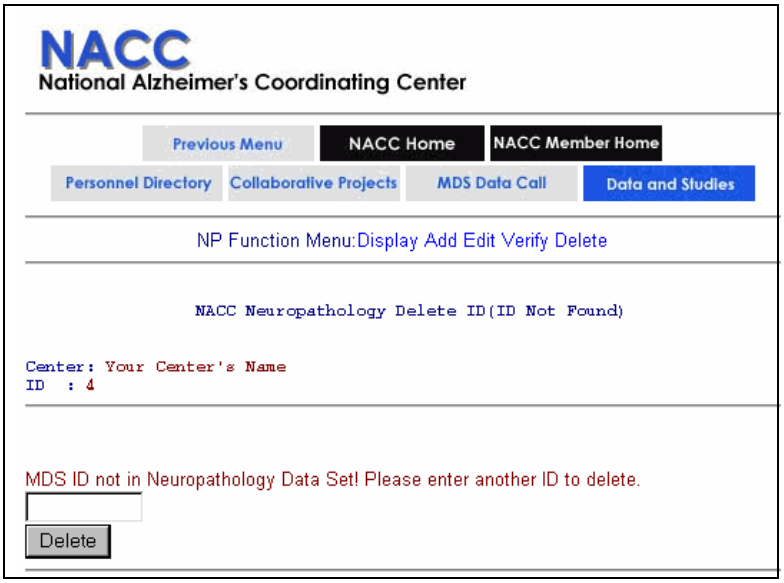

Figure 25.

You may continue to delete additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

d. ID Cannot be Deleted

If the ID could not be deleted because it is located in the MDS with an autopsy value of 'yes', the *NACC Neuropathology Delete ID (ID in MDS)* page is displayed (Figure 26). Check the ID carefully using the "Display" function.

IDs that are in the MDS and have been autopsied cannot be deleted. To delete or change these IDs, contact your Center's data manager prior to the next MDS Data Call.

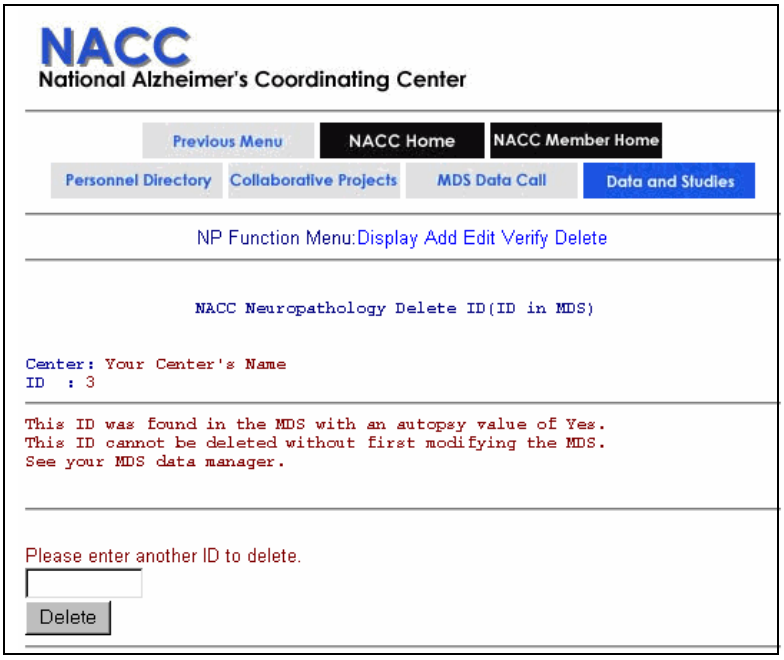

Figure 26.

You may continue to delete additional MDS IDs or click on the "Previous Menu" button to return to your Center's *Neuropathology Data Management* page.

Appendix A

NACC Neuropathology Data Form

National Alzheimer's Coordinating Center
Department of Epidemiology, School of Public Health and Community Medicine, University of Washington
4311 11th Avenue NE #300
Seattle, WA 98105
phone: (206) 543-8637; fax: (206) 616-5927
e-mail: naccmail@u.washington.edu
website: https://www.alz.washington.edu

NEUROPATHOLOGY DATA FORM

ADRC/ADC: _____ **Completed by:** _____

1. MDS Patient ID..... ☐☐☐☐☐☐☐☐☐☐

2. Date form completed..... ☐☐ ☐☐ ☐☐☐☐
month *day* *year*

3. Neuropath ID ..... ☐☐☐☐☐☐☐☐☐☐

4. Gender..... ☐ *(M or F)*

5. Age at death ..... ☐☐☐ *years*

6. Date of death..... ☐☐ ☐☐ ☐☐☐☐
month *day* *year*

7. Does the brain have any gross or microscopic pathology (including any Alzheimer type pathology such as senile plaques and neurofibrillary tangles)?

(*mark one box)*

☐ 1 Yes

☐ 2 No

Code 9 ("No neuropathology diagnosis available") has been removed.
Skip pattern removed. Items 8A through 16A must be answered.

Alzheimer's Disease. For all brains in which there is any degree of Alzheimer type pathology (ranging from a few senile plaques and neurofibrillary tangles to advanced Alzheimer's Disease), please indicate the nature of the pathology according to commonly used pathologic criteria.

8A. NIA/Reagan Institute neuropathological criteria used:

(*mark one box)*

☐ 1 High likelihood of dementia being due to Alzheimer's disease

☐ 2 Intermediate likelihood of dementia being due to Alzheimer's disease

☐ 3 Low likelihood of dementia being due to Alzheimer's disease

☐ 4 Criteria not met

☐ 5 Not done

☐ 9 Missing/unknown

8B. CERAD neuropathological criteria used:

(*mark one box)*

☐ 1 Definite Alzheimer's disease

☐ 2 Probable Alzheimer's disease

☐ 3 Possible Alzheimer's disease

☐ 4 Criteria not met

☐ 5 Not done

☐ 9 Missing/unknown

8C. ADRDA/Khachaturian neuropathological criteria used:

(*mark one box)*

☐ 1 Alzheimer's disease

☐ 2 Criteria not met

☐ 3 Not done

☐ 9 Missing/unknown

8D. Other or unspecified neuropathological criteria used (e.g., Tierney, etc.):

(*mark one box)*

☐ 1 Alzheimer's disease, unspecified

☐ 2 Criteria not met

☐ 3 Not done

☐ 9 Missing/unknown

Neurofibrillary pathology. For all brains in which topographic staging of neurofibrillary degeneration was done, please indicate the stage with a number from 1–7. If Braak staging was not done, use number 8.

9. Braak & Braak Neurofibrillary Stage.

(*mark one box)*

☐ 1 Stage I

☐ 2 Stage II

☐ 3 Stage III

☐ 4 Stage IV

☐ 5 Stage V

☐ 6 Stage VI

☐ 7 Neurofibrillary degeneration not present

☐ 8 Not assessed

☐ 9 Missing/unknown

Plaque score. For the most severely affected cortical region, please indicate the plaque score. Please use the Consortium to Establish a Registry of Alzheimer's Disease (CERAD) standards for sparse, moderate, and frequent.

10. Neuritic plaques (plaques with argyrophilic dystrophic neurites with or without dense amyloid cores).

(*mark one box)*

☐ 1 Frequent neuritic plaques

☐ 2 Moderate neuritic plaques

☐ 3 Sparse neuritic plaques

☐ 4 No neuritic plaques

☐ 5 Not assessed

☐ 9 Missing/unknown

11. Diffuse plaques (plaques with non-compact amyloid and no apparent dystrophic neurites).

(*mark one box)*

☐ 1 Frequent diffuse plaques

☐ 2 Moderate diffuse plaques

☐ 3 Sparse diffuse plaques

☐ 4 No diffuse plaques

☐ 5 Not assessed

☐ 9 Missing/unknown

12. Is ischemic, hemorrhagic or vascular pathology present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

Skip pattern removed. Items 12A through 12L must be answered.

12A. Are one or more large artery cerebral infarcts present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

12B. Are one or more cortical microinfarcts (including "granular atrophy") present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

CONTINUE with 12C on the next page.

12C. Are one or more lacunes (small artery infarcts and/or hemorrhages) present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

12D. Are single or multiple hemorrhages present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

12E. Is subcortical arteriosclerotic leukoencephalopathy present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

12F. Is cortical laminar necrosis present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

12G. Is medial temporal lobe sclerosis (including hippocampal sclerosis) present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

CONTINUE with 12H on the next page.

12H. Is atherosclerotic vascular pathology (of the circle of Willis) present?

(*mark one box)*

☐ 1 None

☐ 2 Mild

☐ 3 Moderate

☐ 4 Severe

☐ 5 Not assessed

☐ 9 Missing/unknown

12I. Is arteriosclerosis (small parenchymal arteriolar disease) present?

(*mark one box*)

☐ 1 None

☐ 2 Mild

☐ 3 Moderate

☐ 4 Severe

☐ 5 Not assessed

☐ 9 Missing/unknown

12J. Is amyloid angiopathy present?

(*mark one box)*

☐ 1 None

☐ 2 Mild

☐ 3 Moderate

☐ 4 Severe

☐ 5 Not assessed

☐ 9 Missing/unknown

12K. Is another type of angiopathy (e.g., CADASIL or arteritis) present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

CONTINUE with 12L on the next page.

12L. Is there other pathology related to ischemic or vascular disease not previously specified present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

Lewy body pathology. For all brains in which Lewy bodies are detected, indicate the presence and distribution of Lewy-related pathology. This classification is independent of the clinical presentation, which may be variable and include Parkinsonism, dementia, psychosis, sleep disorders, etc.

13. Pathology is consistent with criteria of Consortium on Dementia with Lewy Bodies for:

(select only one)

☐ 1 Lewy body pathology, brainstem predominant type

☐ 2 Lewy body pathology, intermediate or transitional (limbic) type

☐ 3 Lewy body pathology, diffuse (neocortical) type

☐ 4 Lewy body pathology, unspecified or not further assessed

☐ 5 No Lewy bodies

☐ 6 Not assessed

☐ 9 Missing/unknown

Frontotemporal degenerations (FTD). (Use this for non-Alzheimer degenerative disorders that commonly have the brunt of cortical changes in frontal and temporal lobes, but may involve other cortical and subcortical regions and have variable clinical presentations, including frontal lobe dementia, progressive aphasia, progressive apraxia, etc.)

14A. Pick's Disease:

(mark one box)

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

CONTINUE with 14B on the next page.

14B. Corticobasal degeneration:

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

14C. Progressive supranuclear palsy:

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

14D. Frontotemporal dementia and Parkinsonism with tau-positive or argyrophilic inclusions:

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

14E. Tauopathy, other (e.g., tangle-only dementia and argyrophilic grain dementia):

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

14F. FTD with ubiquitin-positive (tau-negative) inclusions:

(*mark one box)*

☐ 1 FTD with motor neuron disease

☐ 2 FTD without motor neuron disease

☐ 3 None present

☐ 4 Not assessed

☐ 9 Missing/unknown

CONTINUE with 14G on the next page.

14G. Is there FTD with no distinctive histopathology (tau-negative, ubiquitin-negative, and no argyrophilic inclusions)?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

14H. Was FTD "not otherwise specified" present (e.g., "immunostaining for ubiquitin and tau not done")?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

Prion-related disorders:

15A. Is Creutzfeldt-Jakob disease or variant CJD present?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

15B. Are other prion diseases present (e.g., Gerstmann-Straussler syndrome)?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

Other major pathologic disorders (e.g., infectious, immunologic, metabolic, neoplastic, toxic or degenerative).

16A. Are other major pathologic disorders present (not addressed by questions 8–15)?

(*mark one box)*

☐ 1 Yes

☐ 2 No

☐ 3 Not assessed

☐ 9 Missing/unknown

SKIP: If 2, 3 or 9, go to #17A.

16B. If 16A is yes, then specify below (one disorder per line):

1 _____

2 _____

3 _____

17A. Family history information relevant to neuropathologic diagnosis. Choose one of the following categories that most accurately describes the **family** information available:

(mark one box)

☐ 1 Family history of similar neurodegenerative disorder

☐ 2 Family history of other (dissimilar) neurodegenerative disorder

☐ 3 No family history of similar or dissimilar neurodegenerative disorder

☐ 4 Family history of both similar and dissimilar neurodegenerative disorder

☐ 9 Family history unknown/not available/missing

SKIP: If 1, 3 or 9, go to #18A.

17B. If 17A is 2 or 4, then specify: _____

Genetic variants or polymorphisms. For each of the following three common genetic variants or polymorphisms, choose the patient's genotype, if known; select "not available or not assessed" if unknown:

18A. Apolipoprotein-E:

(*mark one box)*

☐ 1 e3, e3

☐ 2 e3, e4

☐ 3 e3, e2

☐ 4 e4, e4

☐ 5 e4, e2

☐ 6 e2, e2

☐ 9 Missing/unknown/not assessed

18B. Tau haplotype:

(*mark one box)*

☐ 1 H1, H1

☐ 2 H1, H2

☐ 3 H2, H2

☐ 4 Other polymorphism (e.g., A0)

☐ 9 Missing/unknown/not assessed

18C. PRNP codon 129:

(*mark one box)*

☐ 1 M, M

☐ 2 M, V

☐ 3 V, V

☐ 9 Missing/unknown/not assessed

19. Genetic or chromosomal abnormalities. Choose below the ONE known genetic or chromosomal abnormality that best describes the subject:

(mark one box)

☐ 1 APP mutation

☐ 2 PS1 mutation

☐ 3 PS2 mutation

☐ 4 Tau mutation

☐ 5 α-Synuclein mutation

☐ 6 Parkin mutation

☐ 7 PRNP mutation

☐ 8 Huntingtin mutation

☐ 9 Notch 3 mutation (CADASIL)

☐ 10 Other known genetic mutation (e.g., ABri, neuroserpin)

☐ 11 Down syndrome

☐ 12 Other chromosomal abnormality

☐ 13 No known genetic or chromosomal abnormality

☐ 50 Not assessed

☐ 99 Missing/unknown

Appendix B

NACC Neuropathologic Diagnosis Coding Guidebook

NACC Neuropathologic Diagnosis Coding Guidebook

The NACC Neuropathologic Diagnosis Coding Guidebook contains procedures to be followed when completing the NACC Neuropathology Data Form. The authors of this Guidebook are the members of the ADC Neuropathology Core Leaders' Steering Committee:

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Dennis Dickson, MD, Mayo Clinic

Bernardino Ghetti, MD, Indiana University

INTRODUCTION

1. *Please answer ALL items for ALL subjects. Previous "skip" patterns caused data interpretation problems.*

2. *All instructions and reference citations within this Guidebook are printed in italicized text.*

3. *Explanation of allowable codes:*

   "Not done" and "Not assessed" - these responses are equivalent and some questions use one version or the other.

   "Missing/unknown" - this response indicates the data is not available because it has been lost or is no longer retrievable.

1.– 6. DEMOGRAPHICS

Please provide identification and demographic neuropathology information in questions 1 through 6.

7. Does the brain have any gross or microscopic pathology (including any Alzheimer type pathology such as senile plaques and neurofibrillary tangles)?

Answer "no" only if the brain is completely devoid of any histopathologic changes. If there are only minimal Alzheimer type changes, please indicate this in the following questions.

1. Yes
2. No

ALZHEIMER TYPE PATHOLOGY

For all brains in which there is any degree of Alzheimer type pathology, ranging from a few senile plaques and neurofibrillary tangles to advanced Alzheimer's disease, please indicate the nature of the pathology according to commonly used pathologic criteria. Follow the published guidelines for these entries. Answer "not done" for all criteria not used.

8A. NIA/Reagan Institute neuropathological criteria

(Hyman BT, Trojanowski JQ. Editorial on Consensus recommendations for the postmortem diagnosis of Alzheimer's Disease from the National Institute on Aging and Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Assessment of Alzheimer's Disease. J Neuropathol Exp Neurol 1997;56:1095-1097.)

1. High likelihood of dementia being due to Alzheimer's disease
2. Intermediate likelihood of dementia being due to Alzheimer's disease
3. Low likelihood of dementia being due to Alzheimer's disease
4. Criteria not met
5. Not done
9. Missing/unknown

8B. CERAD neuropathological criteria

(Mirra SM, Hart MN, Terry RD. Making the diagnosis of Alzheimer's disease. A primer for practicing pathologists. Arch Pathol Lab Med 1993;117:132-144.)

1. Definite Alzheimer's disease
2. Probable Alzheimer's disease
3. Possible Alzheimer's disease
4. Criteria not met
5. Not done
9. Missing/unknown

8C. ADRDA/Khachaturian neuropathological criteria

(Khachaturian S. Diagnosis of Alzheimer's disease. Arch Neurol 1985;42:1097-1105.)

1. Alzheimer's disease
2. Criteria not met
3. Not done
9. Missing/unknown

8D. Other or unspecified neuropathological criteria

1. Alzheimer's disease, unspecified
2. Criteria not met
3. Not done
9. Missing/unknown

Neurofibrillary Pathology

For all brains in which topographic staging of neurofibrillary degeneration was done, please indicate the stage according to the scheme proposed by Braak and Braak. While the original methods employed Gallyas stains, other stains for neurofibrillary pathology (e.g., tau immunostains, other silver stains or thioflavin-S) may be used. The focus is on the distribution of neurofibrillary tangles. (Nagy Z, Yilmazer-Hanke DM, Braak H, et al. Assessment of the pathological stages of Alzheimer's disease in thin paraffin sections: a comparative study. Dementia & Geriatric Cognitive Disorders 1998;9:140-144; Braak H, Braak E. Neuropathological stageing of Alzheimer-related changes. Acta Neuropathol 1991;82:239-259.)

9. Braak & Braak Stage

Stages I–II correspond to NFT limited to the transentorhinal/entorhinal region; Stages III–IV to limbic stages; and Stages V–VI to neocortical stages. Stage VI implies involvement of primary cortices. Answer "not assessed" if topographic staging has not been done.

1. Stage I
2. Stage II
3. Stage III
4. Stage IV
5. Stage V
6. Stage VI
7. Neurofibrillary degeneration not present
8. Not assessed
9. Missing/unknown

Plaques

For the most severely affected cortical region, please indicate the plaque score. For an illustration of ratings of frequent, moderate and sparse, please refer to: Mirra SM, Hart MN, Terry RD. Making the diagnosis of Alzheimer's disease. A primer for practicing pathologists. Arch Pathol Lab Med 1993;117:132-144.

10. Neuritic plaques

Neuritic plaques are considered to be plaques with argyrophilic, thioflavin-S-positive or tau-positive dystrophic neurites with or without dense amyloid cores. Answer "not assessed" if neuritic plaques have not been specifically analyzed.

1. Frequent neuritic plaques
2. Moderate neuritic plaques
3. Sparse neuritic plaques
4. No neuritic plaques
5. Not assessed
9. Missing/unknown

11. Diffuse plaques

Diffuse plaques are considered to be plaques with non-compact amyloid and no apparent dystrophic neurites. Answer "not assessed" if diffuse plaques have not been specifically analyzed.

1. Frequent diffuse plaques
2. Moderate diffuse plaques
3. Sparse diffuse plaques
4. No diffuse plaques
5. Not assessed
9. Missing/unknown

ISCHEMIC, HEMORRHAGIC AND VASCULAR PATHOLOGY

This section is meant to indicate the presence of vascular pathology, but not the absolute burden, volume, or severity of change. More detailed information about lesion distribution, burden, etc is presumed to be part of a research database. Questions about severity of vascular pathology are of necessity subjective, since current methods to easily and consistently assess severity of vascular disease have not been validated or widely implemented. Even if infarcts, focal sclerosis and hemorrhages are not present, and there is evidence of vascular pathology, be sure to answer questions 12I through 12K to record information about severity of atherosclerotic, arteriosclerotic, and amyloid vascular pathology.

12. Is ischemic, hemorrhagic or vascular pathology present?

Please include atherosclerosis, arteriosclerosis or amyloid angiopathy.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12A. One or more large artery cerebral infarcts

This category refers to infarcts larger than 1-cm in diameter in the distribution of large and medium sized meningocerebral vessels rather than small parenchymal vessels. Infarcts meeting these criteria are included regardless of the histologic age and include acute lesions as well as chronic cystic lesions.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12B. One or more cortical microinfarcts (including “granular atrophy”)

This category refers to infarcts that are detected microscopically and may not be grossly visible, or may appear to the naked eye as cortical granularity. Microinfarcts in non-cortical areas should not be included in this category. Infarcts meeting these criteria are included regardless of the histologic age and include acute lesions as well as chronic cystic lesions.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12C. One or more lacunes (small artery infarcts and/or hemorrhages)

This category refers to cystic/old infarcts or hemorrhages 1-cm or less in diameter that are usually grossly identified and in the distribution of small parenchymal vessels, most often in basal ganglia, thalamus, pons, cerebellum and cerebral white matter.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12D. One or more hemorrhages

This category refers to cerebral hemorrhages, regardless of size in any region of the brain.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12E. Subcortical arteriosclerotic leukoencephalopathy

This category refers to multifocal or diffuse white matter pathology attributable to arteriosclerotic small vessel disease and will be associated with axonal and myelin loss in the centrum ovale, often associated with brain infarcts. White matter rarefaction confined to the immediate periventricular region (so-called periventricular "capping") should not be included. (Roman GC. Senile dementia of the Binswanger type, a vascular form of dementia in the elderly; JAMA 1987;258:1782-1788 and Caplan LR. Binswanger's disease – revisited. Neurology 1995;45:626-633.)

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12F. Cortical laminar necrosis

This category refers to selective cortical necrosis of middle and lower cortical lamina most often associated with cerebral hypoperfusion and concentrated in border zones between major cerebral arteries.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12G. Medial temporal lobe sclerosis (including hippocampal sclerosis)

This category refers to selective neuronal loss and gliosis ("sclerosis") of medial temporal lobe structures. In the hippocampus, this is often limited to CA1 and the subiculum with variable involvement of endplate and CA2. The amygdala and entorhinal cortex may also be affected. In some cases there is a clear history of cerebral hypoperfusion. In others there may be a history of epilepsy. Similar pathology can also be seen in the setting of neurodegenerative disorders (e.g., FTD).

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12H. Atherosclerotic vascular pathology (of the circle of Willis)

Use this item to indicate the severity of atherosclerotic (intimal and medial fibrofatty atheromatous plaques) disease in the large (named) arteries at the base of the brain (i.e., the circle of Willis). The assessment is qualitative and subjective and should indicate an estimate of overall severity rather than an individual vessel.

1. None
2. Mild
3. Moderate
4. Severe
5. Not assessed
9. Missing/unknown

12I. Arteriosclerosis (small parenchymal arteriolar disease)

Use this item to indicate the severity of arteriosclerosis (arteriolosclerosis) (hyalinosis of the media and adventitia) of small parenchymal and/or leptomeningeal vessels. The assessment is qualitative and subjective and should indicate an estimate of overall severity rather than an individual vessel.

1. None
2. Mild
3. Moderate
4. Severe
5. Not assessed
9. Missing/unknown

12J. Amyloid angiopathy

Use this item to indicate the severity of cerebral amyloid angiopathy as demonstrated with special stains for amyloid (e.g., Congo red, thioflavin-S, or Aβ immunostaining). The assessment is qualitative and subjective, and should indicate an estimate of overall severity rather than an individual vessel.

1. None
2. Mild
3. Moderate
4. Severe
5. Not assessed
9. Missing/unknown

12K. Another type of angiopathy (e.g., CADASIL or arteritis)

Use this item to indicate the presence of other forms of arteriopathy not mentioned in the above categories.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

12L. Other pathology related to ischemic or vascular disease not previously specified

This category refers to ischemic or vascular disease not specifically mentioned in the above categories.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

LEWY BODY PATHOLOGY

For all brains in which Lewy bodies are detected, indicate the presence and distribution of Lewy-related pathology. This classification is independent of the clinical presentation, which may be variable and include Parkinsonism, dementia, psychosis, sleep disorders, etc.

Characterization of Lewy body pathology should use guidelines set forth by "Consortium on Dementia with Lewy bodies." (McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): Report of the consortium on DLB international workshop. Neurology 1996;47:1113-1124)

The preferred method of assessment is with immunohistochemistry for synuclein. While ubiquitin has been used in the past, it is less specific than synuclein. If Lewy body pathology was assessed only with H&E stains (neither synuclein or ubiquitin), please specify "4 – Lewy body pathology, unspecified" as your answer.

While the published criteria recommend counts of Lewy bodies, this may not be necessary if one can indicate the topographic distribution of Lewy bodies in accordance with the scheme adopted. The criteria consider a cortical region to be positive if more than isolated neurons are affected (more than 5 Lewy bodies per region). The diffuse (neocortical) type implies involvement of neocortical areas beyond the limbic lobe. The transitional (limbic) type implies cortical involvement limited to limbic lobe. Cases with Lewy bodies limited to the amygdala were not specifically addressed in the Consortium criteria, but should be included in the transitional (limbic) type for the sake of this database.

Pathologic characterization of Lewy body pathology is to be performed independent of Alzheimer related pathology for the sake of this neuropathologic database. Alzheimer pathology on these cases will be recorded in the previous section, "Alzheimer Type Pathology" (questions 8A through 11).

13. Pathology is consistent with criteria of Consortium of Dementia

1. Lewy body pathology, brainstem predominant type
2. Lewy body pathology, intermediate or transitional (limbic) type
3. Lewy body pathology, diffuse (neocortical) type
4. Lewy body pathology, unspecified
5. No Lewy bodies
6. Not assessed
9. Missing/unknown

FRONTOTEMPORAL DEGENERATIONS (FTD)

Use this category for non-Alzheimer degenerative disorders that commonly have the brunt of cortical changes in frontal and temporal lobes, but may involve other cortical and subcortical regions and have variable clinical presentations, including frontal lobe dementia, progressive aphasia, progressive apraxia, etc. (Trojanowski JQ, Dickson D: Update on the neuropathological diagnosis of frontotemporal dementias. J Neuropathol Exp Neurol 2001;60:1123-1126.)

14A. Pick's disease

For sake of uniformity and consistency, Pick's disease in this database is considered to be the classic form of the disease, the form referred to as type A Pick's disease in the classification of Constantinidis (Constandinidis J, Richard J, Tissot R. Pick's disease. Histological and clinical correlations. Eur Neurol 1974;11:208.) Such cases have sharply circumscribed frontotemporal atrophy with argyrophilic Pick bodies and ballooned neurons ("Pick cells"). If there are no Pick bodies, then an alternative diagnosis should be used.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

14B. Corticobasal degeneration

Corticobasal degeneration should refer to a condition in which there is circumscribed atrophy, often in a parasagittal distribution and microscopically characterized by extensive tau-positive or Gallyas-positive thread-like structures in gray and white matter of affected cortices, as well as the basal ganglia, thalamus and rostral brainstem. While ballooned neurons were emphasized in original description and are usually present, they are not essential to the diagnosis. Most cases will have tau-positive plaque-like structures, so-called astrocytic plaques.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

14C. Progressive supranuclear palsy

Progressive supranuclear palsy should refer to a condition with tau pathology in the basal ganglia, thalamus, brainstem and cerebellum. Original descriptions emphasized globose neurofibrillary tangles, but tau-positive or Gallyas-positive glial inclusions, both astrocytic (tufted astrocytes) and oligodendroglial (coiled bodies) are a constant finding. Thread-like structures are also common, especially in the diencephalon and brainstem. Cortical involvement is variable, but often relatively restricted to the peri-Rolandic region.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

14D. Frontotemporal dementia and Parkinsonism with tau-positive or argyrophilic inclusions

This classification will be used most often for cases of frontotemporal dementia and Parkinsonism linked to chromosome 17 (FTDP-17). Most cases have pathology that overlaps with CBD, PSP or Pick's disease and are associated with mutations in the Tau gene. Occasional cases with similar and extensive tau pathology in neurons and/or glia of the cortex and deep gray matter will have no family history or Tau mutations.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

14E. Tauopathy, other (e.g., tangle-only dementia and argyrophilic grain dementia)

Use this for non-Alzheimer degenerative disorders that have tau-positive or Gallyas-positive neuronal and/or glial lesions, but do not fit into any of the above groups. Argyrophilic grain disease should be used for cases with tau-positive or Gallyas-positive grains restricted to limbic and peri-limbic regions as originally described by Braak et al. (Braak H, Braak E. Cortical and subcortical argyrophilic grains characterize a disease associated with adult onset dementia. Neuropathol Appl Neurobiol 1989;15:13-26) Most cases also have a few ballooned neurons in the limbic lobe. Tangle-only or tangle-predominant dementia should have the brunt of neurofibrillary degeneration in the medial temporal lobe, often with many extracellular neurofibrillary tangles (Jellinger KA, Brancher C. Senile dementia with tangles (tangle predominant form of senile dementia.) Brain Pathol 1998;8:367-376). Presence of non-neuritic, diffuse amyloid plaques does not exclude this diagnosis.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

14F. FTD with ubiquitin-positive (tau-negative) inclusions

Use this for non-Alzheimer degenerative disorders with focal atrophy of frontal, temporal or frontotemporal regions and relatively nonspecific histopathology with routine histopathologic methods, as well as with tau and synuclein immunostaining. Ubiquitin immunostaining will show perikaryal inclusions in affected cortices and often in the dentate fascia of the hippocampus. Many cases will show striatal or substantia nigra pathology and many have white matter changes, as well. Some cases will have clinical and/or pathologic evidence of motor neuron disease, but others will not. If immunohistochemical characterization has not been performed, list the case as FTD "not otherwise specified" (see question 14H).

1. FTD with motor neuron disease
2. FTD without motor neuron disease
3. None present
4. Not assessed
9. Missing/unknown

14G. FTD with no distinctive histopathology (tau-negative, ubiquitin-negative & no argyrophilic inclusions)

Use this for non-Alzheimer degenerative disorders with focal atrophy of frontal, temporal or frontotemporal regions and relatively nonspecific histopathology with routine histopathologic methods, as well as with tau, synuclein and ubiquitin immunostaining. If immunohistochemical characterization has not been performed, list the case as FTD "not otherwise specified" (see question 14H).

1. Yes
2. No
3. Not assessed
9. Missing/unknown

14H. FTD "not otherwise specified" (e.g., "immunostaining for ubiquitin and tau not done")

Use this for non-Alzheimer degenerative disorders with nonspecific histopathology that do not clearly fit the above categories or in which immunohistochemical or biochemical characterization is not available or has not been done.

1. Yes
2. No
3. Not assessed
9. Missing/unknown

PRION-RELATED DISORDERS

15A. Creutzfeldt-Jakob disease or variant CJD

Respond "yes" if the case has definite CJD. Such cases would have confirmation with either immunohistochemistry or western blot. If the case has spongiform change, but has not been confirmed with immunohistochemistry or western blot, it should be listed under "Other Major Pathologic Disorders" as "CJD, unconfirmed" (see question 16B).

1. Yes
2. No
3. Not assessed
9. Missing/unknown

15B. Other prion diseases (e.g., Gerstmann-Straussler syndrome)

Respond "yes" if the case has definite prion disease, other than CJD or variant CJD. Such cases would have confirmation with either immunohistochemistry or western blot. If the case has spongiform change, but has not been confirmed with immunohistochemistry or western blot, it should be listed under "Other Major Pathologic Disorders" as "CJD, unconfirmed" (see question 16B).

1. Yes
2. No
3. Not assessed
9. Missing/unknown

OTHER MAJOR PATHOLOGIC DISORDERS

Use this section to record infectious, immunologic, metabolic, neoplastic, toxic or degenerative disease processes.

16A. Other major pathologic disorders

1. Yes
2. No
3. Not assessed
9. Missing/unknown

SKIP: If 2, 3 or 9, go to question 17A.

16B. If 16A is "yes", then specify.

GENETICS & FAMILY HISTORY

17A. Family history information relevant to neuropathologic diagnosis.

Choose one of the following categories that most accurately describes the family information available.

1. Family history of similar neurodegenerative disorder
2. Family history of other (dissimilar) neurodegenerative disorder
3. No family history of similar or dissimilar neurodegenerative disorder
4. Family history of both similar and dissimilar neurodegenerative disorder
9. Family history unknown or not available

SKIP: If 1, 3 or 9, go to question 18A.

17B. If 17A is "2" or "4", then specify.

18A. Apolipoprotein-E genotype

One of the major genetic risk factors for Alzheimer's disease is apolipoprotein-E. Please note the genotype, if known.

1. e3, e3
2. e3, e4
3. e3, e2
4. e4, e4
5. e4, e2
6. e2, e2
9. Missing/unknown/not assessed

18B. Tau haplotype

For tauopathies such as PSP and CBD, there is increased frequency of the H1 haplotype in the tau gene. It may also be increased in Parkinson's disease. Other polymorphisms in the tau gene have also been described, such as the A0 dinucleotide repeat. If known, please include. (Baker M, Litvan I, Houlden H, et al. Association of an extended haplotype in the tau gene with progressive supranuclear palsy. Hum Molec Genetics 1999;8:711-715.)

1. H1, H1
2. H1, H2
3. H2, H2
4. Other polymorphism (e.g., A0)
9. Missing/unknown/not assessed

18C. PRNP codon 129

For prion cases the polymorphism (methionine or valine) at codon 129 influences the phenotype.

1. M, M
2. M, V
3. V, V
9. Missing/unknown/not assessed

19. Genetic or chromosomal abnormalities

Genetic information on the case is recorded here. Please choose "13" when a reasonable clinical evaluation has provided no indication that one of the specific known genetic or chromosomal abnormalities listed should be used to characterize this case. Please choose "50" when neither sufficient clinical work-up nor genetic testing to reasonably observe whether one of the conditions listed might be present has been performed.

1. APP mutation
2. PS1 mutation
3. PS2 mutation
4. Tau mutation
5. α-Synuclein mutation
6. Parkin mutation
7. PRNP mutation
8. Huntingtin mutation
9. Notch 3 mutation (CADASIL)
10. Other known genetic mutation (e.g., ABri, neuroserpin)
11 Down syndrome
12. Other chromosomal abnormality
13. No known genetic or chromosomal abnormality
50. Not assessed
99. Missing/unknown

REFERENCE CITATIONS

Page 2:

Hyman BT, Trojanowski JQ. *Editorial on Consensus recommendations for the postmortem diagnosis of Alzheimer's Disease from the National Institute on Aging and Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Assessment of Alzheimer's Disease*. J Neuropathol Exp Neurol 1997; 56:1095-1097.

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Khachaturian S. *Diagnosis of Alzheimer's disease.* Arch Neurol 1985; 42:1097-1105.

Nagy Z, Yilmazer-Hanke DM, Braak H, et al. *Assessment of the pathological stages of Alzheimer's disease in thin paraffin sections: a comparative study.* Dementia & Geriatric Cognitive Disorders 1998; 9:140-144.

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