NATIONAL INSTITUTE ON AGING

ALZHEIMER DISEASE

FAMILY BASED STUDY

PROCEDURES MANUAL

May 2022

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1.0 Abbreviations

AD	Alzheimer's Disease
ADRC	Alzheimer Disease Research Center
CT	Computer assisted Tomography
CUMC	Columbia University Medical Center
DNA	Deoxyribonucleic Acid
DQ	Dementia Questionnaire
EDTA	Ethylene Diamine Tetra-acetic Acid
FBS	Family Based Study
FTD	Frontotemporal Dementia
GUID	Globally Unique Identifier
IATA	International Air Transport Association
IRB	Internal Review Board
LBD	Lewy Body Dementia
LOAD	Late Onset Alzheimer's Disease
EOAD	Early Onset Alzheimer's Disease
MDS	Minimum Data Set
MRI	Magnetic Resonance Imaging
NaHep	Sodium Heparin (Green-Top) Blood Collection Tube (10 ml)
NCRAD	National Centralized Repository for Alzheimer's Disease and Related Dementias
NYBB	New York Brain Bank
NIA	National Institute on Aging
NINCDS-ADRDA	National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease Related Disorders Association
NPIQ-CBRS	Integrated Neuropsychiatric Inventory questionnaire and the Behavior Rating Scale for dementia
PBMC	Peripheral Blood Mononuclear Cell
PCS	Personal, Cultural and Structural analysis

2.0 Purpose

The purpose of this manual is to provide NIA AD-FBS staff (PIs and study coordinators) at the various study sites with instructions for family recruitment, sample collection and data submission. The following may be collected at each study visit:

- Medical History
- Family History
- Risk factors
- Dementia Questionnaire (optional- for deceased individuals)
- Psychometrics
- NPIQ-CBRS
- Whole Blood (for DNA and plasma extraction)
- PBMC (for extraction of white blood cells)

These procedures are relevant to all study personnel responsible for data and biological specimen collection.

3.0 NIAAD-FBS Information

The National Institute on Aging -Alzheimer's Disease Family Based Study (NIAAD-FBS) is a U24 proposal in which the main purpose is to develop or maintain unique resources to be shared with the scientific community. Dr. Richard Mayeux at Columbia University, Dr. Tatiana Foroud at Indiana University, and Dr. Alison Goate at the Icahn School of Medicine at Mount Sinai, are the co-principal investigators for this study.

3.1 Participating Sites

Site #	Site Name
4	**Columbia University (coordinating center)**
8	**Indiana University**
15	**Rush University**
22	**University of Pittsburgh**
25	**University of Texas Southwestern**
26	**University of Washington**
27	**Washington University**
61	**University of Miami**
62	**North Carolina A & T**
63	**Case Western University**
10R	**Mayo Clinic Rochester**
ISMMS	**Icahn School of Medicine at Mount Sinai**
64	**University of California, Los Angeles**
65	**Rutgers University**

3.2 NIAAD- FBS Contacts

Site Name	PI	PI Email	Site Coordinator	Coordinator Email
Case Western	Jonathan Haines	Jonathan.haines@case.edu	Renee Laux	Ral119@case.edu
Columbia	Richard Mayeux	rpm2@columbia.edu	Dolly Reyes-Dumeyer	dr22100@cumc.columbia.edu
Indiana	Jared Brosch	jbrosch@iupui.edu	Kelly Horner	kjhorner@iu.edu
ISMMS	Alison Goate	alison.goate@mssm.edu		
Mayo Rochester	Brad Boeve	bboeve@mayo.edu	Amber O'Reilly	oreilly.amber@mayo.edu
Miami	Margaret Pericak-Vance	MPericak@med.miami.edu		
NCRAD	Tatiana Foroud	tforoud@iu.edu	Kelley Faber	kelfaber@iu.edu
NCAT	Goldie S Byrd	gsbyrd@ncat.edu	Takiyah D. Starks	tdstarks@ncat.edu
Rush	David Bennett	dbennett@rush.edu	Celina Pavon	CELINA_PAVON@rush.edu
UPitt	Robert Sweet	SweetRA@upmc.edu	Elise Weamer	weamerea@upmc.edu
UTSW	Roger Rosenberg	Roger.Rosenberg@UTSouthwestern.edu	Amy Browning	Amy.Browning@UTSouthwestern.edu
UWash	Debby Tsuang	dwt1@uw.edu	Sarah Peterson	sk.peterson1@outlook.com
WashU	Carlos Cruchaga	cruchagc@psychiatry.wustl.edu	Joanne Norton	nortonj@psychiatry.wustl.edu

UCLA	Keith Vossel	kvossel@mednet.ucla.edu	Aisha Mohammed	amohammed@mednet.ucla.edu
Rutgers	Mark Gluck	Gluck@Newark.rutgers.edu	Genesis Tan	gt308@sph.rutgers.edu

4.0 Family Recruitment and Evaluation

Sites will typically recruit individuals from their memory clinics, referrals from other sites, NCRAD or the Alzheimer's Association, as well as previously unidentified members of existing families. We might also use advertisements such as radio, television and newspapers. We will recruit participants who meet the criteria as described in section 4.1.

4.1 Recruitment Inclusion/Exclusion Criteria

A. Inclusion criteria

INCLUSION CRITERION	METHOD OF ASCERTAINMENT
3 living relatives willing to participate. • **2 of them should be siblings** • **The 3rd could be any other family member (e.g. cousin, aunt/uncle, etc)**	Documented by history, medical records and/or examination
• First sibling with established diagnosis of definite AD (autopsy/tissue as described on the brain donation section 7.0**), probable AD OR a diagnosis of a related neurodegenerative disorder such as FTD or LBD. • Second sibling with established diagnosis of definite AD (autopsy/tissue as described on the brain donation section 7.0**), probable AD, or possible AD OR a diagnosis of a related neurodegenerative disorder such as FTD or LBD. 3rd family member with established diagnosis of definite AD (autopsy/tissue as described on the brain donation section 7.0**), probable AD, or possible AD OR a diagnosis of a related neurodegenerative disorder such as FTD or LBD.	Documented by history, medical records and/or examination
Identified companion to serve as an informant for all participants in the proband's generation;	Self-report or report of family members
Participants who have capacity to consent or participants lacking capacity to consent with a surrogate/proxy in place to provide consent.	Research proxy/surrogate identified and documented in the research chart or next of kin (parent, spouse, adult child) identified and available

**The inclusion of families with only two individuals affected will be permitted with the coordinating site's approval, especially for non-Caucasian families.

Note: To allow flexibility on new recruitments, families will be divided into two tiers:
Tier 1 Families: All the criteria stated above must be met.
Tier 2 Families: Families where the original criteria are not met but there is at least one affected and another family member (cousin, aunt/uncle, parent) is affected, only one affected is alive and willing to participate or a family history of a deceased first degree relative with dementia.

Exclusion criteria

EXCLUSION CRITERION	METHOD OF ASCERTAINMENT
Failure to identify an appropriate informant;	Research staff will document surrogate and/or identify next of kin
Uncertainty of the clinical diagnosis of Alzheimer's disease or other related disorder;	Documented by history, medical records and/or examination
Discovery of additional diagnosis that could account for the clinical manifestations;	Documented by history, medical records and/or examination
Unwillingness to participate;	As indicated verbally or if a participant is not able to speak by a physical sign or refusing blood draw
Failure to identify a living relative with AD or other related disorder;	Family history
Participant lacking the capacity to consent and does not have a surrogate or proxy or next of kin to provide consent.	Research staff must identify proxy or next of kin

4.2 Recruitment Procedures

A. New Families Recruitment

For new families, the research site physicians or NCRAD may refer individuals (probands) who report a known family history of dementia to the research study. Once individuals have been referred to the study, and the family is approved by Columbia University, the coordinator or research staff who are designated to obtain consent will explain study participation and enroll individuals in the study.

B. New Individuals within Existing Families

For new participants from existing families, the proband and/or informant will facilitate participation of other family members by contacting family members about the study. Family members who wish to participate may contact the study coordinator directly or may give permission for the study coordinator or research staff to contact them. Through advertisements and community talks, individuals may directly contact the study staff regarding research participation. Families meeting the inclusion criteria will be enrolled.

4.3 Clinical Evaluation of New and Follow Up Individuals

Evaluations of participants will be the same across all sites. The diagnosis of AD is mainly clinical and rests on the physician, review of medical records and neuropsychological assessment. Computer assisted tomography (CT) of the brain, MRI or other laboratory studies are recommended to ensure full implementation of the NINCDS-ADRDA criteria, but for epidemiological studies this is not always feasible. Participants may also choose to go to their personal physician. We will establish and maintain contact with this individual in order to achieve the goals of confirming diagnoses. Participants may also choose to have imaging studies, laboratory investigations and neuropsychological studies as outpatients with their personal physician. Brain imaging results and laboratory results that are part of the participant's clinical chart may be made available to the research study with consent of release of medical information from the participant or surrogate. These records will be obtained for the purpose of confirming the dementia diagnoses.

Throughout the course of this study, participants who are unaffected or have questionable dementia will have a follow-up study visit every 18 months. At every visit, participants will get repeat neurological and medical examination, and neuropsychological testing in order to detect any change in the individual's cognitive status. Individuals are selected for interviews based on several factors: willingness to continue participation, availability, and if they are still living. Eligible participants will be consented again using verbal consent via telephone (this might be different at every site depending on their IRB mandate). Participants could be given the option to be interviewed via skype.

For deceased participants at follow up, a DQ (Appendix B) or MDS should be completed with the informant or next of kin.

4.4 Minimum Data Set

We established a standardized minimum dataset (MDS – Appendix A) for the study that includes demographic, medical and risk factor information. This process ensured that uniform data is collected across this multi-site study. In many situations, the proband has already been enrolled in other studies and the MDS can be extracted from the study database. De-identified data is transferred electronically to Columbia University on a quarterly basis (section 6.0) and if problems are encountered with the data, Columbia University staff work with the site to resolve the issue. Each site assigns and codes disease status in a standardized way as defined in the MDS data dictionary. The data set is designed to accurately capture not only a subject's diagnosis, but also how the diagnosis was made.

Some fields are designated as "required for all" or "required for sampled". The variables are ordered so that required fields are at the beginning of the data set. Variables designated as "required for all" must be properly coded for every essential subject in a family regardless of whether he/she was sampled ensuring that family structure can be ascertained. "Required for all" fields cannot be left blank or coded as Missing/Unknown for any subject. Variables designated as "required for sampled" are data that are critical for genetic analysis and must be properly coded for sampled subjects as well as for subjects not sampled if the data are available. Columbia University will follow up with sites regarding required fields that are not properly coded. Each site is responsible for providing most recent information for subjects and will maintain one family data file to which new family members are added. When a site has questions regarding the data set, they contact the staff at Columbia.

4.5 Globally Unique Identifier - GUID

The GUID is a subject ID that allows researchers to share data specific to a study participant, without exposing personally identifiable information. A GUID is made up of random alpha-numeric characters and does not include any PHI in the identifier. By using GUIDs in your research data, the system can associate a single research participant's genetic, imaging, clinical assessment data even if the data was collected at different locations or through different studies.

To create a GUID follow these steps:

1. Create an account: https://bricsguid.nia.nih.gov/portal/jsp/login.jsp
2. Once you have an account, go to the GUID Tool – Create GUID
3. To open the 'Launch GUID Tool' you will need to have Java installed on your device
4. In order to generate a GUID, the following PHI is required (Appendix F):
    - Complete legal given (first) name of subject at birth
    - If the subject has a middle name
    - Complete legal family (last) name of subject at birth
    - Day of birth
    - Month of birth
    - Year of birth
    - Name of city/municipality in which subject was born
    - Country of birthcoordinators will be able to create GUID retrospectively on anyone seen before the generator is up and running. The PHI data collected will be kept at the site and will not be shared with Columbia or NCRAD.

*__Note: Please use the GUID Demographics Form in the Appendix of the manual to collect the necessary information. Details about the GUID generator site will be provided when available by NIA.__

5.0 Blood Collection

Research specimen collection kits as well as shipping materials will be provided by NCRAD. These materials include blood tubes, packaging for shipping the blood tubes, as well as partially completed shipping labels to send materials to NCRAD.

Collection tube labels will be pre-printed with study information specific to the type of sample being drawn. Ensure that all tubes are properly labeled during processing and at the time of shipment according to section 5.3.

5.1 Biospecimen Collection

Visit**	#of tubes	Sample Type	Tube Type	Shipment
Follow up	2	Whole blood for PBMC isolation	Sodium Heparin (Green-Top) Blood Collection Tube (10 ml)	Room Temperature. Needs to be at NCRAD within 24 hours of collection. Cannot be shipped on Thursday or Fridays
Initial Visit (and at follow up if needed*)	2	Whole blood for isolation of plasma & buffy coat	EDTA (Lavender-Top) Blood Collection Tube (10 ml)	Dry Ice

*See section 5.8 for sample redraw guidelines. **Visits listed in order of blood draw per industry standards.

5.2 Biospecimen Collection Kit Contents

Collection kits are provided by NCRAD for each subject. Each collection kit provides the necessary supplies to collect samples from a given subject. Do not replace or supplement any of the tubes or kit components provided with your own supplies unless you have received approval from the NCRAD Study team to do so. *Please store all kits at room temperature until use.*

Plasma and Buffy Coat Kit

Quantity	Frozen Shipping Supply Components for Plasma & Buffy Coat
2	EDTA (Lavender-Top) Blood Collection Tube (10 ml)
1	Blue 15 mL conical tube
20	0.5 mL cryovial (purple top)
1	0.5 mL cryovial (blue top)
2	0.5 mL cryovial (gray top)
2	Pipettes
20	Pre-printed labels for plasma
20	Labels for handwritten Site ID, Family ID, and Individual ID
2	Pre-printed labels with kit number
1	Cryovial box
1	Biohazard bag with absorbent pad
1	Frozen shipper box
1	Packing tape strips
1	UPS Return address label

PBMC Kit

Quantity	Ambient Shipping Supply Components for PBMC
2	Sodium Heparin (Green-Top) Blood Collection Tube (10 ml)
2	Pre-printed labels for blood collection
2	Labels for handwritten Site ID, Family ID, and Individual ID
2	Pre-printed labels with kit number
1	Small IATA shipping box
1	Refrigerant pack
1	Absorbent tube sleeve
1	Biohazard bag with absorbent pad
1	List of contents
1	UPS Laboratory Pak
1	UPS Return address label

REMOTE DNA/PBMC Kit (for offsite collection only)

Quantity	Ambient Shipping Supply Components for DNA/PBMC
2	EDTA (Purple-Top) Blood Collection Tube (10ml)
2	PBMC (Green-Top) Blood Collection Tube (10ml)
5	Labels for handwritten Site ID, Family ID, and Individual ID
4	Pre-Printed labels for blood collection tubes
2	Kit number labels
1	Biohazard bag w/absorbent tube sleeves
1	Refrigerant Pack
1	Small IATA shipping box
1	UPS Return Address Label
1	UPS Laboratory Pak

Quantity	Saliva Collection and Shipping Kit
1	Oragene Saliva Collection Kit
2	Kit number labels
1	Label for handwritten Site ID, Family ID, and Individual ID
1	Small Saliva Biohazard Bag with Absorbent Sheet
1	Resealable Bag
1	Exempt Human Specimen Label
1	Shipping Envelope
1	UPS Return Label w/Waybill

5.3 Kit Requests

Each individual site will be responsible for ordering and maintaining a steady supply of kits from NCRAD. Be sure to check your supplies and order additional materials before you run out so you are prepared for study visits. Please go to:

https://redcap.link/FBS request additional kits. Enter your site name from the drop down menu and follow the prompts to request the desired supplies.

When making your order please note:

- If the kit is for a follow up visit the visit number will be needed in the order.. At the bottom of the kit request survey there is a place to indicate which visit you will be using the kits for. The kit will be assigned to the specific visit number for which it will be used. Please only use the kit for the specific visit for which it has been assigned.
- There are 3 types of kits available for the FBS study:
    - Plasma/Buffy Coat kit which will be collected and processed at your site, and shipped frozen back to NCRAD.
    - PBMC kit that will also be collected and shipped ambient from your site.
    - PBMC/DNA kit which is the kit that you will send out to participants to have collected at the location of their choosing and shipped back to NCRAD ambient. The PBMC/DNA kit will also be used for the mobile phlebotomy collection when that program is restarted.

Please allow **2-3 weeks** for kit orders to be processed and delivered.

5.4 Blood Collection and Processing Procedures

EDTA tubes: Two EDTA solution (lavender-top) tubes should be drawn from all participants at the initial visit. Plasma samples need to be spun, aliquoted, and placed on dry ice within 2 hours, preferably within 30 minutes, from the time of collection. Overnight shipment is expected with cryovial on dry ice. Do not draw or ship samples on Thursday or Fridays.

PBMC tubes: At follow up**,** two PBMC (green-top) tubes will be collected from all participants.

For the NaHep tubes to yield the maximum number of viable white blood cells, it is recommended that these **tubes are processed within 24 hours after blood** is drawn. Samples should be sent immediately and by overnight courier to NCRAD. PBMC samples should not be drawn/shipped on Thursday or Fridays.

Important note:

In order to ensure that the highest quality samples are collected, processed, and stored, it is essential to follow the specific collection, processing, and shipment procedures detailed in the following pages. Please read the following instructions first before collecting any specimens. Have all your supplies and equipment out and prepared prior to drawing blood.

SPECIFIC INSTRUCTIONS FOR COLLECTION AND PROCESSING OF EACH SAMPLE ARE DETAILED ON THE FOLLOWING PAGES.

5.4 a Coordinator instructions for collection utilizing contracted Mobile Phlebotomy services

Site coordinators will be tasked to prepare and mail collection kits to the participant for the contracted Mobile Phlebotomy blood collection and schedule appointments for participants. The following instructions will detail this process.

Preparing mailing and kits for remote collection

1. Label all cryovials and collection tubes according to the instructions in this manual. (Section 5.5).

2. Personalize and print Participant Instructions document (Section 5.4c.)

3. Complete Site Coordinator contact information on Mobile Phlebotomy Procedures manual, located inside the Phlebotomist envelope.

4. Prepare Biological Samples and Shipment Notification forms
    a. Print a copy of the appropriate Biological Sample and Shipment Notification Form for each sample type that will be collected.
    b. Complete all areas of form EXCEPT sample specific information to be completed at the time of sample collection.
    c. Affix corresponding Kit labels to forms.
    d. Include UPS tracking number on each Biological Sample and Shipment Notification form from the prepared UPS return mailing stickers included with the kit to ensure the samples are tracked after being shipped by contracted phlebotomist to NCRAD.
    e. Place prepared Biological Sample and Shipment Notification forms inside Phlebotomist envelope.

5. Assemble mailing labels
    a. Affix UPS return mailing label to Ambient shipping box.
    b. Place UPS return mailing label for Frozen shipping box inside Phlebotomist envelope.

6. Assemble mailing to participant. Pack all materials inside of the dry ice shipping box with the Participant Instruction letter on top. Mailing will include:
    a. Collection kit materials with all cryovials labeled per instructions
    b. Participant Instructions letter- with Participant name
    c. Phlebotomist Instruction envelope.
        i. Mobile Phlebotomy Procedures manual- Collection, Processing and Shipping instructions
        ii. Prepared Biological Samples and Shipment Notification Forms
        iii. Preprinted UPS shipping label with each kit (frozen) that will be used to ship the samples to NCRAD after collection and processing.

7. Remove previous UPS shipping label from Dry Ice shipper. Affix FedEx mailing label. Seal box and ship via FedEx to the study participant.

Scheduling Mobile Phlebotomist Blood Collection Appointments:

The participant is instructed to contact the site coordinator to schedule their blood collection appointment. The site coordinator will schedule appointment through the [Company name] website. Coordinators may want to follow up with participant within one (1) week of sending kit to participant to ensure collection kit was received and to schedule appointment.

Scheduling appointments with [Company name] for plasma collections should ONLY be scheduled **Monday through Wednesday**. Please notify the participants of this important scheduling information

Critical note: When scheduling with [Company Name], include "Special Instructions" that 10lbs Dry Ice and Centrifuge are needed for this appointment.

5.4b: Biological Sample and Shipment Notification Form – PBMC

Sample Type	Number of tubes	Tube Type	Shipment
Whole blood for PBMC isolation	2	Sodium Heparin(Green-Top) Blood Collection Tube (10 ml)	Room Temperature Must be shipped and received within 24 hours of collection

Please email this form prior to the date of shipment

To: Kelley Faber Email: alzstudy@iu.edu Phone: 1-800-526-2839

General Information: **UPS tracking #:**_____

Site Coordinator: _____ Date: _____

Phone: _____ Email: _____

Study: AD Family-Based Study **Kit #:**

KIT BARCODE

Site ID: _____ Family ID:_____ Individual ID:_____

Sex: M F **Year of Birth:** _____ **Visit** (please circle one): **1 2 3 4 5 6 7 8 9 10**

*Blood Collection: ***

1. Date Blood Tubes Drawn:_____ (MM/DD/YYYY) _____(time) am/pm

2. Original Volume Drawn (2 x NaHep Green Top):_____ (mL)

Biological Sample and Shipment Notification Form – PBMC and DNA

Sample Type	Number of tubes	Tube Type	Shipment
Whole blood for PBMC isolation	2	Sodium Heparin (Green-Top) Blood Collection Tube (10 ml)	Room Temperature Must be shipped and received within 24 hours of collection
Whole blood for DNA extraction	2	EDTA (Purple-Top) Blood Collection Tube (10ml)	Room Temperature Must be shipped within 24 hours of

Please email this form prior to the date of shipment.

To: Kelley Faber Email: alzstudy@iu.edu Phone: 1-800-526-2839

General Information: **UPS tracking #:**_____

Site Coordinator: _____ Date: _____

Phone: _____ Email: _____

Study: AD Family-Based Study **Kit #:** KIT BARCODE

Site ID: _____ Family ID:_____ Individual ID:_____

Sex: M F **Year of Birth:** _____ **Visit** (please circle one): **1 2 3 4 5 6 7 8 9 10**

*Blood Collection: ***

1. Date Blood Tubes Drawn:_____ (MM/DD/YYYY) _____(time) am/pm
2. Original Volume Drawn (2 x NaHep Green Top):_____ (mL)
3. Original Volume Drawn (2 x EDTA Purple Top):_____(mL)

Comments:

_____

_____

_____

** Completed by contracted mobile phlebotomist at time of blood collection.

*** Blood collection completed by:* _____ *(name)*

Company: _____

Contact phone: _____

Biological Sample and Shipment Notification Form – Plasma and Buffy Coat

Sample Type	Number of tubes	Tube Type	Shipment
Whole blood for isolation of plasma & buffy coat (for DNA extraction)	2	EDTA (Lavender-Top) Blood Collection Tube (10 ml)	Dry Ice

Biological Sample and Shipment Notification Form

Please email this form prior to the date of shipment

To: Kelley Faber Email: alzstudy@iu.edu Phone: 1-800-526-2839

General Information: **UPS tracking #:**_____

Site Coordinator: _____ Date: _____

Phone: _____ Email: _____

Study: AD Family-Based Study **Kit #:**

Site ID: _____ Family ID:_____ Individual ID:_____

Sex: M F **Year of Birth:** _____

Visit: (please circle one) **1 2 3 4 5 6 7 8 9 10**

KIT BARCODE

*Blood Collection: ***

Date Drawn:	[MM/DD/YY]	Time of Draw:	[HH:MM]
Date subject last ate:	[MM/DD/YY]	Time subject last ate:	[HH:MM]

*Blood Processing: ***

Plasma & Buffy Coat (Lavender-top) Tube (2x10 mL)	
Time spin started:	_____ [HH:MM]
Duration of centrifuge:	_____ Minutes
Temp of centrifuge: ____ °C Rate of centrifuge: _____ x g	
Time aliquoted:	_____ [HH:MM]
Number of 0.5 mL plasma aliquots created (lavender cap, up to 20):	
If applicable, volume of residual plasma aliquot (less than 0.5 mL in blue cap):	_____ mL
If applicable, specimen number of residual plasma aliquot (last four digits):	
Buffy coat #1 last four digits of specimen number:	
Buffy coat #1 volume: _____ mL Original blood volume drawn: _____ mL	
Buffy coat #2 last four digits of specimen number:	
Buffy coat #2 volume: _____ mL Original blood volume drawn: _____ mL	

** Completed by contracted mobile remote phlebotomist at time of blood collection.

*** Blood collection completed by:* _____ *(name)*

Company: _____

Contact phone: _____

Notes:

_____

_____

_____

_____

_____

Biological Sample and Shipment Notification Form - Saliva

Sample Type	Number of tubes	Tube Type	Shipment
Saliva	1	Saliva Collection Tube	Ambient

To: Kelley Faber Email: alzstudy@iu.edu FAX: 317-321-2003 Phone: 1-800-526-2839

General Information:

Site Coordinator: _____ Date: _____ Pho

Study: AD Family Based Study

Site: _____ **Family:** _____ **Individual:** _____ **GUID:** _____

Sex: ☐ M ☐ F **Year of Birth:** _____ **Kit #:**

Visit (circle one): 1 2 3 4 5 6 7 8 9 10

Kit Barcode

UPS tracking #: _____

Saliva Collection:

1. Date Saliva Collected: _____ [MMDDYYYY]

2. Time Saliva Collected: _____ [HHMM]

3. Last date subject ate: _____ [MMDDYY]

4. Last time subject ate: _____ [HHMM]

INTERNAL NCARD USE – Do Not

Complete Saliva Volume: ____ml

Notes: _____

5.4 c Participant Instructions

Dear AD ID:

Thank you for your participation in the NIA-AD FBS study. As part of this study, we are collecting blood samples. To make this process as easy as possible, we will schedule the blood collection to be done at your home or another specified location.

Instructions to schedule appointment:

Please call the following phone number to set up your appointment: _____

(coordinator phone)

(NOTE: Appointments can ONLY be scheduled for Monday – Wednesday)

Keep all the boxes in this mailing at room temperature (if possible): 68-77°F (20-25°C)

IMPORTANT! On the day ***prior*** to your scheduled blood collection visit, please place the ice pack (located in the smaller box) in your freezer.

On the day of the visit:

Provide the entire box you received to the blood collection personnel. It is up to you whether you mention the reason for the blood draw, but you do not have to.

Each box has been assigned to an individual study participant. These boxes and their contents are not interchangeable, even for members of the same family. **The name on this participant letter identifies who the supplies have been assigned.**

**Your unique participant ID will be listed on the forms in the envelope labeled “Phlebotomist”, as well as on the labels for each blood collection tube. Please keep these forms and envelopes, along with the collection kit contents all together in the shipping box until your scheduled appointment.

Again, thank you very much for enrolling/re-enrolling and thank you for all that you have done!

Site Coordinator Information

Name:

Phone Number:

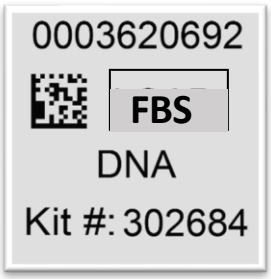
Email Address:

5.5 Labeling Samples

Label Type Summary

1. Kit Number Label
2. Site ID, Family ID, Individual ID Label
3. Collection Tube Label

The **Kit Number Labels** do not indicate a specimen type. They are affixed to the Biological Sample and Shipment Notification Forms and on specific packing materials.



The **Collection Tube Labels** for blood are placed on all collection tubes.

The **Site ID, Family ID, and Individual ID** labels are placed on all collection tubes.

Each kit is supplied with labels for the specimens to be shipped to NCRAD. Place one Kit Number Label within the designated location on the "Biological Sample and Shipment Notification Form". Place the other Kit Number Label on the lid of the shipping canister.

Important Note

Each collection tube will contain two labels: the Collection Tube Label and the Site ID, Family ID, and Individual ID Label. Be sure to place labels in the same configuration consistently among tubes, with the barcoded label near the top of the tube with the handwritten Site ID, Family ID, and Individual ID label below.

Please ensure the barcode is near the cap of the tube.

EDTA Tube

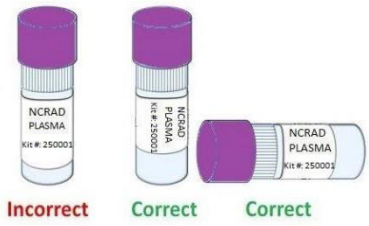
Sodium Heparin Tube

In order to ensure the label adheres properly and remains on the tube, please follow these instructions:

- Place blood collection and aliquot labels on **ALL** collection and aliquot tubes **BEFORE** sample collection, sample processing, or freezing. This should help to ensure the label properly adheres to the tube before exposure to moisture or different temperatures.
- Using a fine point permanent marker, fill-in and place the Site, Family and Ind. ID Labels on the collection tubes only (RNA, Serum, NaHep, EDTA) **BEFORE** sample collection, processing, or freezing. These labels are in addition to the Collection and Aliquot Tube Labels. **DO NOT** place Site, Family, and Individual ID labels on any cryovials.
- Place cryovials in numerical order based on the specimen number, located at the top of the label. This ensures that no aliquot is misplaced or lost during the shipment process.

Specimen Number

- The Collection and Aliquot Tube Labels contain a 2D barcode on the left hand side of the label. Place this barcode toward the tube cap.
- Place label **horizontally** on the tube (wrapped around sideways if the tube is upright) and **just below the ridges** of the aliquot tubes (see labeling diagram below).
- Take a moment to ensure the label is **completely adhered** to each tube. It may be helpful to roll the tube between your fingers after applying the label.



5.6 Instructions for Collection: Sodium Heparin (Green-Top) Blood Collection Tube (10mL) for collection of Peripheral Blood Mononuclear Cells (PBMC) x 2

Sample Type	Number of tubes	Tube Type	Shipment
Whole blood for PBMC isolation	2	Sodium Heparin(Green-Top) Blood Collection Tube (10 ml)	Room Temperature Must be shipped and received within 24 hours of collection

*****Important Visit Scheduling Note*****
Once drawn, Sodium Heparin tubes MUST be shipped to NCRAD on the day of collection via UPS Priority Overnight.
These samples should only be collected Monday-Wednesday.
****NOTE** DO NOT collect these samples on Thursday or Friday.**

Step 1. Preparing for sample draw

CRITICAL STEP: Store empty Sodium Heparin tubes at room temperature, 64°F - 77°F (18°C to 25°C) before use.

Obtain blood collection kit from the participant. This kit was prepared to include all collection and shipping supplies needed for this collection. Confirm all collection tubes and aliquot tubes are labeled. Confirm Kit # and ADFBS ID # on collection tubes match the Biological Sample and Shipment notification form included in the envelope. Note any missing labels on the Biological Sample and Shipment form prior to the collection.

Step 2. Collecting Sample

2.1 Using a blood collection set, collect blood into the 10mL Sodium Heparin tubes using your institution's recommended procedure for standard venipuncture technique.

2.2 The following techniques shall be used to prevent possible backflow:

2.2a Place participant's arm in downward position.
2.2b Hold tube in vertical position, below the participant's arm during blood collection.
2.2c Release tourniquet as soon as blood starts to flow into tube.
2.2 d Make sure tube additives do not touch stopper or end of the needle during venipuncture.

2.3 Document collection on the Biological Sample and Shipment Notification Form - PBMC

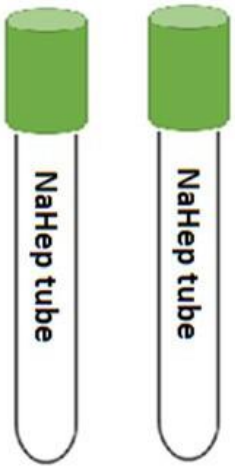
Step 3. Immediately after blood collection, **gently** invert the tubes 8-10 times to mix sample.

Step 4. Seal the Sodium Heparin tubes in the ambient shipment kit. See Shipping instructions for complete packaging and shipping information. Ship the unprocessed tubes ambient to NCRAD.

Samples must be shipped the same day as collection. Samples must be received the following day after collection.

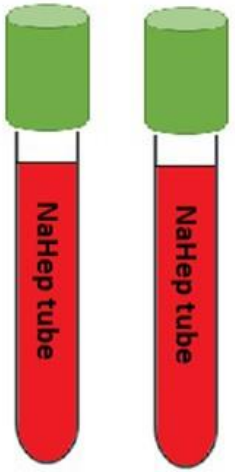
PBMC Preparation (10ml Sodium Heparin Tube x 2)

Step One



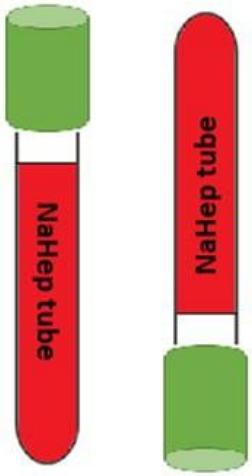
- Store tubes at room temperature.
- Label tubes with pre-printed labels prior to blood draw.

Step Two



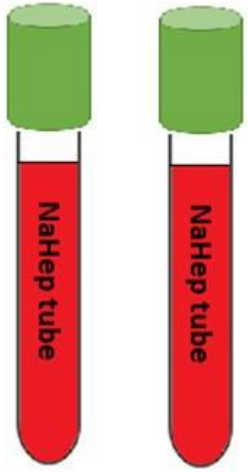
- Collect blood in Sodium Heparin Tubes allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

Step Three



- Immediately after blood draw, invert tubes 8-10 times to mix samples.

Step Four



- Store tubes at room temperature until shipment.
- <u>Ship ambient same day as blood draw</u>

****Please be sure to compare the labels on each tube and cryovial to the Biological Sample Form included with each kit***

5.7 Instructions for Collection: Whole Blood Collection for isolation of Plasma and Buffy Coat: EDTA (Lavender-Top) Blood Collection Tube (10mL)

Sample Type	Number of tubes	Tube Type	Shipment
Whole blood for isolation of plasma & buffy coat (for DNA extraction)	2	EDTA (Lavender-Top) Blood CollectionTube (10 ml)	Dry Ice

Step 1. Preparing for sample draw

Set centrifuge to 4 C to pre-chill before use.

Obtain blood collection kit from the participant. This kit was prepared to include all collection and shipping supplies needed for this collection. Confirm all collection tubes and aliquot tubes are labeled. Confirm Kit # and ADFBS ID # on collection tubes match the Biological Sample and Shipment notification form included in the envelope. Note any missing labels on the Biological Sample and Shipment form prior to the collection.

Keep labels in numerical order (by specimen number) throughout the aliquoting and shipping process.

Step 2. Collecting Whole Blood sample

2.1 Using a blood collection set, collect blood into the **EDTA (Lavender-top) Blood Collection Tube (10mL)** using your institution's recommended procedure for standard venipuncture techniques.

2.2 The following techniques shall be used to prevent possible backflow:

2.2a Place donor's arm in downward position.
2.2b Hold tube in vertical position, below the donor's arm during blood collection.
2.2c Release tourniquet as soon as blood starts to flow into tube.
2.2d Make sure tube additives do not touch stopper or end of the needle during venipuncture.

2.3 Allow at least 10 seconds for a complete blood draw to take place in each tube. Ensure that the blood has stopped flowing into the tube before removing the tube from the holder. The tube with its vacuum is designed to draw 10 mL of blood into the tube.

2.4 Document collection on the Biological Sample and Shipment Notification Form- Plasma/ Buffy Coat

If complications arise during the blood draw, please note the difficulties on the **Biological Sample and Shipment Notification Form. Do not attempt to draw an additional EDTA tube at this time. Process blood obtained in existing EDTA tube.

Step 3. Processing sample following draw

CRITICAL STEP: Immediately after blood collection, gently invert/mix (180 degree turns) the EDTA tube 8-10 times.

Step 4. CRITICAL STEP: Immediately after inverting the EDTA tube, place it on wet ice until centrifugation begins.

Plasma samples need to be spun, aliquoted, and placed on dry ice **within 2 hours**, from the time of collection.

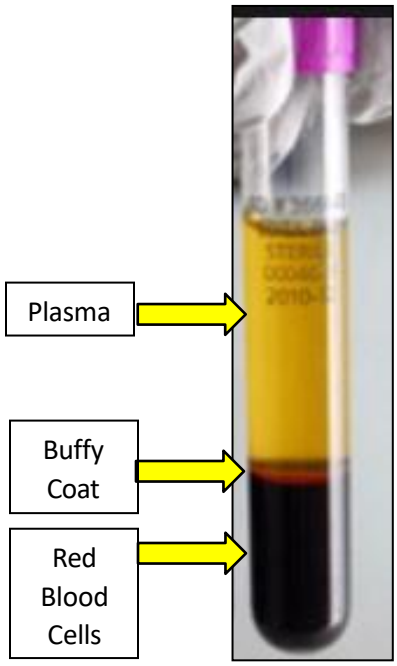
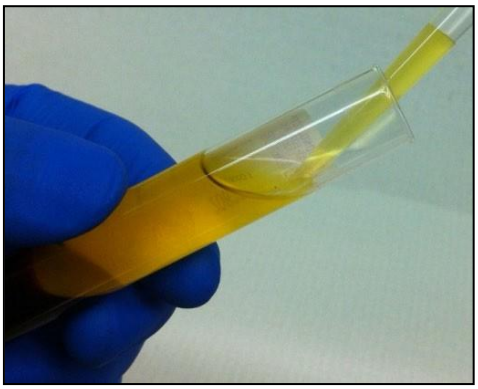
Step 5. CRITICAL: Tubes must be centrifuged at the appropriate speed and temperature to ensure plasma separation.

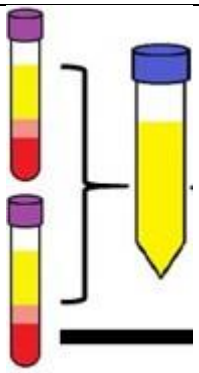
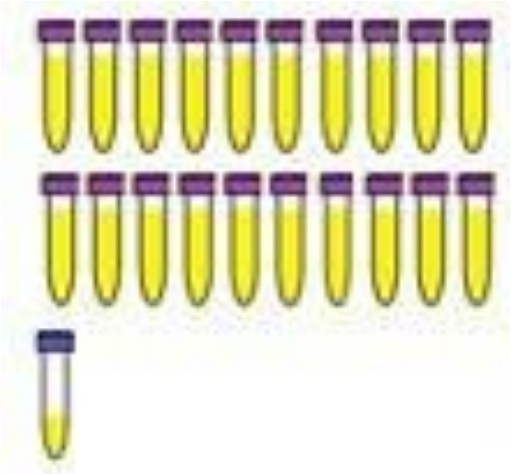
5.1 Centrifuge balanced tubes for 10 minutes at 2000 x g at 4°C. **It is critical that the tubes be centrifuged at the appropriate speed and temperature to ensure proper plasma separation (see worksheet in Appendix C to calculate RPM.)**

5.2 While centrifuging, record all times, temperatures and spin rates on the Biological Sample and Shipment Notification Form.

Spin, aliquot and freeze all plasma and buffy coat aliquots within 2 hours of collection.

Step 6: Pooling Plasma

Instruction	Illustration
Remove the plasma, being careful not to agitate the packed red blood cells at the bottom of the collection tube.	
Tilt the tube and place the disposable pipette tip along the lower side of the wall without touching the pellet (buffy coat) so that plasma is not contaminated	 
NOTE: When pipetting plasma from the plasma tube into the conical, be very careful to pipette the plasma top layer only, leaving the buffy coat and the red blood cell layers untouched.	

Transfer plasma from both EDTA tubes into the blue topped 15 mL conical tubes and gently invert 3 times. NOTE:15 mL blue top conical will not have a label.	
Step 7: Aliquot plasma	
Aliquot plasma into the pre-labeled cryovials. Aliquot 0.5 mL per cryovial (up to 20 vials with 0.5 mL each). Be sure to only place **plasma** in cryovials labeled with “PLASMA” labels. *If there is extra plasma left, use 1 extra cryovial with blue cap provided for another <0.5 mL aliquot of plasma. **If residual aliquot (<0.5 mL) is created, document the sample number and volume on the Biological Sample and Shipment Notification Form.	
After plasma has been removed from the EDTA (Lavender-Top) Blood Collection Tube (10 ml), the top layer of cells is the buffy coat mixed with RBCs	Buffy Coat layer (mixed with RBCs)  

Step 8: Aliquot Buffy Coat	
Aliquot buffy coat layer from each collection tube into separate cryovials with gray cap using a disposable graduated micropipette. The buffy coat aliquot is expected to have a reddish color from the RBCs. Place Buffy Coat cryovials into the same cryovial box with the plasma samples on Dry Ice	 Buffy Coat Aliquot use GRAY cap cryovial "BUFFY COAT" label
Place the labeled cryovials in the cryobox and place upright on dry ice and ship to NCRAD. Record time aliquots placed on dry ice on Biological Sample and Shipment Notification Form.	
Dispose of collection tubes with red blood cell pellet according to your site's guidelines for disposing of biomedical waste.	

Plasma & Buffy Coat Preparation (EDTA Tube x 2)

Step One

- Store tubes at room temp.
- Each tube should be labeled with Collecûon Tube and Site and PTID Labels.

Step Two

- Collect blood into each EDTA Tube, allowing blood to flow for 10 seconds and ensuring blood flow has stopped.

Step Three

- Immediately aûer blood draw, invert tubes 8-10 ûmes to mix samples.

Step Four

- Place thoroughly mixed tube on wet ice unûl centrifugaûon begins.

Step Five

- Centrifuge samples at 2000 x g for 10 minutes at 4°C.

Step Six

- Pool all plasma from the 2 EDTA tubes into a 15 ml conical tube and invert gently 3 ûmes to mix the plasma.

Step Seven

- Label purple-capped cryovials with "PLASMA" labels .
- Aliquot 0.5 ml plasma into each cryovial.
- If residual aliquot is created, document specimen number and volume on Sample Form.
- Store plasma aliquots upright at -80°C unûl shipment to NCRAD.

Step Eight

- Label gray -capped cryovials with "BUFFY COAT" labels.
- Using a clean transfer pipeûe, collect the buffy coat (may have residual plasma and some RBCs included).
- Transfer the buffy coat from each EDTA tube into its own cryovial.
- Store buffy coat aliquots upright at -80°C unûl shipment to NCRAD.
- Spin, aliquot, and freeze all plasma and buffy coat aliquots within 2 hours of collecûon.

***Please be sure to compare the labels on each tube and cryovial to the Biological Sample Form included with each kit**

5.8 Sample Redraws

There may be situations that arise that **require** a patient sample to be redrawn. At those times, NCRAD study staff will alert site coordinators via email that a participant sample has failed and should be redrawn. This can happen for several reasons, including insufficient blood at the time the sample was drawn, temperature storage extremes, or even shipping errors.

Redraw kits may vary depending upon the sample that failed and must be redrawn. Tubes that may be redrawn using the redraw kit include the EDTA (Lavender-Top) Blood Collection Tube (10 ml) and the Sodium Heparin (Green-Top) Blood Collection Tube (10 ml). Both of these tubes should be sent back to NCRAD ambient and unprocessed.

5.9a Packaging and Shipping Instructions

Instructions for Ambient Shipping: Sodium Heparin (Green-Top) Blood Collection Tube (10mL) for collection of Peripheral Blood Mononuclear Cells (PBMC) x 2

Sample Type	Number of tubes	Tube Type	Shipment
Whole blood for PBMC isolation	2	Sodium Heparin(Green-Top) Blood Collection Tube (10 ml)	Room Temperature Must be shipped and received within 24 hours of collection

***** Packing and Labeling Guidelines *****

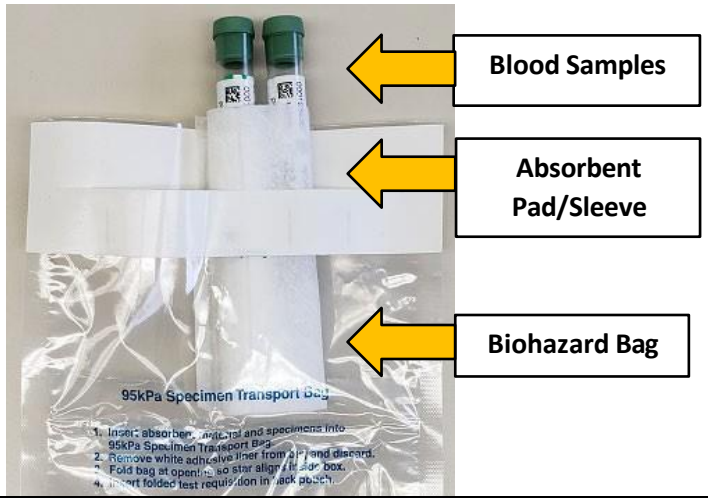
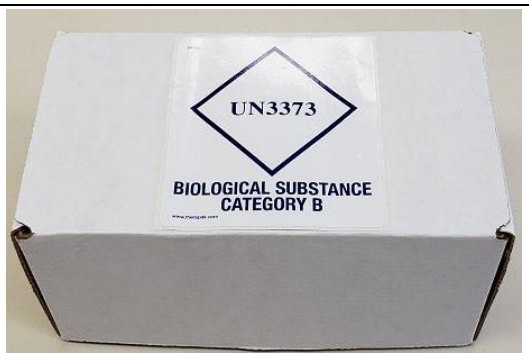
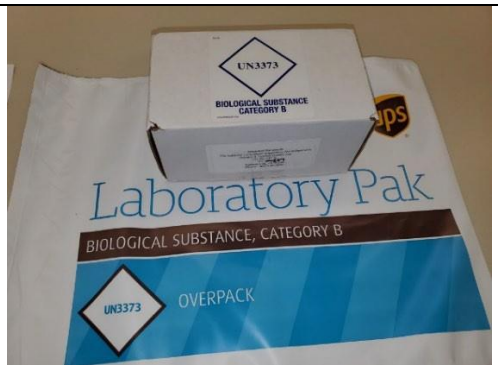
- The primary receptacle (collection tube) must be leak proof and must not contain more than 10 ml total.
- The secondary packaging (foam box) must be leak proof.
- Absorbent material must be placed between the primary receptacle (collection tube) and the secondary packaging (foam box). The absorbent material should be of sufficient quantity in order to absorb the entire contents of the specimens being shipped. Examples of absorbent material are paper towels, absorbent pads, cotton balls, or cellulose wadding.
- A copy of the Biological Sample and Shipment Notification Form must be included between the secondary and outer packaging.
- The outer shipping container must display the following labels:
  - ✓ Sender's name and address
  - ✓ Recipient's name and address
  - ✓ Responsible Person
  - ✓ The words "Biological Substance, Category B"
  - ✓ UN3373

PMBC Blood Collection Tube (10 ml) shipments should be considered as Category B UN3373 and as such must be tripled packaged and compliant with the IATA Packing Instructions 650. *See the Latest Edition of the IATA Regulations for complete documentation.*

Triple packaging consists of a primary receptacle(s), a secondary packaging, and a rigid outer packaging. The primary receptacles must be packed in secondary packaging in such a way that, under normal conditions of transport, they cannot break, be punctured or leak their contents into the secondary packaging. Secondary packaging must be secured in outer packaging with suitable cushioning material. Any leakage of the contents must not compromise the integrity of the cushioning material or of the outer packaging.

IMPORTANT!
AMBIENT SAMPLES <u>MUST</u> BE SHIPPED MONDAY-WEDNESDAY ONLY! Do NOT draw blood for ambient shipments on Thursday or Friday

Retrieve refrigerant pack from participant. It was placed in freezer at least 24 hours prior to shipment.	
Contact UPS 1-800-742-5877 to locate the closest UPS store location to drop off the package for same day shipping. **Do NOT** ship from UPS drop box location.	
Scan or take a picture with a cell phone of completed Biological Sample and Shipment notification form- PBMC	
Notify NCRAD of shipment by emailing alzstudy@iu.edu. If email is unavailable, please call NCRAD **1-800-526-2839** Do not ship until you have notified NCRAD coordinators of the shipment in advance.	**Content of email:** 1. **Completed Biological Sample and Shpment notification form- PBMC (scanned)** 2. **UPS Shipment tracking number** Email to alzstudy@iu.edu

Place filled and labeled sodium heparin (green-top) tubes within the slots in the absorbent pad provided, and place into the plastic biohazard bag with absorbent sheet. Remove as much air as possible from the plastic biohazard bag and seal the bag according to the directions printed on the bag.	
Place the refrigerant pack into the cooler on top of the filled biohazard bag. Place the Styrofoam lid onto the cooler inside the shipping box.	
Place the Biological Sample and Shipment Notification Form within the shipping box and list of contents form in the shipping box before closing and securing box top. Secure box with packing tape. Confirm UN3373 (Biological Substance Category B) label is on outside of the cardboard box	
Place shipping box inside UPS Next Day mailing envelope with the pre-printed return address label	
Specimens should be sent via UPS Next Day Air. Samples must be sent next day and on **Monday through Wednesday** to avoid any potential shipping delays.	**NCRAD** **IU School of Medicine** **351 W. 10th Street, TK 217** **Indianapolis, IN 46202** **Phone: 1-800-526-2839**

Remember to complete the Biological Sample and Shipment Notification (A), include a copy in your shipment AND include a scanned copy in the email notification to alzstudy@iu.edu IN ADVANCE to confirm the shipment.

In addition to tracking and reconciliation of samples, the condition and number of samples received are tracked by NCRAD for each sample type. Investigators and clinical coordinators for each project are responsible to ensure the requested amounts of each fluid are collected to the best of their ability.

5.9b **Instructions for Frozen Shipping: Whole Blood Collection for isolation of Plasma and Buffy Coat: EDTA (Lavender-Top) Blood Collection Tube (10mL)

Sample Type	Number of tubes	Tube Type	Shipment
Whole blood for isolation of plasma & buffy coat (for DNA extraction)	2	EDTA (Lavender-Top) Blood CollectionTube (10 ml)	Dry Ice

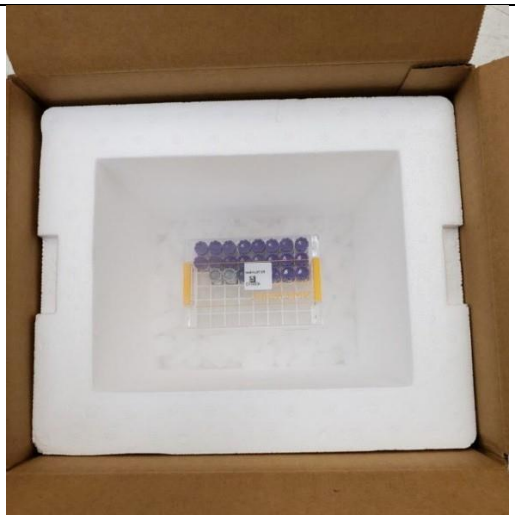
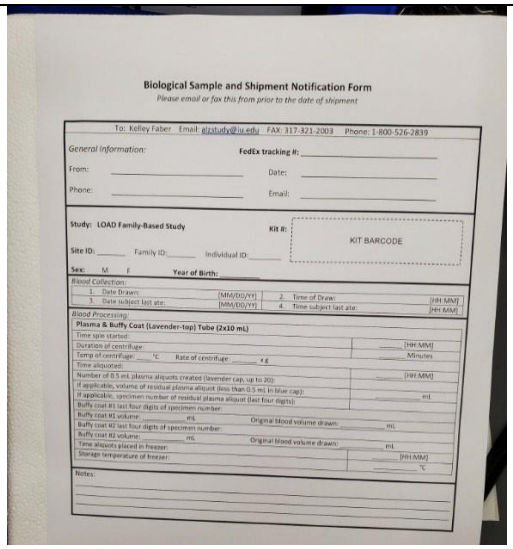
IMPORTANT!
FROZEN SAMPLES MUST BE SHIPPED MONDAY-WEDNESDAY ONLY! Do NOT draw blood on Thursday or Friday

***** Packing and Labeling Guidelines *****

- The primary receptacle (frozen cryovials) must be leak proof and must not contain more than 1L total.
- The secondary packaging (biohazard bag) must be leak proof and if multiple blood tubes are placed in a single secondary packaging, they must be either individually wrapped or separated to prevent direct contact with adjacent blood tubes.
- Absorbent material must be placed between the primary receptacle (within the cryovial box containing the frozen cryovials) and the secondary packaging. The absorbent material should be of sufficient quantity in order to absorb the entire contents of the specimens being shipped. Examples of absorbent material are paper towels, absorbent pads, cotton balls, or cellulose wadding.
- A copy of the Biological Sample and Shipment Notification Form must be included between the secondary and outer packaging.
- The outer shipping container must display the
- following labels:
  - ✓ Sender's name and address
  - ✓ Recipient's name and address
  - ✓ Responsible Person
  - ✓ The words "Biological Substance, Category B"
  - ✓ UN3373
  - ✓ Class 9 label including UN 1845, and net weight of dry ice contained

Steps for completing Shipping process for FROZEN Shipping

Contact UPS 1-800-742-5877 to locate the closest UPS store location to drop off the package for same day shipping. **Do NOT** ship from UPS drop box location.	
Scan or take a picture with a cell phone of completed Biological Sample and Shipment notification form- Plasma/ Buffy Coat	
Email NCRAD notification of shipment alzstudy@iu.edu. If email is unavailable, please call NCRAD **1-800-526-2839** **Do** not ship until you have notified NCRAD coordinators of the shipment in advance.	**Content of email:** 1. **Completed Biological Sample and Shipment Notification Form- Plasma/ Buffy Coat (scanned)** 2. **UPS Shipment tracking number** Email to alzstudy@iu.edu
Place all labeled and frozen plasma and buffy coat aliquots in a cryovial box.	
Place cryovial box in a clear biohazard bag. Do **not** remove absorbent material found in the bag and seal according to the instructions on the bag.	

Place approximately 2-3 inches of dry ice in the bottom of the Styrofoam shipping container. Place the biohazard bag with cryovial box into the Styrofoam-lined shipping container on top of the dry ice. Ensure cryovial box is placed so the cryovials are upright in the shipping container.	
The dry ice should entirely fill the inner box and be placed on top of the biohazard bags to ensure the frozen state of the specimens. The inner Styrofoam shipping container must contain approximately 10 lbs. (or 4.5kg) of dry ice.	
Replace the lid of the Styrofoam container. Place the completed Biological Sample and Shipment Notification Form in the package on top of the Styrofoam lid. Close and seal the outer cardboard shipping carton with package tape. **<u>DO NOT</u>** completely seal the outer cardboard box with tape, as the dry ice needs to vent.	 **Biological Sample and Shipment Notification Form** *Please email or fax this from prior to the date of shipment* To: Kelley Faber Email: alzstudy@iu.edu FAX: 317-321-2003 Phone: 1-800-526-2839 General Information: FedEx tracking #: From: Date: Phone: Email: Study: LOAD Family-Based Study Kit #: KIT BARCODE Site ID: Family ID: Individual ID: Sex: M F Year of Birth: Blood Collection: 1. Date Drawn: [MM/DD/YY] 2. Time of Draw: [HH:MM] 3. Date subject last ate: [MM/DD/YY] 4. Time subject last ate: [HH:MM] Blood Processing: Plasma & Buffy Coat (Lavender-top) Tube (2x10 mL) Time spin started: [HH:MM] Duration of centrifuge: Minutes Temp of centrifuge: °C Rate of centrifuge: x g Time aliquoted: [HH:MM] Number of 0.5 mL plasma aliquots created (lavender cap, up to 20): If applicable, volume of residual plasma aliquot (less than 0.5 mL in blue cap): mL If applicable, specimen number of residual plasma aliquot (last four digits): Buffy coat #1 last four digits of specimen number: Buffy coat #1 volume: mL Original blood volume drawn: mL Buffy coat #2 last four digits of specimen number: Buffy coat #2 volume: mL Original blood volume drawn: mL Time aliquots placed in freezer: [HH:MM] Storage temperature of freezer: °C Notes:

Apply the provided, pre-printed UPS shipping label to the outside of the box. **Important:** Remove any previous shipping labels prior to shipping	
Specimens should be sent via UPS Next Day Air. Frozen specimens should be sent **Monday through Wednesday** to avoid any potential shipping delays.	**NCRAD** **IU School of Medicine** **351 W. 10th Street, TK 217** **Indianapolis, IN 46202** **Phone: 1-800-526-2839**

DRAW AND SHIP ALL FROZEN SAMPLES MONDAY - WEDNESDAY ONLY!
BE AWARE OF INCIPIENT INCLEMENT WEATHER THAT MAY DELAY SHIPMENT/DELIVERY OF SAMPLES!

Remember to complete the Biological Sample and Shipment Notification (A), include a copy in your shipment AND include a scanned copy in the email notification to alzstudy@iu.edu IN ADVANCE to confirm the shipment.

In addition to tracking and reconciliation of samples, the condition and number of samples received are tracked by NCRAD for each sample type. Investigators and clinical coordinators for each project are responsible to ensure the requested amounts of each fluid are collected to the best of their ability and that samples are packed with sufficient amounts of dry ice to avoid thawing in the shipment process.

5.9c

FBS Saliva Collection Instructions

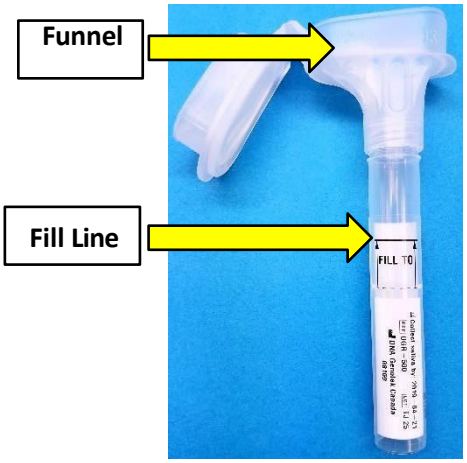
Do not eat, drink, smoke, or chew gum for 30 minutes prior to giving your sample.

Note: Do not rinse your mouth prior to giving your sample. Most people take between 2 and 5 minutes to deliver a saliva sample following steps 1 through 7 below. Before spitting, relax and rub your cheeks gently for 30 seconds to create saliva.

To review a video of the saliva collection procedure, please visit:
http://www.dnagenotek.com/ROW/support/ciOG500.html

STEP 1

- Do NOT remove the plastic film from the lid of the container.
- Spit directly into the funnel at the top of the tube until the amount of liquid saliva (not including bubbles) reaches the fill line shown in picture #1.
- **The saliva tube has a false bottom, so you will only need to provide 2 milliliters (less than ½ teaspoon) of saliva to reach the fill line.**
- Do NOT fill above the line.



STEP 2

- Once the saliva level reaches the fill line, hold the tube upright with one hand.
- Close the lid with the other hand (as shown) by firmly pushing the lid until you hear a loud click.
- The liquid in the lid will be released into the tube to mix with the saliva. Make sure that the lid is closed tightly.

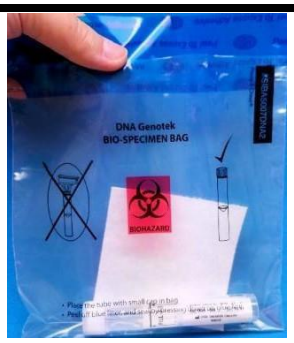
STEP 3

- Hold the tube upright.
- Unscrew the funnel from the tube.
- Pick up the small cap for the tube.
- Use the small cap to close the tube tightly.

FBS Saliva Collection Instructions

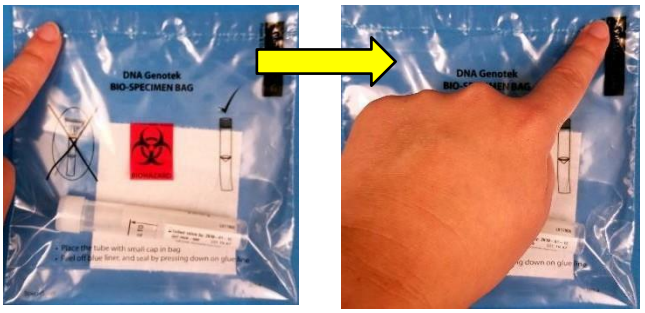
STEP 4

- Shake the capped tube for 5 seconds.
- Discard or recycle the funnel.
- Place sample in provided specimen bag for shipment to Indiana University (IU).



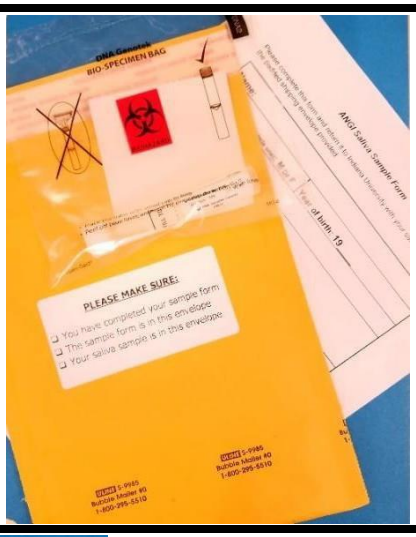
STEP 5

- Peel off blue plastic liner at the top of the specimen bag to expose the adhesive.
- Seal bag by pressing down across the top of the bag.



STEP 6

- Fill out sample form with Sex, Year of Birth, Date Collected, Time of Collection, Last date subject ate, Last time subject ate
- Fold sample form and place into prepaid shipping envelope.
- Also put your specimen (in the provided specimen bag) into this shipping envelope.



STEP 7

- Peel off the white paper at the top of the envelope to expose the adhesive, fold this flap down, and press firmly to seal envelope.
- Send the envelope via U.S. Mail as soon as possible after sample collection. The envelope may be placed in your mailbox with any outgoing mail or mailed through any USPS drop box or post office location.

Questions? Please contact a study coordinator at 1-800-526-2839 or email alzstudy@iupui.edu

Intended Use: This product is designed for the safe collection of human saliva samples.

Contents: The funnel lid contains 2 mL of liquid. The solution should be clear and colorless.

Warnings: Do not ingest this liquid. Wash with water if the saliva container liquid comes in contact with eyes or skin. Small Cap, choking hazard.

Storage: Store at room temperature 15-30˚C (59-86˚F).

6.0 Data Collection

6.1 Data Collection Schedule

Each site is responsible for providing the NIA-AD FBS with the most recent information for participants. All data should be sent to the coordinating site (CUMC) every quarter. The project manager will send a reminder to all coordinators and provide a template for the data submission. Data calls are scheduled to happen in January, April, July and October. Identity of participants will not be shared with Columbia, NCRAD or with any investigators.

6.2 Data Cleaning

The MDS must be completed on each participant as accurately as possible. Every effort is made to ensure that required fields are not left blank or coded as Missing/Unknown; Columbia will follow-up for required fields not properly coded. Information that appears incorrect in the NIA-AD FBS database, will be queried through the standard system. Queries (if any) will be sent to the sites after each data call. Additional discrepancies that may be unrelated to data entry will be resolved with the Principal Investigator in a separate follow up communication. The data queries dictionary and guide can be found on Appendix E.

7.0 Brain Autopsy

Brain donation is useful to confirm the clinical diagnosis of AD or the absence of AD pathology and the tissue is useful for genetic research studies.

7.1 Deceased Family Member with a Previous Autopsy:

For deceased individuals who have previously participated in brain donation/autopsy, their brain tissue and neuropathological diagnosis may be used in the study. If an individual is deceased, DNA can be extracted from an autopsy specimen. 2-3 grams of frozen tissue is required. Families may have obtained an autopsy through their own healthcare provider. The research staff will assist the family in obtaining autopsy tissue to send to NCRAD. Family members must obtain copies of medical records for deceased individuals including records that confirm a clinical diagnosis of Alzheimer's disease or other related neurodegenerative disorder.

7.2 Current Participants and Family Members Program Enrollment:

Participating (living) individuals and/or their next of kin/surrogate in these families, will be informed of the brain donation program through the Columbia ADRC and/or the Rush University ADRC. Families who wish to plan for brain donation may call their site coordinator who will put them in touch with one of the brain donation sites. Brain donation flyers may be given to participants in the study. All study staff should be able to answer initial questions about the role of brain donation in the study of Alzheimer's disease and related neurological disorders. The autopsy consent and intent forms are approved by the IRB under Columbia's and Rush's Alzheimer's Diseases Resource Center and ADFBS can cross-reference those forms.

After autopsy is completed, ~20 grams of frozen dorsal lateral/pre-frontal cortex and/or ~20 grams of fixed dorsal lateral/pre-frontal cortex tissue will be sent to NCRAD for sharing with the scientific community. We will request the same amount of tissue from autopsies done at other institutions. See Appendix H for sample form.

7.3 Autopsy Results:

Once autopsy and the pathology report is completed (usually takes 3-4 months), CU/Rush personnel will return the report to the site where the participant was originally enrolled. The site PI or an appropriate staff member will contact the next of kin or surrogate to explain the autopsy results. A copy of the pathology report may be sent to the family.

7.4 Brain shipment and Coordinator Contacts:

For fresh brain shipment instructions, please refer to Appendix G. For any inquiries about brain donation and autopsy, please contact:

Scott M. Reid, MA
Clinical Research Coordinator
Phone: (212) 305-10086
Fax: (212) 342-5323
Email: SMR2212@COLUMBIA.EDU

Address:
The Taub Institute for Research on
Alzheimer's Disease and the Aging Brain
Columbia University Medical Center
630 West 168th Street, P&S Box 16
New York, NY 10032-37105

Rush Contact: TBA

8.0 Informed Consent

Each site will need to obtain an approved consent form from their institution to conduct this study (see appendix C for sample language). Written informed consent should be obtained from the participant and informant prior to any study related procedures. Capacity of assent should be evaluated throughout the study (based on each site's IRB requirements). Trained research staff will be responsible for leading the potential participant through the entire consent process.

8.1 Consent Procedures

The following is just general guidelines for consenting participants. Each site's procedures may vary as required by local IRBs.

1. Capacity to consent will be determined and documented by trained and experienced research staff.

2. All aspects of the study, as described in the consent form, are first discussed with the potential subject.

3. The consent form is thoroughly reviewed with the potential subject and answers to the potential subject's questions are provided.

4. While reviewing the consent form, the person obtaining consent (reviewer) asks questions designed to assess the potential subject's understanding of the material. The reviewer will specifically state this intent to the potential subject. Responses to these questions are the basis of the assessment of capacity to consent. The consent issues can be repeated and explained in more detail by the research staff during the determination of capacity to consent.

5. The potential subject is given ample opportunity to decide, without coercion or undue influence, whether or not to participate in the study.

6. The potential subject's capacity to understand, appreciate, reason with, and express a choice about this specific protocol will be documented in our progress note. Specifically, we will make a note of the potential subject's knowledge of critical elements in the informed consent form: nature of the illness being studied, voluntary nature of participation, ability to withdraw at any time, consequences of withdrawing, possible risks and benefits of participating, procedures involved, time required, confidentiality, and whom to call with any questions.

All participants who have capacity to consent to research participation will be asked to decide and document whether or not they will appoint a research health care proxy should they lose decision making capacity by the time of follow up. If appointed, the research health care proxy would make decisions regarding enrollment in this study once capacity is lost.

At follow up, the appointed proxy may provide consent on subject's behalf.

When no proxy is assigned in advance and the subject has not previously indicated that he/she would like to terminate participation in case of incapacity, consent may be provided by next of kin (parent, spouse, adult child). If next of kin is not available, and participant is determined to retain capacity to appoint a surrogate, then research staff will use the PCS model to appoint any trusted individual.

Although many subjects will have capacity to consent to research participation at the onset, it is likely that many will have diminished capacity over time. Capacity and loss of capacity will be determined and documented by trained research staff. Cognitive functioning and capacity to consent to research participation will be reassessed at follow-up research visits.

A waiver of consent for information obtained for family members without their consent is justified under the 45CFR46.116 (d). Consent, assent and research participation will be conducted in the presence of the surrogate (or surrogate choice). Research health care proxy will be identified if possible.

Documentation of assent. If the research participant lacks capacity to give consent, assent will be documented on the consent form. The designated individual will provide consent.

For follow-up participants, since they have previously consented to be part of the study and to participate in follow-up evaluations, site's IRB may or may not ask for verbal consent to be obtained from the participant and noted in chart. In case of incapacity, verbal consent will be obtained from surrogate/proxy and noted in chart Informed Consent.

For participants living out of the research site area, both initial and follow-up assessments will be done remotely by email, phone or via skype.

9.0 Trainings and Certifications

All study coordinators are required to complete training on the neuropsychological battery, the NPIQ-CBRS and the Dementia Questionnaire.

Training	Site	Contact	Recurrence
Neuropsychological Battery	**Rush University**	**Celina Pavon CELINA_PAVON@rush.edu**	**Once a year**
NPIQ-CBRS	**University of Pittsburgh**	**Elise Weamer weamerea@upmc.edu**	**One time only**
Dementia Questionnaire	**Columbia University**	**Dolly Reyes-Dumeyer Dr22100@cumc.columbia.edu**	**One time only**

10.0 Appendices

10.1 Appendix A: ADFBS Minimum Data set

VARIABLE	QUESTION
ADCID Required for all **Overwrite**	1. Site ID — — –
FAMID Required for all **Overwrite**	2. Family ID ——— —
INDID Required for all **Overwrite**	3. Individual ID ——— —
FATHID Required for all **Overwrite**	4. Father ID ——— — **"Founders" are 0**
MOTHID Required for all **Overwrite**	5. Mother ID ——— — **"Founders" are 0**
CONTROL Required for all **Overwrite**	6. Is the subject a control? 1 Yes 2 No
CONTYPE Required for control **Overwrite**	6a. Type of control 1 Unaffected spouse 2 Population control 3 Convenience control
RELDEM Required for control **Overwrite**	6b. How many first degree relatives (parents, siblings, or children of subject) were reported to have had dementia (by symptoms, history, or diagnosis)? — — 99 Missing/Unknown
8PROBAND Required for all **Overwrite**	7. Is the subject the proband? 1 Yes 2 No
TWIN Required for all **Overwrite**	7a. Is this person a twin? 1 Yes 2 No

TWINTYPE Required for all **Overwrite**	7b. If yes, indicate twin type: 1 Monozygotic (Identical) 2 Dizygotic (Fraternal) 9 Unknown
TWINID Required for all **Overwrite**	7c. If yes, indicate twin individual ID (INDID):
SEX Required for all **Overwrite**	8. Subject's sex: 1 Male 2 Female
INF **Longitudinal**	9. Relation of Informant to Subject (primary informant) 1 Spouse 2 Child 3 Sibling 4 Other Family 5 Friend 6 Professional 7 Other Note: 6 and 7 require specific informant information in 9a.
INFCOM	9a.
INFID	9b. Individual ID of primary informant (if known): _____
INF2 **Longitudinal**	9c. Relation of Informant to Subject (second informant) 1 Spouse 2 Child 3 Sibling 4 Other Family 5 Friend 6 Professional 7 Other Note: 6 and 7 require specific informant information in 9d.
INF2COM **Longitudinal**	9d.
INF2ID	9e. Individual ID of secondary informant (if known): _____
INF3 **Longitudinal**	9f. Relation of Informant to Subject (third informant) 1 Spouse 2 Child 3 Sibling 4 Other Family 5 Friend 6 Professional 7 Other Note: 6 and 7 require specific informant information in 9g.

INF3COM **Longitudinal**	9g.
INF3ID	9h. Individual ID of tertiary informant (if known): _____
INFA **Longitudinal**	9i. At Least One Informant Lives with Subject 0 No 1 Yes
INFB **Longitudinal**	9j. Total Contact of All Informant(s) with Subject (Combined) 0 < 2 days a week 1 2 days/week 2 3-4 days/week 3 5 or more days/week
SAMPLED Required for all **Overwrite**	10. Is the subject sampled or will the subject be sampled (blood, cell lines, brain tissue)? 1 Yes 2 No If **Yes**, please continue. If **No**, please code any of the following variables for which you have data (specifically 12-29); if you have no data for the variable(s), please leave blank OR fill in with the appropriate code for missing values.
LTF **Overwrite**	10b. Lost to follow-up 1 Yes 2 No
COMREQ Required for all **Overwrite**	11. Does the subject consent to for-profit organizations (pharmaceutical and biotechnology companies) having access to his/her clinical data and DNA? 1 Yes 2 No 3 Subject was not specifically asked/consented 9 Missing/Unknown
GENRSCH Required for all **Overwrite**	11b. Does the subject consent to researchers studying the genetics of any human disease having access to his/her clinical data and DNA? 1 Yes 2 No 3 Subject was not specifically asked/consented 9 Missing/Unknown
BIRTHYR Required for all **Overwrite**	12. Subject's year of birth __ _____ 9999 Missing/Unknown *If exact date is not known, please approximate to nearest decade.*
VITALST Required for all **Overwrite**	13. The subject's last known vital status was: 1 Alive 2 Dead 9 Missing/Unknown

	SKIP? If 1 or 9, skip to #14 RACE If 2, continue with next item, #13a AGEDEATH
AGEDEATH Required for sampled if subject is dead (VITALST = 2) **Overwrite**	13a. At what age did the subject die? — ——— 999 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
AUTOPSY Required for sampled if subject is dead (VITALST = 2) **Overwrite**	13b. Has an autopsy been performed that resulted in data or a report that is available or will be available at your Center? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 2 or 9, skip to #14 RACE If 1, continue with next item, #13c CERAD
CERAD Required for sampled if autopsy report available (AUTOPSY = 1) **Overwrite**	13c. Was CERAD criteria used? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 2 or 9, skip to #13e REAGAN If 1, continue with next item, #13d CERADCT
CERADCT Required for sampled if CERAD criteria used (CERAD = 1) **Overwrite**	13d. If CERAD was used, what category was assigned? 1 Definite 2 Probable 3 Possible 4 Normal 9 Missing/Unknown
REAGAN Required for sampled if autopsy report available (AUTOPSY = 1) **Overwrite**	13e. Was NIA-Reagan criteria used? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 2 or 9, skip to #13g BRAAK If 1, continue with next item, #13f REAGANCT
REAGANCT Required for sampled if REAGAN criteria used (REAGAN = 1) **Overwrite**	13f. If NIA-Reagan criteria was used, what category was assigned? 1 High 2 Intermediate 3 Low 9 Missing/Unknown
BRAAK Required for sampled if autopsy report available (AUTOPSY = 1) **Overwrite**	13g. Was Braak and Braak criteria used? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 2 or 9, skip to #13i OTHCRI If 1, continue with next item, #13h BRAAKCT
BRAAKCT Required for sampled if	13h. If Braak and Braak was used, what category was assigned?

BRAAK criteria used (BRAAK = 1) **Overwrite**	1 Stage I 2 Stage II 3 Stage III 4 Stage IV 5 Stage V 6 Stage VI 9 Missing/Unknown
OTHCRI Required for sampled if autopsy report available (AUTOPSY = 1) **Overwrite**	13i. Was another neuropathological criteria used? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 2 or 9, skip to #13k LEWYBODY If 1, continue with next item, #13j TYPECRI
TYPECRI Required for sampled if other criteria used (OTHCRI = 1) **Overwrite**	13j. Describe the type of neuropathological criteria and the assigned category.
LEWYBODY Required for sampled if autopsy report available (AUTOPSY = 1) **Overwrite**	13k. If Lewy bodies were present, in what part of the brain were they found? 1 Substantia nigra/brain stem 2 Limbic/amygdala 3 Neocortex 4 Substantia nigra/brain stem and limbic/amygdala 5 Substantia nigra/brain stem and neocortex 6 Limbic/amygdala and neocortex 7 Substantia nigra/brain stem, limbic/amygdala and neocortex 8 Lewy bodies present but location not specified 9 Missing/Unknown/Lewy bodies not present
LEWYSTAIN Required for sampled if autopsy report available (AUTOPSY = 1) **Overwrite**	13l. What stain was used to look for Lewy bodies? 1 Hematoxylin and eosin (H&E) alone 2 alpha-synuclein and H&E 3 Ubiquitin and H&E 4 Ubiquitin, alpha-synuclein and H&E 5 Other 9 Missing/Unknown ***SKIP?*** If 1-4 or 9, skip to #14 RACE If 5, continue with next item, #13m LSTAINTY
LSTAINTY Required for sampled if other stain used (LEWYSTAIN = 5) **Overwrite**	13m. Describe the type of stain used to look for Lewy bodies.
RACE Required for sampled **Overwrite**	14. Subject's race/ethnic group: 1 White 2 Black 3 American Indian or Alaskan Native 4 Asian or Pacific Islander 54 Other 99 Missing/Unknown

HISPANIC Required for sampled **Overwrite**	15. Is the subject Spanish/Hispanic/Latino? 1 Yes 2 No 9 Missing/Unknown
EDUC **Overwrite**	16. Subject's education: Highest grade or number of years of school completed. __ _ 99 = Missing/Unknown
VISIT Required for ALL **Longitudinal**	17. What is the visit number? __ __ 98 = Not applicable *Baseline/initial visit = 1, 2nd visit (follow-up) = 2, etc. If a diagnosis changes, you must change the VISIT number, e.g., if a subject goes to autopsy and is diagnosed with Definite AD.* *For individuals that will never be sampled/evaluated and are included for pedigree structure, code as 98*
EVALMETH Required for sampled **Longitudinal**	18. How was disease status assigned? 1 Autopsy 2 Examination (in-person at your ADC/institution or by your genetics staff) 3 Medical record review from formal dementia evaluation with or without a telephone interview 4 Review of general medical records AND informant and/or subject telephone interview 5 Review of general medical records *only* 6 Subject and/or informant telephone interview 7 Family report 9 Missing/Unknown
EVALYR Required for sampled **Longitudinal**	19. When was the last assessment by examination, medical record review, or telephone interview? Year _____ _ Missing/Unknown = 9999 NOTE: If EVALMETH = Family report, record as Missing/Unknown.
EVALTEST Required for sampled **Longitudinal**	20. Was cognitive testing administered to the subject? 1 Yes 2 No 9 Missing/Unknown
NEUROIM Required for sampled **Longitudinal**	21. Has brain imaging been performed? 1 Yes 2 No 9 Missing/Unknown
CLINDEM Required for sampled **Longitudinal**	22. Is the subject demented? 1 Yes 2 No (includes questionable dementia or diagnosis not completed) 9 Missing/Unknown ***SKIP?*** If 1, skip to #23 DEMDX If 2, continue with next item, #22a NOTDEMCI If 9, please code any of the following variables for which you have data; if you have no data

	for the variable(s), please leave blank OR fill in with the appropriate code for missing values.
NOTDEMCI Required for sampled if subject is not demented (CLINDEM = 2) **Longitudinal**	22a. If the subject does not meet criteria for dementia, what is the diagnosis? 1 Not demented, no neurological disorder 2 Not demented, but has other neurological disorder (such as Parkinson's, MS, etc.) 3 Questionable dementia (e.g., CDR=0.5) or cognitive impairment (MCI, AAMI) 4 Down syndrome, but not demented 5 Other 6 No diagnosis made 9 Missing/Unknown ***SKIP?*** Skip to #31 CDR
DEMDX Required for sampled if subject is demented (CLINDEM = 1) **Longitudinal**	23. Is the primary clinical dementia diagnosis Alzheimer's disease? 1 Definite AD (autopsy confirmed) 2 Probable AD 3 Possible AD 4 Dementia, unspecified 5 Non-Alzheimer's dementia 6 Dementia by family report 9 Missing/Unknown ***SKIP?*** If 1 through 3 continue with next item, #24 CLDEMLEW If 4, 6 or 9, skip to #25 COMDXAD If 5, skip to #26 NONADDEM
CLDEMLEW **Longitudinal**	24. If the primary clinical dementia diagnosis is Alzheimer's disease (CLDEMX = 1 through 3), does the subject also meet clinical criteria for dementia with Lewy bodies, Lewy body variant Alzheimer's disease, or diffuse Lewy body disease? 1 Yes 2 No 9 Missing/Unknown
COMDXAD **Longitudinal**	25. Please note any comments for DEMDX and/or CLDEMLEW or any comments regarding diagnosis, e.g., interesting neuropathological data. ***SKIP?*** Skip to #28 AGEDEM
NONADDEM Required for sampled if subject has non-AD dementia (DEMDX = 5) **Longitudinal**	26. If the primary clinical dementia diagnosis is non-Alzheimer's dementia, what is the suspected etiology? 1 Frontal lobe dementia (e.g., Pick's, FTD) 2 Parkinson's disease dementia 3 Huntington's disease (HD) 4 Progressive supranuclear palsy (PSP) 5 Alcohol related dementias 6 Corticobasal degeneration 7 Communicating, obstructive, or normal pressure hydrocephalus 8 Vascular dementia (e.g., dementia due to stroke) 9 Dementia with Lewy bodies (not Parkinson's dementia) 10 Prion-associated dementia (e.g., Creutzfeldt-Jakob) 11 Human immunodeficiency virus (HIV) encephalopathy 12 Primary progressive aphasia 13 Posterior cortical dysfunction 14 Down syndrome 15 Dementia due to multiple non-Alzheimer's etiologies 16 Dementia due to other general medical conditions 17 Other (dementia not otherwise specified) 99 Missing/Unknown

COMDXNAD **Longitudinal**	27. Please note any comments for **NONADDEM**
AGEDEM Required for sampled if subject is demented (CLINDEM = 1) **Overwrite**	28. At what age did the subject *develop* dementia symptoms (AAO)? __ ___ 999 Missing/Unknown *If exact age is not known, please approximate to nearest five year period.*
AAOSYMP **Overwrite**	29. What presented as the first dementia symptom? 1 Memory change 2 Performance change (in daily activities) 3 Language change 4 Disorientation 5 Personality change (e.g. outgoing to withdrawn) 6 Depressed mood 7 Behavior change (e.g. dropped hobbies) 8 Psychosis (includes paranoia, hallucinations, etc.) 9 Missing/Unknown
AGEDXDEM **Overwrite**	30. At what age was the subject *diagnosed* with Alzheimer's disease or other non-Alzheimer's dementia? __ ___ 999 Missing/Unknown *If exact age is not known, please approximate to nearest five year period.*
CDR **Longitudinal**	31. What is the most recent CDR score? __ _ 99 Missing/Unknown
CDRYR **Longitudinal**	31a. What YEAR was the most recent CDR Scale administered? __ __ __ _ 9999 Missing/Unknown
CDRVER **Longitudinal**	31b. What version of the CDR was used? 1 Short Form 2 Long Form 9 Missing/Unknown
STROKE **Overwrite**	32. Does the subject have a history of stroke(s)? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue with next item, #32a STROKETY If 2 or 9, skip to #33 HYPERTEN
STROKETY **Overwrite**	32a. What type of stroke did the subject have? 1 Ischemic 2 Hemorrhagic 9 Missing/Unknown *If multiple strokes, record type of first stroke.*
STROKEAGE **Overwrite**	32b. At what age did the subject have a stroke?

	__ ____ 999 Missing/Unknown *If multiple strokes, record age at first stroke.* *If exact age is not known, please approximate to nearest decade.*
HYPERTEN **Overwrite**	33. Does the subject have a history of hypertension? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue with next item, #33a HYPERAGE If 2 or 9, skip to #34 HEART
HYPERAGE **Overwrite**	33a. At what age was the subject diagnosed with hypertension? __ ____ 999 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
HEART **Overwrite**	34. Does the subject have a history of heart disease? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue with next item, #34a HEARTAGE If 2 or 9, skip to #35 DIABETES
HEARTAGE **Overwrite**	34a. At what age was the subject diagnosed with heart disease? __ ____ 999 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
DIABETES **Overwrite**	35. Does the subject have a history of diabetes? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue with next item, #35a DIABETAG If 2 or 9, skip to #36 PDNODEM
DIABETAG **Overwrite**	35a. At what age was the subject diagnosed with diabetes? __ __ __ 999 Missing *If exact age is not known, please approximate to nearest decade.*
DIABETX **Overwrite**	35b. Has the subject undergone treatment for diabetes? 1 Yes, diet alone 2 Yes, hypoglycemics 3 Yes, insulin 4 Yes, both hypoglycemics and insulin 5 No 9 Missing/Unknown
PDNODEM **Overwrite**	36. Does the subject have a history of Parkinson's disease?

	1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue with next item, #36a PDCLINDX If 2 or 9, skip to #37 DEPR
PDCLINDX **Overwrite**	36a. What category of Parkinson's disease was the subject diagnosed with? 1 Definite PD (autopsy confirmed) 2 Probable PD 3 Possible PD 9 Missing/Unknown
PDAGE **Overwrite**	36b. At what age was the subject diagnosed with Parkinson's disease? __ ____ 999 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
DEPR **Overwrite**	37. Does the subject have a history of depression? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue with next item, #37a DEPRTX If 2 or 9, skip to #38 HEADINJ
DEPRTX **Overwrite**	37a. Has the subject undergone treatment for depression? 1 Yes, therapy alone 2 Yes, antidepressants with or without therapy 3 Yes, electroconvulsive therapy with or without antidepressants/therapy 4 No 9 Missing/Unknown
DEPRAGE **Overwrite**	37b. At what age was the subject diagnosed with depression? __ ____ 999 Missing *If subject has multiple depressive episodes, record age at first episode.* *If exact age is not known, please approximate to nearest decade.*
HEADINJ **Overwrite**	38. Does the subject have a history of head injury? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue to next item, #38a HEADAGE If 2 or 9, skip to #39 ALCDRUG
HEADAGE **Overwrite**	38a. At what age did the subject have the head injury? __ ____ 999 Missing/Unknown *If multiple head injuries, record age at first head injury.* *If exact age is not known, please approximate to nearest decade.*
ALCDRUG **Overwrite**	39. Does the subject have a history of alcohol or drug abuse?

	1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue to next item, #39a ABUSEAGE If 2 or 9, skip to #40 COM28_36
ABUSEAGE **Overwrite**	39a. At what age was the subject initially diagnosed with alcohol or drug abuse? __ ____ 999 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
COM28_36 **Overwrite**	40. Please note any comments for fields #31 through #39a
SMOKE **Longitudinal**	41. Have you ever smoked one or more cigarettes, cigars, or pipes a day for at least a year? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue to next item, #41a SMOKEAGE If 2 or 9, skip to #46 PHYSACT
SMOKEAGE **Longitudinal**	41a. How old were you when you started smoking? __ ____ 999 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
SMOKENOW **Longitudinal**	41b. Do you still smoke? 1 Yes 2 No ***SKIP?*** If 2, continue to next item, #41c SMOKESTOP If 1, skip to #46 PHYSACT
SMOKESTOP **Longitudinal**	41c. How old were you when you stopped smoking? __ ____ 999 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
PREG **Overwrite**	42. How many pregnancies did you have? __ _ 99 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
PREGLIVE **Overwrite**	42a. How many live born children did you have? __ _ 99 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*

HRT **Overwrite**	43. Have you ever taken any form of hormone replacement therapy (HRT) or medication for menopause? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue to next item, #43a HRTAGEA If 2 or 9, skip to #44 HYST
HRTAGEA **Overwrite**	43a. How old were you when you started taking HRT? __ _ 99 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
HRTAGEB **Overwrite**	43b. How old were you when you last took HRT? __ _ 99 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
HRTYRS **Overwrite**	43c. For how many years total did you take any form of HRT? __ _ 99 Missing/Unknown *If exact time is not known, please approximate to nearest 5 yr period.*
HYST **Overwrite**	44. Have you had a hysterectomy? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue to next item, #44a HYSTAGE If 2 or 9, skip to #45 OVAR
HYSTAGE **Overwrite**	44a. At what age did you have a hysterectomy? __ _ 99 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
OVAR **Overwrite**	45. Have any of your ovaries been removed? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 1, continue to next item, #45a OVARAGE If 2 or 9, skip to #46 PHYSACT
OVARAGE **Overwrite**	45a. At what age were your ovaries removed? __ _ 99 Missing/Unknown *If exact age is not known, please approximate to nearest decade.*
OVARBOTH	45b. Were both ovaries removed?

Overwrite	1 Yes 2 No 9 Missing/Unknown
OVARHRT **Overwrite**	45c. Was hormone replacement therapy given at the time your ovaries were removed? 1 Yes 2 No 9 Missing/Unknown
PHYSACT **Longitudinal**	46. In the past 14 days, have you participated in your typical number of recreational or leisure-time activities? 1 Yes 2 No 9 Missing/Unknown ***SKIP?*** If 2, continue to next item, #46aPHYSACTNO If 1, skip to #47a. VIGACTA1
PHYSACTNO **Longitudinal**	46a. What prevented you from engaging in your usual number of recreational or leisure-time activities during the past 14 days? 1 Poor Health 2 No desire 3 Other responsibilities 4 Weather 5 Vacation/Holiday 6 Other
VIGACTA1 **Longitudinal**	47a. In the past 2 weeks, did you take part in any vigorous activities (aerobic dancing, playing handball) more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #47b.VIGACTA2 If 2, skip to #47d. VIGACTB1
VIGACTA2 **Longitudinal**	47b. How many times in the past 2 weeks did you take part in any vigorous activities? __ __ _ 999 Missing/Unknown
VIGACTA3 **Longitudinal**	47c. For how many minutes did you participate in vigorous activities each time? __ __ _ 999 Missing/Unknown
VIGACTB1 **Longitudinal**	47d. From ages 12-25, did you take part in any vigorous activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #47e.VIGACTB2 If 2, skip to #47f. VIGACTC1
VIGACTB2 **Longitudinal**	47e. How would you describe your level of vigorous activity from ages 12-25? 1 Almost all the time 2 Very frequently 3 Frequently

	4 Rarely
VIGACTC1 **Longitudinal**	47f. From ages 26-50, did you take part in any vigorous activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #47g.VIGACTC2 If 2, skip to #47h. VIGACTD1
VIGACTC2 **Longitudinal**	47g. How would you describe your level of vigorous activity from ages 26-50? 1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
VIGACTD1 **Longitudinal**	47h. From ages 50 and up, did you take part in any vigorous activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #47i. VIGACTD2 If 2, skip to #48a. MODACTA1
VIGACTD2 **Longitudinal**	47i. How would you describe your level of vigorous activity from ages 50 and up? 1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
MODACTA1 **Longitudinal**	48a. In the past 2 weeks, did you take part in any moderate activities (bicycling, swimming, hiking, playing tennis) more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #48b.MODACTA2 If 2, skip to #48d. MODACTB1
MODACTA2 **Longitudinal**	48b. How many times in the past 2 weeks did you take part in any moderate activities? __ __ _ 999 Missing/Unknown
MODACTA3 **Longitudinal**	48c. For how many minutes did you participate in moderate activities each time? __ __ _ 999 Missing/Unknown
MODACTB1 **Longitudinal**	48d. From ages 12-25, did you take part in any moderate activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #48e.MODACTB2 If 2, skip to #48f. MODACTC1
MODACTB2 Longitudinal	48e. How would you describe your level of moderate activity from ages 26-50?

	1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
MODACTC1 **Longitudinal**	48f. From ages 26-50, did you take part in any moderate activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #48g.MODACTC2 If 2, skip to #48h. MODACTD1
MODACTC2 **Longitudinal**	48g. How would you describe your level of moderate activity from ages 26-50? 1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
MODACTD1 **Longitudinal**	48h. From ages 50 and up, did you take part in any moderate activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #48i MODACTD2 If 2, skip to #49a. LITEACTA1
MODACTD2 **Longitudinal**	48i. How would you describe your level of moderate activity from ages 50 and up? 1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
LITEACTA1 **Longitudinal**	49a. In the past 2 weeks, did you take part in any light activities (walking, dancing, calisthenics, bowling, gardening, horseback riding) more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #49b. LITEACTA2 If 2, skip to #49d. LITEACTB1
LITEACTA2 **Longitudinal**	49b. How many times in the past 2 weeks did you take part in any light activities? __ __ _ 999 Missing/Unknown
LITEACTA3 **Longitudinal**	49c. For how many minutes did you participate in light activities each time? __ __ _ 999 Missing/Unknown
LITEACTB1 **Longitudinal**	49d. From ages 12-25, did you take part in any light activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #49e. LITEACTB2 If 2, skip to #49f. LITEACTC1

LITEACTB2 **Longitudinal**	49e. How would you describe your level of light activity from ages 12-25? 1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
LITEACTC1 **Longitudinal**	49f. From ages 26-50, did you take part in any light activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #49g.LITEACTC2 If 2, skip to #49h. LITEACTD1
LITEACTC2 **Longitudinal**	49g. How would you describe your level of light activity from ages 26-50? 1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
LITEACTD1 **Longitudinal**	49h. From ages 50 and up, did you take part in any light activities more than 10 times? 1 Yes 2 No ***SKIP?*** If 1, continue to next item, #49i. LITEACTD2 If 2, skip to #50 VERSION
LITEACTD2 **Longitudinal**	49i. How would you describe your level of light activity from ages 50 and up? 1 Almost all the time 2 Very frequently 3 Frequently 4 Rarely
VERSION **Longitudinal**	50. What version of the cognitive measures was given? LC01 Load Cognitive version 1 LC02 Load Cognitive version 2 (vegetables) 9999 Missing/Unknown
INTID **Longitudinal**	51. What is the interviewer ID? NOTE: This is an open text field. You may use any scheme for assigning Interviewer ID, such as initials.
DATEINT **Longitudinal**	52. What is the month and year of the cognitive testing interview? __ __ / __ __ __ __
PHONE **Longitudinal**	53. Was the interview in person or via telephone? 1 In person 2 Phone 8 Refusal 9 Missing/Unknown

STORY **Longitudinal**	54. Logical Memory IA-- Story Score 0-25 — — 96 Physical problem 97 Cognitive/behavioral problem 98 Other problem 99 Verbal refusal
DIGFOR **Longitudinal**	55. Digit Span Forward Score 0-12 — — 96 Physical problem 97 Cognitive/behavioral problem 98 Other problem 99 Verbal refusal
DIGBAK **Longitudinal**	56. Digit Span Backward Score 0-12 — – 96 Physical problem 97 Cognitive/behavioral problem 98 Other problem 99 Verbal refusal
ANIMALS **Longitudinal**	57. Category Fluency-- Animals Score 0-79 — – 96 Physical problem 97 Cognitive/behavioral problem 98 Other problem 99 Verbal refusal
FRUITS **Longitudinal**	58. Category Fluency-- Fruits and Vegetables Score 0-79 — – 96 Physical problem 97 Cognitive/behavioral problem 98 Other problem 99 Verbal refusal
DIGORD **Longitudinal**	59. Digit Ordering Score 0-16 — – 96 Physical problem 97 Cognitive/behavioral problem

	98 Other problem 99 Verbal refusal
DELAY **Longitudinal**	60. Logical Memory IIA-- Story Score 0-25 __ _ 96 Physical problem 97 Cognitive/behavioral problem 98 Other problem 99 Verbal refusal
HOWWELL **Longitudinal**	61. How well do you think the subject understood the questions? 1 Quite well 2 Fairly well 3 Somewhat 4 Very little 5 Not at all 8 Refusal 9 Missing/Unknown
HEARIMP **Longitudinal**	62. Does the participant have substantial hearing impairment? 1 Yes 2 No
CSTATUS **Longitudinal**	63. What is the cognitive testing status of the subject? 1 Complete 2 Incomplete, refused 3 Incomplete, too impaired 4 Incomplete- interim, complete later 10 Not tested, out of town 11 Not tested, moved 12 Not tested, refused 13 Not tested, hospitalized 14 Not tested, other 20 Deceased 21 Withdrawn

COMM **Longitudinal**	64. Please note any comments for fields #41 - #60
VEG **Longitudinal**	65. Category Fluency-- Vegetable Score 0-79 __ _ 96 Physical problem 97 Cognitive/behavioral problem 98 Other problem 99 Verbal refusal
COM_ANY **Longitudinal**	66. Please note any comments for any field

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VARIABLE	QUESTION
NPIQDATE **Longitudinal**	67. What is the month and year of the interview? _ _ / _ _ _ _ NOTE: Please format as MM/YYYY
INITIALS Required **Longitudinal**	68. Psychiatric Rater Initials
NPIQNA **Longitudinal**	68a. Assessment Was Not Administered due to (Circle one): 1 No Informant 2 Subject Refused 3 Other NOTE: 3 requires specific information.
NPIQNACOM **Longitudinal**	68b. If 68a = 3 (other), please provide specific information.
NPIQTYPE **Longitudinal**	69. Interview Type 1 Visit 2 Telephone
NPIQSOURCE **Longitudinal**	69a. What is source of the data submitted? 1 LOAD Integrated Interview 2 UDS 3 Other NOTE: See Data Element Dictionary for more information
NPIQSOURCECOM **Longitudinal**	69b. Document comments about the source of NPIQ data if NPIQSOURCE = 3 (other)
NPIQVITAL **Longitudinal**	69c. Was NPIQ data collected on a living or deceased individual? 1 Living Individual 2 Deceased Individual NOTE: See Data Element Dictionary for more information
AGIT **Longitudinal**	70. Is the patient stubborn and resistive to help from others? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#12a AGITSEV) if 0, skip to #71 DEPD.
AGITSEV **Longitudinal**	70a. Severity of agitation or aggression. 1-3 Scale.
DEPD **Longitudinal**	71. Does the patient act as if he or she is sad or in low spirits? Does he or she cry? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#71a DEPDSEV) if 0, skip to #67 ANX.
DEPDSEV **Longitudinal**	71a. Severity of depression or dysphoria. 1-3 Scale
ANX **Longitudinal**	72. Does the patient become upset when separated from you? Does he or she have any other signs of nervousness, such as shortness of breath, sighing, being unable to relax, or feeling excessively tense? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#72a ANXSEV) if 0, skip to #73 ELAT.
ANXSEV **Longitudinal**	72a. Severity of anxiety. 1-3 Scale
ELAT **Longitudinal**	73. Does the patient appear to feel too good or act excessively happy? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#73a ELATSEV) if 0, skip to #74 APA.
ELATSEV **Longitudinal**	73a. Severity of elation or euphoria. 1-3 Scale
APA **Longitudinal**	74. Does the patient seem less interested in his or her usual activities and in the activities and plans of others? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#74a APASEV) if 0, skip to #70 DISN.

APASEV **Longitudinal**	74a. Severity of Apathy or Indifference. 1-3 Scale
DISN **Longitudinal**	75. Does the patient seem to act impulsively? For example, does the patient talk to strangers as if he or she knows them, or does the patient say things that may hurt people's feelings? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#75a DISNSEV) if 0, skip to #76 IRR.
DISNSEV **Longitudinal**	75a. Severity of disinhibition. 1-3 Scale
IRR **Longitudinal**	76. Is the patient impatient or cranky? Does he or she have difficulty coping with delays or waiting for planned activities? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#76a IRRSEV) if 0, skip to #77 MOT.
IRRSEV **Longitudinal**	76a. Severity of irritability or lability. 1-3 Scale
MOT **Longitudinal**	77. Does the patient engage in repetitive activities, such as pacing around the house, handling buttons, wrapping string, or doing other things repeatedly? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#77a MOTSEV) if 0, skip to #78 NITE.
MOTSEV **Longitudinal**	77a. Severity of motor disturbance. 1-3 Scale
NITE **Longitudinal**	78. Does the patient awaken you during the night, rise too early in the morning, or take excessive naps during the day? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#78a NITESEV) if 0, skip to #79 APP.
NITESEV **Longitudinal**	78a. Severity of nighttime behaviors. 1-3 Scale
APP **Longitudinal**	79. Has the patient lost or gained weight, or had a change in the food he or she likes? 0 No 1 Yes ***SKIP:*** if 1, continue with next item (#79a APPSEV) if 0, skip to #80 DEL.
APPSEV **Longitudinal**	79a. Severity of appetite and eating. 1-3 Scale
DEL **Longitudinal**	80. Does the patient believe that others are stealing from him or her, or planning to harm him or her in some way? 0 No 1 YES ***SKIP:*** if 1, continue with next item (#80a DELSEV) if 0, skip to #80b PARA.
DELSEV **Longitudinal**	80a. Severity of Delusions. 1-3 Scale
Paranoid (PARA) **Longitudinal**	80b. How often has that happened this past month? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate **SKIP:** If 1-8, continue with next item (#80c PARAB). If 0 or 9, skip to #81 (HALL). **Note:** If '8' was circled, please also complete #80d (PARAC) and #80e (PARAD).
ParanoidB (PARAB) **Longitudinal**	80c. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 NA
ParanoidC (PARAC) **Longitudinal**	80d. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests {S} believes people are harming, threatening or taking advantage of {S} in some way? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month)

	4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #80b. Paranoid (PARA) was '8'.
ParanoidD (PARAD) Longitudinal	80e. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #80b (PARA) is '8'.
HALL Longitudinal	81. Does the patient act as if he or she hears voices? Does he or she talk to people who are not there? 0 No 1 Yes ***SKIP:*** If 1, continue with next item #81a (HALLSEV). If 0, skip to #82 (VISHALL).
HALLSEV Longitudinal	81a. Severity of Hallucinations. 1-3 Scale
AuditoryHallucinations (AUDHALL) Longitudinal	81b. How often has that happened this past month? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** If 1-8, continue with next item #81c (AUDHALLB). If 0 or 9, skip to #82 (VISHALL). **Note:** If 8 was circled, please also complete #81c (PARAC) and #81e (PARAD).
AuditoryHallucinationsB (AUDHALLB) Longitudinal	81c. Rate for clarity. 0 Vauge 1 Clear
AuditoryHallucinationsC (AUDHALLC) Longitudinal	81d. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests {S} believes people are harming, threatening or taking advantage of {S} in some way? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #81b (AUDHALL) is '8'.
AuditoryHallucinationsD (AUDHALLD) Longitudinal	81e. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #81b (AUDHALL) is '8'.
VisualHallucinations (VISHALL) Longitudinal	82. Has {S} seen things or people that were not there? *If yes, describe.* 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** I f 1-8, continue with next item #82a (VISHALLB). If 0 or 9, skip to #83 (MISIDP). **Note:** If '8' was circled, please also complete #82b (VISHALLC) and #82c (VISHALLD).
VisualHallucinationsB (VISHALLB) Longitudinal	82a. Rate for clarity. 0 Vague 1 Clear
VisualHallucinationsC (VISHALLC) Longitudinal	82b. In the month when this symptom was most persistent, how often has {S} seen things or people that were not there? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month)

	4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #82 (VISHALL) is '8'.
VisualHallucinationsD (VISHALLD) Longitudinal	82c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #82 (VISHALL) is '8'.
MisidentifyPeople (MISIDP) Longitudinal	83. Has {S} misidentified people? (For example, has {S} confused one familiar person with another, or has {S} thought that a familiar person was a stranger?) ***NOTE:*** *'Misidentification' means an actual belief that one person was another, not simply a misnaming or failure to remember who someone is, and it refers to someone actually seen by {S}.* 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** If 1-8, continue with next item #83a (MISIDPB). If 0 or 9, skip to #84 (MISIDSEL). **Note:** If '8' was circled, please also complete #83b (MISIDPC) and #83c (MISIDPD).
MisidentifyPeopleB (MISIDPB) Longitudinal	83a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 N/A
MisidentifyPeopleC (MISIDPC) Longitudinal	83b. In the month when this symptom was most persistent, how often has {S} misidentified people? (For example, has {S} confused one person with another, or has {S} thought that a familiar person was a stranger?) 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #83. MisidentifyPeople (MISIDP) was '8'.
MisidentifyPeopleD (MISIDPD) Longitudinal	83c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #83. MisidentifyPeople (MISIDP) was '8'.
MisidentifySelf (MISIDSEL) Longitudinal	84. Has {S} looked at {S's} self in a mirror and not recognized {S's} self? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** If 1-8 , continue with next item #84a (MISIDSB). If 0 or 9, skip to #85 (MISIDT). **Note:** If '8' was circled, please also complete #84b (MISIDSC) and #84c (MISIDSD).
MisidentifySelfB (MISIDSB) Longitudinal	84a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 NA
MisidentifySelf C (MISIDSC) Longitudinal	84b. In the month when this symptom was most persistent, how often has {S} looked at {Ss} self in a mirror and not recognized {Ss} self? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #84. MisidentifySelf (MISIDSEL) was '8'.

MisidentifySelfD (MISIDSD) Longitudinal	84c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #84. MisidentifySelf (MISIDSEL) was '8'.
MisidentifyThings (MISIDT) Longitudinal	85. Has {S} misidentified things? Has {S} thought common things were something else? (For example, has {S} said that a pillow was a person or that a light bulb was a fire?) *If yes, describe.* 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** If 1-8, continue with next item #85a (MISIDTB). If 0 or 9, skip to #86 (INFID). **Note:** If '8' was circled, please also complete #85b (MISIDTC) and #85c (MISIDTD).
MisidentifyThingsB (MISIDTB) Longitudinal	85a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 NA
MisidentifyThingsC (MISIDTC) Longitudinal	85b. In the month when this symptom was most persistent, how often has {S} misidentified things? Has {S} thought common things were something else? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #85. MisidentifyThings (MISIDT) was '8'.
MisidentifyThingsD (MISIDTD) Longitudinal	85c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #85. MisidentifyThings (MISIDT) was '8'.

Infidelity (INFID) Longitudinal	86. Has {S} done or said anything that suggests {S} thinks {S's} spouse is unfaithful? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** If 1-8, continue with next item #86a.(INFIDB). If 0 or 9, skip to #87 (ABND). **Note:** If '8' was circled, please also complete #86b (INFIDC) and #86c (INFIDD).
InfidelityB (INFIDB) Longitudinal	86a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 N/A
InfidelityC (INFIDC) Longitudinal	86b. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests {S} thinks {Ss} spouse is unfaithful? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to
InfidelityD (INFIDD) Longitudinal	86c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #86. Infidelity (INFID) was '8'.

Abandonment (ABND) Longitudinal	87. Has {S} done or said anything that suggests {S} thinks {S's} spouse or caregiver is plotting to abandon {S}? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** If 1-8, continue with next item #87a (ABNDB). If 0 or 9, skip to #88 (IMP) **Note:** If '8' was circled, please also complete #87b (ABNDC) and #87c (ABNDC).
AbandonmentB (ABNDB) Longitudinal	87a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 N/A
AbandonmentC (ABNDC) Longitudinal	87b. In the month when this symptom was most persistent, how often has {S}done or said anything that suggests {S} thinks {Ss} spouse or caregiver is plotting to abandon {S}? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #87. Abandonment(ABND) was '8'.
AbandonmentD (ABNDD) Longitudinal	87c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #87. Abandonment(ABND) was '8'.
Imposter (IMP) Longitudinal	88. Has {S} done or said anything that suggests {S} thinks {S's} spouse or caregiver is an imposter? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** if 1-8, continue with next item #88a (IMPB). If 0 or 9, skip to #89 (TVR) . **Note:** If '8' was circled, please also complete #88b. (IMPC) and #88c (IMPD).
ImposterB (IMPB) Longitudinal	88a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 N/A
ImposterC (IMPC) Longitudinal	88b. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests {S} thinks {S's} spouse or caregiver is an imposter? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #88. Imposter (IMP) was '8'.
ImposterD (IMPD) Longitudinal	88c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #88. Imposter (IMP) was '8'.
TelevisionIsReal (TVR) Longitudinal	89. Has {S} done or said anything that suggests {S} thinks that characters on television are real? (For example, has {S} talked to them, acted as if they could hear or see {S}, or said that they were friends or neighbors?) 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month)

	4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** if 1-8, continue with next item (#89a. TVRB if 0 or 9, skip to #90 OPI) . **Note:** If '8' was circled, please also complete #89b. TVRC and #89c. TVRD.
TelevisionIsRealB (TVRB) **Longitudinal**	89a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 NA
TelevisionIsRealC (TVRC) **Longitudinal**	89b. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests {S} thinks that characters on television are real? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #89. TVR was '8'.
TelevisionIsRealD (TVRD) **Longitudinal**	89c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #89. TVR was '8'.
OtherPeopleInHouse (OPIH) **Longitudinal**	90. Has {S} done or said anything that suggests {S} believes that there are people in or around the house beyond those who are actually there? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** if 1-8, continue with next item #90a. OPIHB. If 0 or 9, skip to #91 DPSA . **Note:** If '8' was circled, please also complete #90b. OPIHC and #90c. OPIHD.
OtherPeopleInHouseB (OPIHB) **Longitudinal**	90a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 NA
OtherPeopleInHouseC (OPIHC) **Longitudinal**	90b. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests {S} believes that there are people in or around the house beyond those who are actually there? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #90. OtherPeopleInHouse (OPIH) was '8'.
OtherPeopleInHouseD (OPIHD) **Longitudinal**	90c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #90. OtherPeopleInHouse (OPIH) was '8'.
DeadPersonStillAlive (DPSA) **Longitudinal**	91. Has {S} done or said anything that suggests {S} believes that a dead person is still alive, even though {S} used to know they were dead? *Do not rate memory problems. If {S} simply cannot remember whether a particular person has died, it should not be rated as a mistaken belief.* 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month)

	4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** if 1-8, continue with next item (#91a. DeadPersonStillAliveB (DPSAB). If 0 or 9, skip to #92 HouseNotHome (HNH)) . **Note:** If '8' was circled, please also complete #91b. DPSAC and #91c. DPSAD.
DeadPersonStillAliveB (DPSAB) Longitudinal	91a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 NA
DeadPersonStillAliveC (DPSAC) Longitudinal	91b. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests a dead person is still alive even though {S} used to know they were dead? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #91. DeadPersonStillAlive (DPSA) was '8'.
DeadPersonStillAliveD (DPSAD) Longitudinal	91c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #91. DeadPersonStillAlive (DPSA) was '8'.
HouseNotHome (HNH) Longitudinal	92. Has {S} done or said anything that suggests {S} thinks where {S} lives is not really {S's} home, even though {S} used to consider it home? 0 Has not occurred since illness began 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 8 Occurred since illness began, but not in past month 9 Unable to rate ***SKIP:*** if 1-8, continue with next item #87a. HouseNotHomeB (HNHB). If 0 or 9, skip to #93 INTQUAL . **Note:** If '8' was circled, please also complete #92b.HNHC and #92c. HNHD.
HouseNotHomeB (HNHB) Longitudinal	92a. If you try to correct {S}, will {S} accept the truth? 0 No 1 Yes 9 NA

HouseNotHomeC (HNHC) Longitudinal	92b. In the month when this symptom was most persistent, how often has {S} done or said anything that suggests {S} thinks where {S}lives is not really {S's}home, even though {S} used to consider it home? 1 1-2 days in past month 2 3-8 days in past month (up to twice per week) 3 9-15 days in past month (up to half the days in past month) 4 16 days or more in past month 9 Unable to rate **Note:** To be completed if the answer to #92. HouseNotHome (HNH) was '8'.
HouseNotHomeD (HNHD) Longitudinal	92c. Was this symptom ever a focus of medication treatment? 0 No 1 Yes 9 Unknown **Note:** To be completed if the answer to #92. HouseNotHome (HNH) was '8'.
INTQUAL Longitudinal	93. Quality of interview (Rater's judgment) *Rater should record the basis for judging the interview of questionable or doubtful validity.* 0 Interview appeared valid. 1 Some question about interview, but interview is probably acceptable. 2 Information from interview is of doubtful validity.
MEDS Longitudinal	94. Please list medications subject is currently taking:

10.2 Appendix B: Dementia Questionnaire

Memory:

Does the subject have any problems with:	Yes	No	Don't know	Date
1. Memory				
2. Remembering people's names				
3. Recognizing familiar faces				
4. Finding way about indoors				
5. Finding way on familiar streets				
6. Remembering a short list of items				
7. Did trouble with memory begin:				
Suddenly_____ or slowly _____				
8. Has the course of memory problems been :				
a steady downhill progression _____				
or have there been abrupt declines _____				
9. Ever see a doctor for memory problems				
10. If yes, what was the cause given:				

Expression

11. Ever have trouble finding the right word or expressing self				
12. Talking less over time				
13. Tendency to dwell in the past				

Daily Functioning

14. Trouble with household tasks				
15. Handling money				
16. Grasping situations or explanations				
17. Difficulty at work (Check if N/A) _____				
Age Retired_____ Date Retired _____				
Date significant change in work status _____				
18. Trouble dressing or caring for self				
19. Trouble feeding self				
20. Controlling bladder and bowels				
21. Agitation and nervousness				

Other Problems

22. High blood pressure				
23. Stroke				
24. More that one (1) stroke				
25. Is one side of the body weaker than the other				
26. Parkinson's Disease (tremors, shuffling gait, rigidity of limbs)				
27. Injury to head resulting in loss of consciousness for more than a second or two				
28. Seizure or fits				
29. Syphilis				
30. Diabetes				
31. Drinking problem (If alcoholism suspected, explore further SADS Sxs)				
32. Did memory problems coincide with drinking				
33. Ever depressed or sad for 2 weeks or more				
34. If yes, ever seek treatment				
35. Ever very high, euphoric, top of the world				
36. If yes, ever seek treatment				

37. Ever seek psychiatric or psychological help for any reason _____ _____ _____ _____

38. If yes, ever hospitalized for psychiatric illness _____ _____ _____ _____

Where? _____

39. Down's Syndrome _____ _____ _____ _____

40. Other medical problems we have not talked about _____

Medical Contacts

41. Name and address of first doctor seen for problems:

_____

_____

_____

42. Ever receive medications
43. A neurological or psychiatric examination
44. CAT scan of head
45. Ever in an institution (Nursing home)
Where? _____
46. What was diagnosis given for problems _____

Recognition of Problem

47. Who was first person to notice something wrong?_____

48. What was noticed? _____
49. When was the last time (the subject) seemed to be really well or his/her olf self? _____

10.3 Appendix C: Sample Consent form

Site Name

Consent to Participate in A Research Study

(Study Participant)

Research studies only include people who choose to be involved in the study. Please read this consent form carefully and take your time making your decision. This consent form may contain words that are hard to understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand.

Study title: Late Onset Alzheimer's Disease Study - LOAD study

IRB study number:

Contact information: _____, Principal Investigator

_____Address

_____ (name/phone #), Site coordinator 1

_____ (name/phone #), Site coordinator 2 (if needed)

Study Purpose

You are invited to participate in a research study funded by the National Institutes of Health (NIH). The purpose of this study is to identify risk factors, which might be associated with the development of diseases of the nervous system associated with late-onset Alzheimer's disease (AD) (late onset is defined as symptoms of AD beginning at age 60 or older), aging and other related disorders. Other related disorders may include early-onset Alzheimer's disease, frontotemporal degeneration (FTD), lewy body dementia, corticobasal degeneration and progressive supranuclear palsy. **[SITE PI]** and his associates hope to learn about factors that might increase the risk of developing late-onset Alzheimer's disease or other related disorders and study genes that are associated with late-onset Alzheimer's disease, aging and other related disorders in extended families or in the general population.

Should you choose to participate in this study, you will be asked to provide a biological sample, medical records, and family history information. You may also receive a clinical examination by a neurologist and complete neuropsychological testing to fully evaluate your memory and thinking skills.

This research study examines the genetic code to help understand why some people develop Alzheimer's disease or other related disorders and others do not. The cells of your body contain the genetic code or DNA. DNA is passed down from your parents, in the form of genes, which determines your physical characteristics, such as the color of your hair and eyes; and risk for some diseases. Just as differences in our genetic code help explain why we all look different, these differences can also help to explain why some people develop certain diseases and others do not.

Our study seeks to identify, evaluate, and follow individuals with AD and individuals without AD. Specifically, we are seeking families who have at least 2 members with late onset (signs and symptoms of dementia started at 60 years of age or older) AD who have been diagnosed by a neurologist, gerontologist or other specialist in the diseases of the elderly. In addition, we are seeking healthy, unrelated individuals over the age of 60 who do not have a family history of AD. Information gathered from the individuals and families that participate in this research study will be used by researchers to identify genetic factors that contribute to this disease. Families will be seen at various sites throughout the United States.

Alternative to study participation

This is not a treatment study. Information being collected is for research purposes only and will not provide information that will be medically useful for you. The alternative to participating would be simply not to participate.

Study Procedures

If you decide to participate, you may receive a neurological examination from a physician and you may also be asked to take a pencil and paper test, to assess memory and other cognitive functions including reasoning, attention and language (neuropsychological testing). Additionally, you will be asked to complete an interview of risk factors and family history. This interview may take 30-40 minutes and consists of questions regarding habits and behavior such as smoking, alcohol intake, physical activities and your past medical history. We will ask you about the state of health of many of your close relatives (mother, father, brother, sister and children). We will ask you about a number of conditions in those individuals such as whether or not they had Alzheimer's disease or other related disorders. Since we wish to study the relationship between heart disease and these neurological disorders, we will ask you about previous heart attacks and related disorders. You may also be asked to provide medical records. You will be also asked to give a blood sample (3 tablespoons)**.**

The complete evaluation including the neurological examination, memory testing (neuropsychological testing), family history and risk factor interview and blood draw, should take approximately 2-3 hours to complete.

You may be invited to participate in this study on a yearly basis, during which you may be asked to complete all or some of the interview, clinical exam or memory testing. This is done in order to detect any change in the individual's cognitive status. In addition, you may be asked to give another blood sample. If you are asked to give another blood sample, the appropriate consent will be obtained from you. The total amount of time required for each yearly visit will be approximately two to three hours.

Your blood samples will be sent to the National Centralized Repository for Alzheimer's Disease and Related Dementias (NCRAD) at Indiana University and will be stored indefinitely. Your blood will be used to examine some of your genetic material (DNA), extract white blood cells, and grow cell lines that will be invaluable to researchers who are interested in studying AD and other diseases. We will also freeze these cells in a special way so that we can re-examine other genes that may cause or increase the risk of AD or other related disorders later. Your biological sample may undergo genetic analysis and genomic sequencing which involves determining the arrangement and sequence of all the genes in your DNA. As this is done for research purposes, you will not be given the results of this genetic analysis.

A unique subject identifier will be used to link your blood sample and clinical information. Only de-identified (coded) data will be kept on a secure computer at the data-coordinating center at Columbia University and the biological specimen repository at NCRAD. These data can be accessed only by authorized investigators. De-identified (all identifying information has been removed) clinical, biological sample and genetic data may be provided to qualified researchers at academic institutions, hospitals, and biotechnology/pharmaceutical companies. Results of analyses performed using the biological samples collected as part of this study may be submitted, along with de-identified clinical data, to a government health research database that will assist other researchers investigating various diseases, including AD and dementia. This government health research database will have access limited to approved researchers. Your data may be withdrawn at any time, upon your request. However, data that has already been distributed for approved research will not be retrieved.

Taking part in this study is voluntary. You may choose to take part or may refuse to participate in the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are otherwise entitled. You will continue to have access to health care at **[SITE NAME]** Medical Center. If you do withdraw from the study, then you may request that your demographic and clinical data and any unused samples be destroyed. However, data and samples that have already been distributed to approved researchers will not be retrieved. If you do decide to withdraw, we ask that you contact **[SITE PI NAME]** in writing to let him know that you are withdrawing from the study.

Voluntary Autopsy Program and Specimen

The only means to definitively diagnose AD is through examination of the brain at the time of death (termed autopsy). For this reason, many families choose to have an autopsy performed when a family member with Alzheimer's disease or memory loss dies. In addition, autopsy can also be informative when completed for individuals without memory loss. If you are interested in learning more about autopsy, our study staff will provide additional information and can also assist in autopsy planning. If you choose to plan an autopsy for yourself or a family member, you will be asked to sign a separate

consent form. The Late Onset Alzheimer Disease study will pay for costs associated with an autopsy. An autopsy report will be provided to the subject's legal next-of-kin, guardian or representative.

Some families will meet criteria for this study due to the availability of an autopsy specimen from a family member. If we find that this autopsy sample has been stored under conditions that will allow it to still be used for genetic research, we may request that you sign a separate consent form allowing us to obtain a piece of the autopsy specimen. Just like a blood sample, DNA can be extracted from an autopsy specimen that has been stored under the proper conditions. A cell line cannot be grown from an autopsy specimen. The autopsy specimen will be assigned a unique subject identifier and will never be identified using the name of the individual.

Study Risks

A possible risk from your participation in the Late Onset Alzheimer Disease study involves loss of privacy as a result of providing biological samples for research. Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, other blood relatives, and other members of your ethnic group. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them. While information traditionally used to identify you will not be released (i.e. name, date of birth, address, telephone number), people may develop ways in the future that would allow someone to link your genetic or medical information back to you.

Similarly, when information about you and your family are sent to the National Centralized Repository for Alzheimer's Disease and Related Dementias and Columbia University, a unique subject identifier is assigned to this information. A unique subject identifier is a combination of numbers and/or letters that do not correspond to any information you have provided to us (i.e. birth date, age, name) and which is different for each person who participates in this study. The National Centralized Repository for Alzheimer's Disease and Related Dementias and Columbia University use a secure computer system. There is a slight risk that there could be a breach of the security of these computer systems resulting in the access of information about family or medical history. Safeguards are in place to minimize this risk.

Some de-identified data may be provided to a government health research database for broad sharing to approved investigators. This information will be de-identified and will not contain any traditional identifiers (i.e. name, date of birth, address, telephone number). There is a slight risk that there could be a breach in the security of this database system resulting in the access of information. Safeguards are in place to minimize this risk.

Your participation in this study might be associated with slight pain due to the blood test. For most people, drawing blood does not cause any serious problems. However, there is a risk of bruising, discomfort, dizziness, infection, and pain at the needle site. To reduce any risk, we will take every precaution using skilled individuals to obtain blood from you. If there is any difficulty in obtaining the blood or if there is some medical reason you cannot allow us to perform the blood draw, we will omit this part of the study.

You may also be slightly embarrassed, tired, or anxious about the memory testing or answering questions about your habits such as smoking and alcohol use, but we assure you that you can choose not to answer a specific question or we can stop at any time. There may be other privacy risks that we have not foreseen.

Study Benefits

You are not expected to benefit personally from this study. However, the greatest benefit will be to society where you will assist us in identifying important risk factors for the cause of diseases of the nervous system in the elderly.

If you have concerns about memory problems or other health related questions, the research team will refer you to appropriate medical resources (i.e. your primary care physician, a memory disorders specialist).

Costs/Compensation

There will be no costs to you for participating in this study**. [Insert language regarding payment if applicable]** Samples and data sent to the National Centralized Repository for Alzheimer's Disease and Related Dementias may be shared with companies and there is the possibility that the research done may be used to develop new products. You will receive no financial compensation for the development of new products that result from the use of your biological sample (blood, cell line, autopsy tissue), clinical and demographic data, and/or genetic data.

In the event of physical injury resulting from your participation in this research, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

Confidentiality

Confidentiality is a central concern of this study of Alzheimer's disease and other related disorders. Every possible effort will be made to maintain the research information in the strictest confidence. We cannot absolutely guarantee that disclosure might not occur unintentionally. We remind all persons participating in this research that maintaining complete confidentiality is a responsibility of both the investigator and his/her staff (US), and the participant (YOU). If you are concerned about these issues, you should consider them carefully before telling anyone that you are participating in a genetic study of Alzheimer's disease.

Any information and blood samples obtained during this study and identified with you will remain confidential. To protect your identity, we have assigned you a unique code number. This means that we will not send the participant's name, address, phone number or other identifying information to Columbia University or the National Centralized Repository for Alzheimer's Disease and Related Dementias. Coded data linked to the sample will be kept on a secure computer that can only be accessed by authorized individuals. Research records are maintained in locked paper files and secured computer files, available only to research staff and institutional personnel as part of routine audits.

In addition to the confidentiality protections described in this consent form, a Federal law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. **[Sites insert their own GINA language here]** GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance or by adoption agencies. GINA also does not protect you against discrimination based on an already diagnosed genetic condition or disease. If you would like to know more about it you can discuss this with the principal investigator of this study or you can go to the following website www.genome.gov/10002328.

The researchers for this study have obtained a Certificate of Confidentiality issued by the Department of Health and Human Services (DHHS) that will help them protect your privacy during this study. With this certificate, the research staff cannot be forced (for example by court subpoena) to disclose research information that may identify you as a research participant, without your written consent. However, if the researchers learn that you are in real danger of physical or serious mental harm (example, suspected or known sexual or physical abuse of a child or threatened violence to self or others) they will release study related information to protect you and the other persons. Such information must be reported to the appropriate authorities. You should also understand that this Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about you or your participation in this research. If an insurance company asks you to release information and you choose to do so, the Certificate of Confidentiality will not protect your privacy. The **[SITE NAME]** Human Research Protection Office and the Office of Human Research Protection (OHRP) are entities that may have access to the data collected as part of this research.

Research Standards and Rights of Participants

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. You can contact **[STUDY COORDINATOR NAME & PHONE #]** to stop participating. If you agree to be in this study, you are free to change your mind. Participants will be

notified of significant new findings that may relate to their willingness to continue to participate. Signing this form does not waive any of your legal rights.

Questions

You can reach the investigator, **[SITE PI, PHONE NUMBER]**. He will answer to the best of his ability any questions that the participant may have now or in the future about the research procedures, or about the subject's response to the procedures.

If you have any questions about your rights as a research subject, you should contact the Institutional Review Board by phone at **[SITE IRB Phone #]** or by email at **[SITE IRB EMAIL]**
More information about taking part in a research study can be found on the IRB website at **[SITE IRB'S WEBSITE]**

Taking part in this research study may result in injury or harm to you. In the event of an injury resulting from your participation in this study, you should seek appropriate medical care and inform the study doctor. In the event of an emergency you should go to an emergency room.

If you are injured or harmed as a result of participating in the study and receive medical care through the **[SITE]**, or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance.

Consent by participant: I have had the opportunity to review the information and ask questions regarding this consent form. I voluntarily consent to participate in this research study. I may drop out of or be withdrawn from this study at any time without fear of changing the investigator's interest or the quality of medical care that I may seek or receive in the future from the doctor's participating in this study. I have received (or will receive) a copy of this form for my records and future reference. In consideration of all of the above, I give my consent to participate in a Study Visit.

_____

Signature of participant *Date*

_____

Name of participant (printed)

I have discussed the proposed research with this participant, and, in my opinion, this participant understands the benefits, risks and alternatives (including non-participation) and is capable of freely consenting to participate in research.

_____

Signature of person obtaining consent *Printed name* *Date*

Documentation of Assent

To be completed by research staff if participant is not able to provide consent and consent provided by surrogate.

Assent by participant:

I voluntarily agree to participate in the research study described above.

I understand that _____ will provide consent for my research participation.

(name of surrogate)

_____

Signature of participant *Date*

_____

Printed name of participant

Consent by surrogate: I was present when the proposed research study was described to the above patient and in my opinion, she or he agrees to participate, or does not object to participation.

_____

Signature of Surrogate *Date*

_____

Name of Surrogate (printed) *Relationship to participant*

I have discussed the proposed research with this participant and the participant's surrogate, and, in my opinion, the surrogate understands the benefits, risks and alternatives (including non-participation) for this participant.

_____

Signature of person obtaining consent *Printed name* *Date*

Assessment of capacity by research staff

I assessed _____ (Name of subject) on _____(Date), for the purpose of determining whether he/she is capable of understanding the purpose, nature, risks, benefits and alternatives (including non-participation) of the research, making a decisions about participation, and understanding that the decision about participation in the research will involve no penalty or loss of benefits to which the patient is otherwise entitled, for [SITE PI] research project of Late onset Alzheimer's disease and related disorders. On the basis of this assessment I have arrived at the conclusion that:

___ A. This patient has this capacity at this time.

___ B. There is a question about this patient's capacity at this time.

___ C. This patient clearly lacks this capacity.

Print Name _____

Signature _____ Date _____

For telephone assessments and remote annual follow up visits:

Has verbal consent from the participant been obtained?

☐ Yes, participant has consented to the telephone assessment.

☐ No, participant does not wish to continue participation.

Participant's Name (Printed) Date

I have discussed the proposed research with this participant, and, in my opinion, this participant understands the benefits, risks and alternatives (including non-participation) and is capable of freely consenting to participate in research.

10.5 Appendix E: MDS/Queries/Discrepancies Guide

Minimum Data Set Query Guide

There are many queries in place to insure the validity of data sets submitted by all participating centers. Quarterly, reports will be generated from these queries and distributed to the appropriate centers by NCRAD or Columbia.

All data errors or missing entries MUST BE CORRECTED before the next data submission. It is imperative that data is valid at the source, as this data overwrites the information housed at Columbia each time it is imported.

Columbia will pool all reports together when notifying centers in hopes that this will be more

Required Variables

The following variables are required in order for the data to import. Please complete these variables before first data submission.

ADCID ---------- Center ID

FAMID ---------- Family ID
INDID ---------- Individual ID
FATHID---------- Father ID
MOTHID--------- Mother ID
CONTROL------ Is the subject a control?
PROBAND ----- Is the subject the proband?
SEX---------- Subject's gender
SAMPLED------ Is the subject sampled or will be sampled?
VISIT ---------- What is the visit number?

Reporting Queries- Dataclean file 1

File I (name of site_dataclean file_month_year) contains the following variables. These data errors need to corrected and updated in the center's database/file before the next datacall; the file *does not* have to be sent back to Columbia. A detailed explanation of each query can be found below.

1. Qualifying families (lists all families that meet qualifying family criteria-nothing needs to be done excepted checked over to be sure you agree with total list)
2. Nearly Qualifying families
3. Dead end families (lists all families that have been noted to be dead end-nothing needs to be done except checked over to be sure you agree with total list)
4. Qualifying families-Non Qualifying (summarizes families not meeting the qualifying family criteria and shows key variables that can indicate why the family does not qualify)
5. Overwrite, but no Long data
6. Long data, but no Overwrite
7. Samples without data
8. Samples without data-Controls
9. Autopsy, only 1 visit
10. All autopsy info null
11. All autopsy info 9
12. All autopsy info, no sample
13. Sampled=Yes, no sample at NCRAD
14. Sampled=No, sample at NCRAD

1. Qualifying Families

This program screens for families with at least **three sampled** individuals that meet the following conditions:

1. At least 1 individual diagnosed with Definite (Def) and/or Probable AD (PRAD) with AAO of 60 or older.
2. At least 1 individual diagnosed with Def, PRAD, Possible AD with AAO of 60 or older.
3. At least 1 individual diagnosed with Def, PRAD, Possible AD with AAO of 50 or older; OR at least 1 individual diagnosed with MCI or normal that is 60 or older.
4. The two affected, sampled individuals must be full-siblings.

The logic/fields we consider in the query that checks for qualifying families are:

1. Moth and Fath ID to be sure there are at least 2 full sibs
2. AgeDem OR AgeDxDem >=60 AND diagnosis of confirmed or probable AD (DemDx=1 or 2) in the first full sib
3. AgeDem OR AgeDxDem >=60 AND diagnosis of confirmed, probable, possible AD (DemDx=1 or 2 or 3) in the second full sib
4. AgeDem OR AgeDxDem >=50 AND diagnosis of confirmed, probable or possible AD (DemDx=1 or 2 or 3) in the 3rd family member OR is Not demented (Clindem=2) and over age 60.

2.Nearly Qualifying Families

We now have a spreadsheet that searches all data sets for families that almost meet the minimum LOAD criteria. This program screens for families with at least **two sampled** individuals that meet the following conditions:

1. At least 1 individual diagnosed with Definite (Def) and/or Probable AD (PRAD) with AAO of 60 or older.
2. At least 1 individual diagnosed with Def, PRAD, or Possible AD with AAO of 60 or older.
3. The two affected, sampled individuals must be full-siblings.

**this query NO LONGER CONTAINS families that meet the "Qualifying Family" criteria.

3. Dead End Families

We now have a spreadsheet that searches all data sets for families that have been deemed to be dead end by the site. This means that this family will never make "Qualifying Family" status.

4. Qualifying_Fams-NonQualifying

This query lists individuals in families not meeting the qualifying family criteria and shows key variables that can indicate why the family does not qualify.

5. Overwrite, No Long
Overwrite data has been submitted but no longitudinal data. All individuals need to have a record in both datasets. If the individual will never be seen, please use a visit=98. Please check that there are no typos in ADCID, FAMID or INDID fields.

6. Long, No Over
Longitudinal data has been submitted but no corresponding overwrite data. Please check that there are no typos in site, fam or ind fields.

7. Samples without Data
Compares samples submitted by ADCs to data sets submitted for all subjects. All samples submitted by an ADC should also have a corresponding data set. Records will appear when data is not submitted for a particular sampled individual.

Queries Important for Autopsy Data

8. Autopsy only 1 visit
Individuals will be listed if EvalMeth is autopsy on visit 1. There should be medical records available to indicate status prior to autopsy. It is important to document the clinical vs. pathological diagnoses.

9. All Autopsy Info is Null
Individual is listed as "yes" for autopsy but all of the autopsy variables are null. This report serves as a reminder of autopsy data that needs to be submitted. Please fill in as soon as possible. We realize that there is often a significant lag between the time of death and the time the autopsy report is available.

10. All Autopsy Info is 9
Individual is listed as "yes" for autopsy but all of the autopsy variables are 9. Please fill in as much data as possible.

11. All Autopsy info, No Sample
Individuals will be listed if autopsy is "yes" but there is no sample available at NCRAD. Please try to obtain brain tissue if possible.

12.Sampled = Yes, No Sample at NCRAD
Compares information from the data set to sample information at NCRAD. Indicates individuals coded as sampled (SAMPLED = 1), with no corresponding sample in the repository. Many of you will code an individual as sampled before you send the sample in to NCRAD. This is fine, however be sure to update the record to SAMPLED = 2 if you are not able to obtain a sample. This information needs to be accurate in the data set.

13.Sampled = No, Sample at NCRAD
Compares information from the data set to sample information at NCRAD. Indicates individuals coded as not sampled (SAMPLED = 2), who do have a sample present in the repository. Results of this query need to be updated and changed to SAMPLED = 1.

Cleaning Queries- Dataclean file 2

File II contains data errors that need to be corrected and sent back to Columbia ASAP. The following variables should be included in **File II (name of site_dataclean File II_month_year)**. A detailed explanation of each query can be found below.

1. Required for sampled
2. Required for sampled-controls
3. Autopsy Status
4. ClinDem and AgeDem
5. ClinDem and NotDemCi
6. Deceased, no AgeDeath
7. DemDx and ClinDem
8. DemDx and NonADDem
9. Sampled=1, Visit=98
10. Visit=98 with other visits
11. AgeDeath >100
12. AgeDeath<20
13. Birth Yr vs. AgeDeath
14. AgeDem or AgeDxDem <50
15. AgeDem or AgeDxDem = 99
16. AgeDxDem or AgeDem vs. YOB
17. AgeDem>AgeDxDem
18. Alive but has AgeDeath
19. Child vs. Parent YOB
20. No Proband in Family
21. More Than One Proband
22. Proband Not Affected
23. Sex and YOB don't match sample
24. Sampled under 20
25. Control is 1, sample not control
26. Control is 2, control sample
27. AgeDxDem Clean
28. CDR Clean
29. Educ clean
30. Co-morbidity Age
31. CogDateIntCheck
32. CogVersion
33. LC02 Update
34. CStatusNull
35. NPIQ
36. Fath ID= Moth ID
37. Ind ID= Mother or Fath ID
38. Missing one parent ID
39. Missing all data

1. Required for Sampled Variables

The following variables are required if the individual is sampled. In most cases, missing/unknown values will not be accepted.

COMREQ ------- Does subject consent to for-profit organizations (pharmaceutical and biotechnology companies) having access to his/her clinical data and DNA? Record will be listed if 9 or null.

GENRSCH----Does subject consent to researchers studying the genetics of any human disease having

access to his/her clinical data and DNA? Record will be listed if 9 or null.
BIRTHYR ------- Subject's year of birth. Record will be listed if 9999 or null.
VITALST -------- Subject's last known vital status. Record will be listed if 9 or null.
AGEDEATH ---- At what age did subject die?
RACE ---------- Subject's race/ethnic group Record will be listed if 99 or null.
HISPANIC ------ Is the subject Spanish/Hispanic/Latino? Record will be listed if 9 or null.
VISIT----------What is the visit number? Null is not accepted. Data will not be imported if null.
EVALMETH ---- How was the disease status assigned? Record will be listed if 9 or null.
EVALYR -------- When was the last assessment by examination, medical record review, telephone interview, or family report? Record will be listed if 9999 or null.
EVALTEST ----- Was cognitive testing administered to the subject? Record will be listed if 9 or null.
NEUROIM ------ Has brain imaging been performed? Record will be listed if 9 or null.
CLINDEM------- Is the subject demented? Record will be listed if 9 or null.

2. Required for Sampled Controls Variables

The following variables are required if the individual is sampled control. Columbia will run queries periodically to determine if these variables contain valid information. In most cases, missing/unknown values will not be accepted.
RELDEM ---- How many first degree relatives (parents, siblings or children of subject) were reported to have had dementia (by symptoms, history, or diagnosis)? Record will be listed if anything other than 0 for control.
BIRTHYR --- Subject's year of birth. Record will be listed if subject's age <60 for a control.
EVALTEST -- Was cognitive testing administered to the subject? Record will be listed if anything but "yes" for a control.
PDNoDem -- Does the subject have a history of Parkinson's disease? Record will be listed if anything but "no" for a control.
DEPR ------ Does the subject have a history of *major* depression? Record will be listed if anything but "no" for a control.
STROKE----Does the subject have a history of stroke? Record will be listed if anything but "no" for a control. **Will not disqualify control. Included to be sure that subject really had a stroke and not a TIA. Stroke is not desirable in a control.
HEADINJ---Does the subject have a history of head injury? Record will be listed if anything but "no" for a control. **Will not disqualify control. Head injury is not desirable in a control.
CLINDEM --- s the subject demented? Record will appear if anything but "no" listed for a control at visit=1.
NOTDEMCI-If the subject does not meet the criteria for dementia, what is the diagnosis? Record will be listed if anything but "not demented, no neurological disorder."is listed for a control.

Conditional Requirements

Certain variables in the data set are required pending the entry of a specific value in another variable. Columbia will run the following queries to look for these conditional requirements. Missing or unknown (999) variables will not be accepted, and these requirements only apply to **sampled** subjects.

3. Autopsy Status ----------alue in AUTOPSY required if subject is deceased, VITALST = 2
4. ClinDem and AgeDem ----------alue in AGEDEM required if subject is demented, CLINDEM = 1
5. ClinDem and NotDemCi ---------alue in NOTDEMCI required if subject is not demented, CLINDEM = 2
And NOTDEMCI should be Null if CLINDEM=1
6. Deceased, no AgeDeath --------alue in AGEDEATH required if subject is deceased, VITALST = 2
7. DemDx and ClinDem ----------alue in DEMDX required if subject is demented, CLINDEM = 1
8. DemDx and NonADDem ------Value in NONADDEM required if subject has non-AD dementia, DEMDX = 5

Logic Queries

The following queries were designed to find common errors in the data sets. Most of these errors result from data entry mistakes, but need to be corrected for data validity.

9. Sampled=1 Visit=98
Compares visit number to sampled status. Visit 98 should only be used if subject will never ever have a visit or sample. Therefore record will be listed if a sampled individual has a visit number 98. This will be checked before the data is imported into the database!

10. Visit=98 with other Visits
Compares visit numbers. Visit 98 should only be used if a subject will never ever have a visit or sample. Therefore record will be listed if an individual has multiple visit entries, one of which is number 98. This will be checked before the data is imported into the database!

11. AgeDeath > 100
Looks for any individual with an age of death (AGEDEATH) greater than 100 in order to be sure this information is valid. We realize that it will be valid in some cases.

12. AgeDeath < 20
Looks for any individual with an age of death (AGEDEATH) less than 20 in order to be sure this information is valid. We realize that it will be valid in some cases.

13. BirthYr vs AgeDeath
Looks for any individual with an age of death (AGEDEATH) greater than the value produced by this formula, Current Year – Year of Birth = ?.

14. AgeDem or AgeDxDem <50
Indicates subjects with a reported age at onset or age of diagnosis less than 50. Only looks at sampled subjects (Sampled = 1).

15. AgeDem or AgeDxDem =99
Indicates subjects with a reported age at onset or age of diagnosis equal to 99. This may be a valid response but is a very late onset age and is close to the missing/unknown value of 999. This query checks to make sure the age is really 99 and not 999 mistyped.

16. AgeDxDem or AgeDem vs YOB
Compares subject's YOB to age at onset or age of diagnosis.

17. AgeDem > AgeDxDem
Looks for individuals with an age of onset after age of diagnosis.

18. Alive but has AgeDeath
Looks for individuals who are coded as alive (VITALST = 1), but have a value other than 999 listed in the AGEDEATH field. AGEDEATH needs to be corrected, or VITALST updated to deceased.

19. Child vs. Parent YOB
Compares year of birth between parents and child. Will pull the record if the age difference is less than 12 or greater than 60. We realize this may be valid in some cases.

20. No Proband in Family
Checks Proband variable within all non-control families to make sure family contains a proband. Lists all members of the family who are not controls. PROBAND variable needs to be changed to 1 for the individual in the family who is the proband.

21. More Than 1 Proband
Checks families for number of probands and lists all individuals within a family where PROBAND=1. Families must have only one proband.

22. Proband Not Affected
Checks Clindem for all individuals with PROBAND=1. Probands must be affected.

23. Sex and YOB Don't Match Sample
Compares gender and year of birth provided when the sample is sent to NCRAD (listed on sample tubes and LOAD Study Sample Form), to the gender and year of birth listed in the corresponding data set for an individual. Will list the record if either the gender or the year of birth on the sample do not match the gender or year of birth in the data set.

24. Sampled under 20
Compares year of birth to date when sample is drawn (listed on sample tubes and LOAD Study Sample Form). Will list the record if the age of the individual sampled is less than 20 years old.

25. Control=1 not Control Sample
Compares information provided when the sample is sent to NCRAD (listed on sample tubes or LOAD Study Sample Form) to the corresponding data set submitted for an individual. Will list the record if data set submitted indicates sample is a control but control was not noted at time of sample submission.

26. Control=2 Control Sample
Compares information provided when the sample is sent to NCRAD (listed on the sample tubes or LOAD Study Sample Form) to the corresponding data set submitted for an individual. Will list the record if the data set submitted indicates the sample is NOT a control but the sample was noted to be a control at time of sample submission.

27. AgeDxDem Clean
Compares NotDemCi to AgeDxDem. If NotDemCi is anything but 9 or 3 (questionable dementia or cognitive impairment) indicating that the individual is not demented, then there should not be an age of diagnosis. Record will be listed if not demented and age of onset is anything but null or 999.

28. CDR Clean
Looks for individuals with a CDR Score other than null, 0, 0.5, 1, 2 or 3. While other CDR scales are often used, for the LOAD study we want the scale certified by Washington University School of Medicine in St. Louis. CDR Scores of 4 or 5 should be recoded as a 3 for the LOAD MDS.

29. EDUC Clean
Checks for valid years of education. Record will be shown if education years are null, less than or equal to 8 or greater than 20. Data should be categorical if possible. If an attempted level is not completed, enter the number of years completed.

12 = High School/GED
16 = College /Bachelor degree
18 = Master degree
20 = Doctorate
99 = Missing/Unknown

30. Co-morbidity Age
Looks for individuals with an age less than 20 for the co-morbidities such as stroke, hypertension, heart disease, and head injury etc. We realize that these may be valid responses in some cases.

Queries Important for Cognitive Data

31. CogDateIntCheck
Looks at the format of the date. DateInt is required to be in **mm/yyyy** format. It is not possible to query for a particular format, therefore, all individuals with cognitive data are listed. Please check that the date is listed in the correct format.

32. CogVersion
Looks to see if the year of evaluation (EvalYr) is greater than or equal to 2004 that the cognitive battery used is LC01 or LC02.

33. LC02Update
Looks to see if the vegetables field is not null then the cognitive battery version should be LC02.

34. CStatusNull
Looks to see if the status field is null when the cognitive battery was administered.

Queries Important for Behavioral Data

35. NPIQ

Uses the logic in the NPIQ and CBRS to check for errors. Looks for errors in logic or missing data. The "check" fields will indicate which data field having missing or erroneous data. Commonly, errors in logic occur for the questions that merge the NPIQ and CBRS fields (DEL/PARA and HALL/AUDHALL). If the NPIQ rating =1 (yes, occurred in the past month), the CBRS field should never = 8 (occurred since the illness began but not in the past month). Similarly, if the NPIQ rating=2 (no, did not occur in the past month), the CBRS field should never= 1, 2, 3, or 4.

Queries Important for Pedigree Linkage

The following queries were designed to validate information that is critical for pedigree analysis of the data sets. If any of these queries return results, this indicates that the pedigree will not plot accurately based on the minimum data sets for that family.

36.FathID = MothID

Looks for individuals in the data set who have the same ID listed for both MothID and FathID.

37.IndID = MothID or FathID

Looks for individuals in the data set who have the same ID as their mother or father, indicating that they are their own parent.

38. Missing one ParentID

Looks for individuals in the data set who have a MothID or FathID listed, but the other parent ID is 0. Both MothID and FathID must be filled in with an actual ID, or both must be 0 if founder.

39. Missing all Data (formerly Fathers Missing Data & Mothers Missing data)

Finds individuals listed in the data set as a father for another subject, but has no data set submitted for themselves. The following variables will need to be completed to correct this problem.

THESE INDIVIDUALS NEED TO BE ADDED TO THE DATAFILE. THE FOLLOWING VARIABLES MUST BE CODED FOR THE HIGHLIGHTED INDIVIDUALS:
ADCID **FAMID** **INDID** **FATHID** (0 IF THE FATHER IS A FOUNDER) **MOTHID** (0 IF THE MOTHER IS A FOUNDER) **CONTROL** **PROBAND** **SEX** **SAMPLED** **VISIT** (98 IF THE SUBJECT WILL NOT EVER BE SAMPLED/EVALUATED)

*We recommend that you keep a print out of your previous data cleaning queries and changes made. Some instances where incorrect data is not fixable, it will continue to appear on all discrepancy reports. We recommend that you refer to previous print outs so you do not have to look this data up in the chart each time.

**If you have any suggestions for additional queries or logic checks, feel free to email Dolly Reyes-Dumeyer at dr2290@cumc.columbia.edu

10.6 **Appendix F: GUID Demographics Form**

LOAD-FBS Additional Demographics

Please be certain to collect the following demographic information to generate a Global Unique Identifier:

1. Compete legal given (first) name of subject at birth: _____
2. Complete additional (middle) name or names at birth: _____
3. Complete legal family (last) name of subject at birth: _____
4. Suffix: _____
5. Date of Birth: _____
6. Name of city/municipality in which subject was born: _____
7. Country of birth: _____

10.7 Appendix G: NYBB Fresh Tissue shipping instructions

New York Brain Bank @ Columbia University (NYBB)

Alzheimer Disease Research Center - Taub Institute

Babies & Children's Hospital of
New York-Presbyterian
3959 Broadway, BHs - T8
New York, NY 10032

Telephone: (212) 305-2299
Fax: (212)342-0083
E-mail: nybb@columbia.edu
http://nybb.hs.columbia.edu

Pathologist Information

Pathologist: _____ Phone: _____

Institution: _____

Address: _____ Fax: _____

_____

_____ E-mail: _____

Donor Information

Donor's Name: _____

Date of Birth: _____ SSN: _____

Autopsy Number: _____

Cause of Death: _____

Clinical Diagnosis: _____

Time of Death (24h): _____ Date: _____

Time Body Placed into Refrigeration (24h): _____ Date: _____

Time Body Removed from Refrigeration (24h): _____ Date: _____

Specimen Information

Fresh Brain Weight (g): _____

Time Fresh Brain Placed in Chilled Water (24h): _____ Date: _____

Time Brain Fixed/Frozen (24h): _____ Date: _____

C. Keller facit 08/03

Instructions for Shipping Fresh Brains to the NYBB – Taub

These instructions outline the procedures of packing a fresh brain for shipment to the NYBB. Upon request, we provide packing material. For further assistance call 212-305-2299.

1. Recommended items to pack a fresh brain:

<table>
<tr><td>Two clean, dry ziploc plastic bags
(about 22.0 x 30.0 cm)
  </td><td>Plastic bucket with a tightly fitting lid
(about 4.0 liters)
  </td></tr>
<tr><td>Large plastic
bag (about 40.0 x 50.0 cm)</td><td>Envelope for documents</td></tr>
<tr><td>Thermosafe polyfoam container
(about 38.0 x 33.0 x 31.0 cm)
  </td><td>Two refrigerant packs about
(17.0 x 10.0 cm)
  </td></tr>
<tr><td colspan="2">Wet ice (about 1.0 kg)</td></tr>
</table>

2. Packing procedure:

Put the fresh brain in the first ziploc bag (A).  A	Ziploc first bag (B).  B
Place bag (B) in second bag and ziploc it (C).  C	Place 0.5 kg of wet ice into the bucket and transfer the double-bagged brain onto the ice (D).  D
Cover double-bagged brain with wet ice (E) and tightly fit the lid on the bucket.  E	Put big plastic bag into the polyfoam container and place wet ice (about 0.3 kg) into the bag (F).  F
Transfer sealed bucket into plastic bag of the container, onto the ice and add refrigerant packs (G).  G	Close plastic bag (H), put polyfoam lid in place, add documents and close cardboard box.  H
Please provide information pertaining to the donor of the specimen and the time intervals between the steps of obtaining and packing the brain. Please refer to the information sheet, which may be downloaded from our Internet site. (http://www.nybb.hs.columbia.edu)	
We use *"Sterling Courier Systems"* as they are familiar with our operations. For pickup call: **1-888-633-6666** and indicate that you would like to send tissue samples to: **"NYBB - Taub"**.	

10.8 Appendix H: Sample form for frozen and fixed brain tissue

AD FBS Brain Tissue Specimens

Please complete this form when sending brain tissue to NCRAD. The contact information for emailing the form is in the box below. **Please email the form as soon as possible after tissue is extracted**. NCRAD would like to receive this form BEFORE tissue arrives.

To: Kelley Faber **Fax: 317-321-2003** **Email: alzstudy@iu.edu**

Phone: 1-800-526-2839 **Phone: 317-274-7360**

From: _____ Site ID: _____

Phone: _____ Fax: _____

Email: _____ Date: _____

Site ID	Family ID	Individual ID	GUID	Tissue Removal Date	Section of Brain	Gender	Year of Birth	Fixed or Frozen Tissue