NIA grant: Ancillary to HCHS/SOL: MRI Measures of Cerebrovascular Injury and AD Atrophy in a Study of Latinos (RF1 AG054548, C DeCarli & H Gonzalez)

HCHS/SOL

Investigation of Neurocognitive Aging and MRI Study

(SOL-INCA-MRI)

MRI Reading Center Manual of Operations

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Version 3.5, February 14, 2019

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Tracking of Revisions to SOL-INCA-MRI MOP –
Highlighted text is new to this version

[Previous Manual, Date, Version]	New MOP Version	Date(s) of Revisions	Revisions Description	Page #s/Section changed	Distribution Date
v3.3, 01/30/18	v3.4	06/07/2018	Table1, forms added to the table	Page 3	6/8/18
	v3.4	06/07/2018	Flowchart 2, update of proxy flow	Page 4	6/8/18
	v3.4	06/07/2018	Section 4.1- Detail information added	Page 5	6/8/18
	v3.4	06/07/2018	Section 5.1 – Clarification added	Page 6	6/8/18
	v3.4	06/07/2018	Section 5.3- Medical Records information added	Page 6	6/8/18
	v3.4	06/07/2018	Section 8.1- Reference to Implant Exception list Appendix A added.	Page 7, Page 23	6/8/18
	v3.4	06/07/2018	Flowchart 4- Reporting section updated	Page 13	6/8/18
	v3.4	06/07/2018	Section 12 added, Reporting results to participants	Page 14-15	6/8/18
	v3.4	06/07/2018	Section 13 added, Adverse events reporting	Page 15	6/8/18
	v3.4	06/07/2018	Appendix C- Research Capacity Policy minor updates, i.e. subject changed to participant.	Page 26-29	6/8/18
V3.4, 06/07/2018	V3.5	02/14/2019	Section 12, minor changes to incorporate report letter 1.5 information	Page 14	2/18/2019

Last updated 2/18/2019 10:50 AM

1. Introduction

Dear Field Center Investigators:

We are pleased to provide you with the Manual of Procedures for the SOL-INCA-MRI study. This procedure manual will provide all the necessary information for the recruitment, MRI safety prescreening, acquisition and electronic transfer of MRI data for this project. Participating site coordinators and MRI technicians should review the protocol upon receipt and familiarize themselves with the requirements. All questions should be addressed as soon as possible to facilitate a clear understanding of the protocol prior to contact of the first participant.

As a participating site, your main responsibility is to perform MRI safety prescreening and schedule the MRI acquisition. You will also be responsible for consenting each participant at the MRI facility and assuring timely transfer of the MRI data to the MRI Reading Center. It is critical that the integrity of the study is maintained through each study site by adherence to this Manual of Procedures. Every site will be asked to electronically ship digitally archived images (in collaboration with your MRI imaging centers) along with data tracking sheets to the MRI Reading Center at UC Davis as well as retain data locally.

Please note that the MRI sequence protocol used for SOL-INCA-MRI may differ from the routine MRI sequences used for clinical practice at your center. Your site must follow the standardized protocol that we have developed to assure consistency of data collection across the sites. The imaging protocol for this study is designed for research purposes only and cannot substitute for a clinical assessment that may be necessary for the evaluation or management of participants. Therefore, any clinically relevant findings must be pursued using clinically applicable MRI assessment under the guidance of a managing physician.

Feel free to contact me or the SOL-INCA-MRI staff if we can help to assist you in carrying out this protocol. We are always available to answer any questions and to guide you through the entire process. Thank you in advance for your commitment to this study. We look forward to working with you.

Sincerely,

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Victor and Genevieve Orsi Chair in Alzheimer's Research
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2. Overall Study Aims and Processes

The overall goal of SOL-INCA-MRI (HCHS/SOL, Investigation of Neurocognitive Aging with MRI) is to acquire research MRI to understand brain structural differences among the heterogeneous ethnic group of Hispanic-Latinos living in the United States. It will also serve to examine potential differences in brain structure related to the aging and cognitive impairment processes in comparison to numerous similar reports in White Americans. Genetic information will be combined with the MRI data to further enhance discovery of biological pathways related to brain aging and dementia.

This is an ancillary study to the NIH funded Hispanic Community Health Study/Study of Latinos (HCHS/SOL), a population-based study of 16,0000 Hispanics. The SOL-INCA-MRI ancillary study will consist of a subsample of 2800 participants from already enrolled in HCHS/SOL across the four US Field Centers (Bronx, NY; Chicago, IL; San Diego,CA; Miami, FL), utilizing a balance enrollment design to obtain near equal numbers of Hispanic subgroup representation. Participants for this ancillary study will be derived from two participant groupings: a subsample of 400 younger individuals ($\leq$50) participating in HCHS/SOL and a larger sample of 2400 older individuals (>50) participating in SOL-INCA.

The data coordinating center located at the UNC-Chapel Hill, in collaboration with Dr. Hector Gonzalez and Dr. Wassim Tarraf will determine participant selection for this ancillary study. Field Centers will then reach out to selected participants to seek participation to acquire state-of-the-art research MRIs on these individuals and transfer this data to the MRI Reading Center. The primary outcomes of this study will be MRI measures of atrophy patterns associated with age and cognitive impairment as well as the presence and extent of MRI identified vascular brain injury. These primary outcome measures will be further associated with known genetic influences to compare with prior research as well as to use genetic association studies to discover potentially new genetic influences on brain structure and function unique to the Hispanic-Latino population living in the United States.

SOL-INCA-MRI will be the first large epidemiological study to utilize MRI and combine MRI with genetics of Hispanic-Latinos with strong subgroup representation living in the United States. This study will specifically explore the role of increased prevalence of vascular risk factors among Latinos on brain aging and cognitive impairment as well as difference in genetic influences on these processes. As such, this study will likely result in a substantial number of new scientific discoveries related to brain aging and impairment and possibly give evidence for new pathways of dementia prevention.

The MRI reading center at UC Davis, housed in the Imaging of Dementia and Aging (IDeA) and directed by Dr. Charles DeCarli laboratory will serve to accomplish the aims of this study in the following ways:

1. Work collaboratively with the Field Centers, the Coordinating Center and SOL-INCA personnel to implement the protocol for data acquisition, quality control and assurance, analysis and reporting of the MRIs including clinically important information when needed.
2. Develop and implement a standardized MR imaging protocol that will result in the highest degree of consistency across the four field centers.
3. Test implementation of this protocol at each Field Center to assure accuracy of acquisition.
4. Track the receipt, reading, quality assessment and storage of each MRI received by the IDeA laboratory and share this information at monthly teleconferences.
5. Quantify MRIs on an ongoing basis and regularly share this information with the coordinating center.
6. Maintain confidentiality and securing of the data files.
7. Make raw and processed data available to approved scientists for expanded use.

Flowchart 1: *SOL-INCA-MRI Flow Chart*

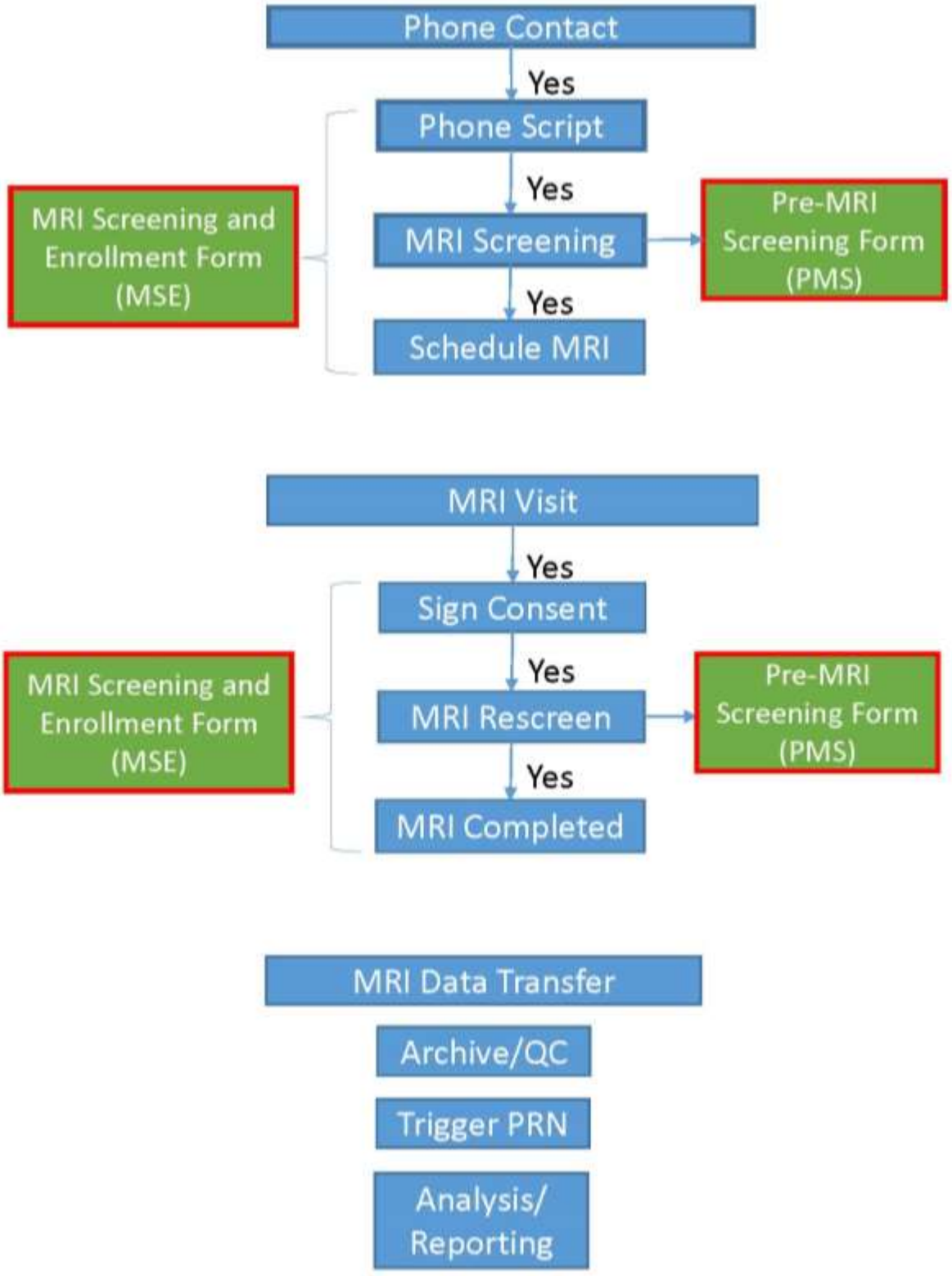


Table 1: *SOL-INCA-MRI-Forms*

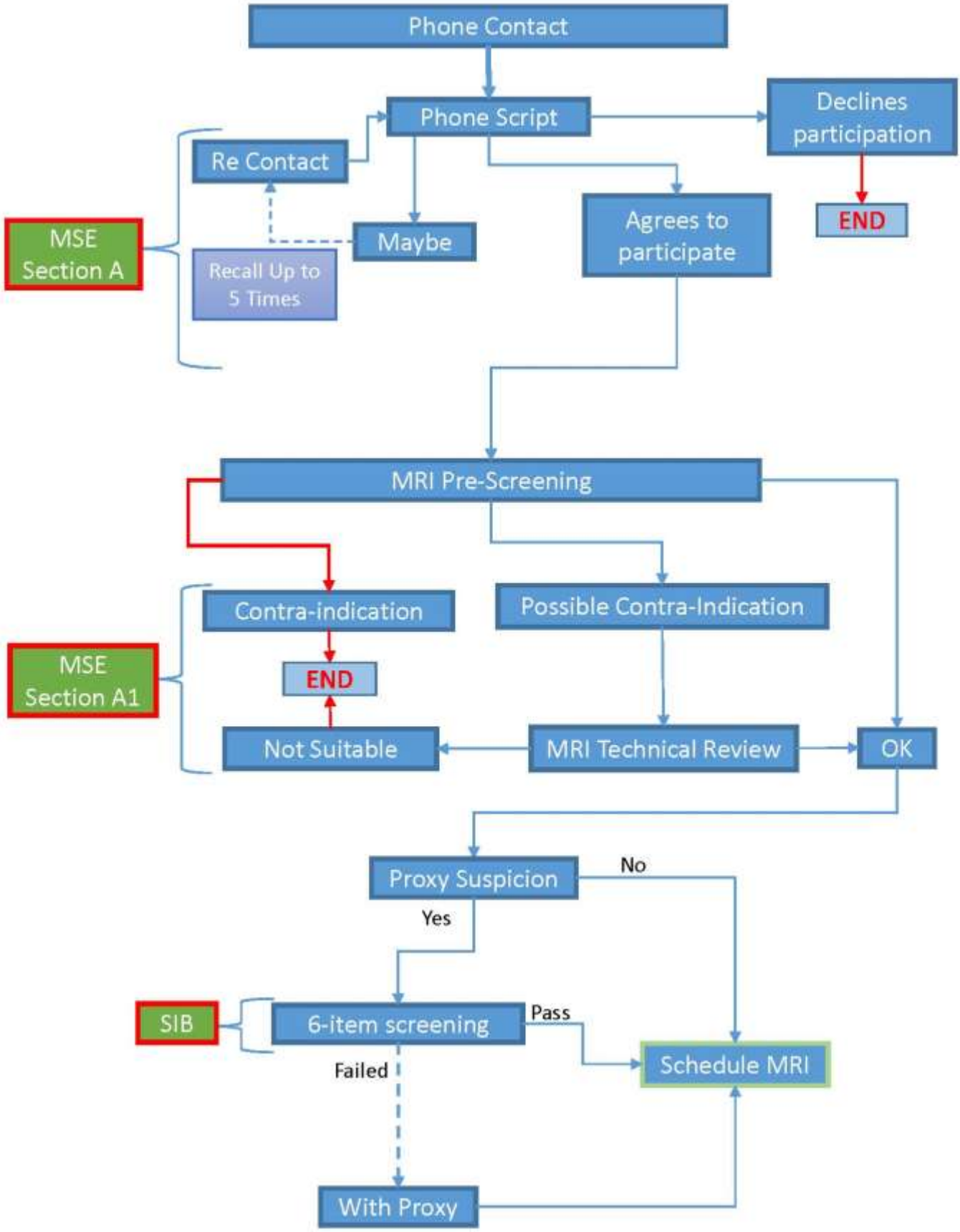
Code or Type	Descripton	VerDate/ Type
Phone Script	Sol-INCA-MRI Phone Script- English/Spanish	2018.01.10
PMS	MRI_Screening form	2017.11.29/ paper
IRI	Implant Required Information	2018.01.19/ paper
Implant	Implant Exception List	2018.03.28 reference
MSE	MSE-SOL INCA MRI Screening-Enrollment-ICT form-2018.01.23	2018.01.23/ CDART
SIB	Cognitive Screener	2015.06.30/ CDART-from parent study
CAC	Capacity Asses Ck Lst.doc (CAR)	2017.11.29/ paper
SSS-Sp	Simplified Study Summary- Spanish	2010.01.10/ paper
SSS-Eng	Simplified Study Summary- English	2010.01.10/ paper

3. MRI Phone Call

Use the phone script (see Appendix A, page 16).

If the person says “maybe” to the offer, ask when is a good time you can call them back and determine a date that would work for the participant. If the person does not give you a time, wait 1 month before calling back. Record offered call back date and time or 1-month date on the **Contact Screening and Enrollment Form (MSE)**. If the person agrees to preliminary participation, move on to the **Pre-MRI screening form (PMS).**

Flowchart 2: *Phone Contact Flow Chart*



4. Pre-MRI Screen

For Pre-MRI screening form questions, please ensure that they are filled out completely and accurately. This will help mitigate any risks to the participant and ensure that scans are not cancelled. If the form is incomplete, it places the MRI technicians in a difficult position because they do not have time to research issues thoroughly if they discovered on the day of a scan. Oversight of such details will likely lead to cancelled scans.

4.1. Pre-MRI Screen Form Questions:

Administrative Information:

Collect date of administration, DOB and Staff ID in the administrative section.

The information for height and weight is participant self-reported. Staff member does not need to take these measurements.

Participants Questions

1) Very important! If they have had an implant, we will need to know the type, facility where it was provided, and the date so that MRI compatibility can be checked.

   Suggested leading question to evaluate the presence of an implant:
   "Do you have anything in your body that you were not born with?"
   ["*¿Tiene usted algún objeto en su cuerpo con el cuál no nació?"]*
   If they answer "yes", the coordinator needs to find out what it is.

2) Not a lot of details necessary, just want to know if they have had an MRI, particularly recently. If participant answered **YES** to question 1, but has had a subsequent MRI, this is extremely helpful.

3) General question to get at metal in the eyes, etc. Re-reviewed in the list.

Female Participants ONLY questions 4-8. Specific to women of childbearing age. Refer to QxQ for additional information.

4) If the participant is pregnant, they not eligible for the study.

5) If the participant is breastfeeding, they are not eligible the study.

6) Date of last menstrual period. If participant does not remember the day/month/year, try to collect at least the approximate month/year.

7) Fertility medication information.

8) Contraceptives question, specific to women of childbearing age, *possibility of pregnancy is exclusionary!*

Please fill out in entirety. Each question must be asked and answered. The pre-MRI-screening will be repeated at the MRI center. This is why it is important to prescreen at time of phone contact to exclude people who would not be able to be imaged. It is important to avoid cancelled scan slots due to incomplete pre-screen at time of phone contact.

If participant has joint replacement, we need to know which joint. Use the body diagram (page 2 of the Pre-MRI-Screening form) to help make this determination. Tattoos are not contraindications, particularly if they are not on the face. However, if you are asked directly, this is what the FDA says: *"There have been reports of people with tattoos or permanent makeup who experienced swelling or burning"*. Reassure the participant that these questions are to let the MRI technician know about anything that could cause problems during MRI and that we will be sure to inform the technician about this.

5. Exclusions:

5.1. Absolute contraindications (exclusions) for MRI include, but not limited to:

1) Pacemaker or implantable defibrillator
2) Aneurysm Clips
3) Metallic Foreign body in the eye
4) “Triggerfish” contact lens
5) Gastric Reflux device
6) Insulin pumps

If the participant has an absolute contraindication to MRI, inform them that they are not qualified for the study and thank them for their time. State that participation in this ancillary study has no effect on participation with HCHS/SOL or other ancillary studies. Reiterate how valuable it is that they continue to participate in HCHS/SOL and the other studies for which they have already enrolled, and **Complete the MSE form**.

If you have any questions or concerns, please contact your MRI technician or feel free to reach out to us at: Oliver Martinez IDeA Laboratory Manager,
omartinez@ucdavis.edu

5.2. Additional information about MRI safety

Food and Drug Administration recommendations. Center for Devices and Radiological Health. MDR data files www.fda.gov/CDRH/mdrfile.html

Institute for Magnetic Resonance Safety, Education, and Research: http://www.MRIsafety.com or http://www.IMRSER.org

5.3. Medical Records

If you cannot obtain medical records for a possible contradiction in a reasonable amount of time (3 months), exclude the participant. Maintain contact with the participant during the course of the study to verify if they have been able to obtain the medical information needed. Maybe the participant can provide records in the future, and participation can be completed.

6. Capacity Concerns

If you believe that the participant may have difficulties with capacity to consent, please follow the procedures defined in HCHS/SOL MOP2 Section 4.5 “Proxy” to screen for proxy need at time of phone call. If a proxy is needed, please be sure to speak to the proxy for scheduling.

The final capacity assessment will be done at time of consent during the MRI visit. See “Assessing Capacity during the consenting process” Section 9.1.1.

7. Helpful Hints to explain MRI study

Participants are generally amenable to MRI, but have common questions, such as:

1) What are the risks? These are listed in the consent, but include the following:
    a. MRI machine acts like a large magnet, it could move iron-containing objects in your body. We will ask you about these. If you have something that prevents MRI, we will not enroll you in the study. If you have something that may not be MRI compatible, we will do research to be sure it is safe. This will take time and we will call you back about the results.
    b. Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study.
    c. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear ear plugs.

2) Will I get the results? Yes, participants may get a report of the imaging if they specifically request one. All MRIs will be reviewed by a specialist and copies can be given to the participant if requested. If there is a medically relevant issue, reassure the participant that we will contact them and share the information with them and any physician they designate. If they don't have a physician, Field Center coordinators will help them find one. UCD will assist if needed. Physicians may request digital copies with the participants permission which the Field Center or UCD will provide.

If the participant agrees to participate, and the Pre-MRI screening form is completed, please share with the MRI technician, and complete the **MRI Screening and Enrollment Form (MSE)**.

8. How to address safety questions

It is best to share these questions with your local MRI facility. There are safety websites that these facilities often use (refer to Section 5) and often they can quickly give you clearance. If clearance cannot be immediately determined, then further information will be required. You will need to find out information about the device as outlined below:

8.1. Determining MRI Safe Implants

1) Participants with any type of implant need operative reports. MRI's should not be scheduled until operative reports have been retrieved and sent to the MRI tech for review. If MRI's are scheduled before the participant's safety is authorized, that scan could be cancelled because they might not able to be authorized at the time of the visit. Refer to Implant Exception list Appendix C.

2) When requesting operative reports, the specifics of the implant must obtained. Complete **MRI Implant Required information form (IRI)** to record:
    a. Location of implant on the body
    b. Date implant was placed
    c. Implant manufacturer
    d. Implant model name/number (e.g. an implant sticker sheet)

3) If the participant does not have an implant, then operative reports aren't required. Dentures, hearing aids, piercings, crowns, etc. are generally ok, but if you are unsure, feel absolutely free to request a report. Better safe than sorry.

8.2. Form Completion

After phone call screening is finalized, make sure to complete all required forms:

- **MSE, Section A**- SOL MRI Screening and Enrollment form, refer to QxQs for details. CDART form.
- **PMS**- Pre-MRI Screening form (paper form only). Make sure you sign the form with your name and designation (most will be “other”, coordinator).
- **SIB**- Six Item Screener when required to assess at time of phone call the need of a proxy. Refer to HCHS/SOL MOP2 Section 4.5 “Proxy” to screen for proxy need. CDART form.
- **IRI**- MRI Implant Required Information form (paper form only) when required.

9. MRI Visit

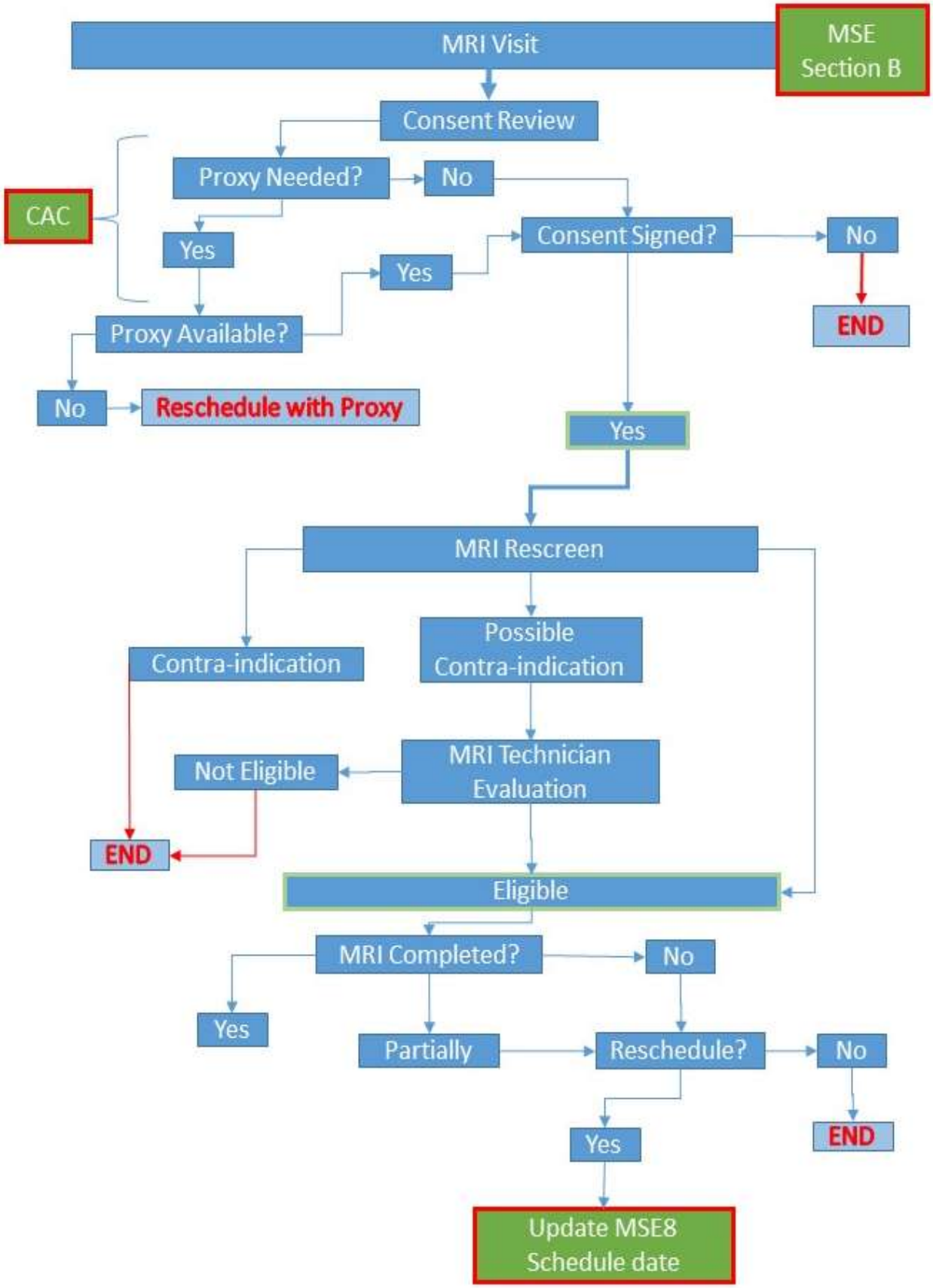
Coordinators and participant must arrive at least 45 minutes before the appointed time.

Coordinators:

Introduce yourself to the participant, stating your role and why you are meeting with the participant:

1) To obtain consent
2) To answer questions
3) To be present for the technician’s MRI safety screen
4) To be available throughout the procedure and afterwards, particularly for Spanish speaking participants
5) To address any last minute questions associated with the procedure

Flowchart 3: *MRI Visit Flow Chart*



9.1. Perform the Consent

Coordinators, please follow the following process while performing the consenting process:

1) State you will review the document that will describe the study in detail
2) Read the first page out loud to the participant, ask the participant if they have any questions
3) At the end of each page, ask if they have any questions about the page you just read
4) Repeat for every page until you come to the signature line
5) Evaluate capacity to consent
6) Complete **Capacity Assessment Checklist for IC form (CAC).** Required for all participants at time of MRI visit.
7) If participant has capacity, then:
    a. Before signing, ask the participant again if they have any questions about the procedure the risks or anything else about the study
8) If the participant is determined not to have capacity by your assessment
    a. Assure that participant assents to the procedure
    b. The Proxy (LAR) must cosign
9) If there are no further questions, please have the participant or Proxy (LAR) sign, date.
10) You as witness sign and date.
11) Make a copy of the consent and give to the participant or Proxy (LAR)

9.1.1. Assessing Capacity during the consenting process

It is important to assume that the participant has full capacity until proven otherwise. Please read the **Policy and Procedures for Assessing Capacity to Consent for Research** supplemental material in the appendix.

9.1.2. Summary of Process

1) Review Informed consent form with participant. Use the simplified study summary (**SSS document**). If he or she cannot participate with the consenting process, then they lack capacity and no further assessment is needed.
2) Question the participant about the study using the simplified study summary (**SSS**).
3) Decide whether or not the participant has capacity.
4) If the participant has capacity and agrees to participate, have them sign the consent form.
5) If the participant lacks capacity or has marginal capacity, ask for the participant's assent to participate.

6) If the participant assents, and the participant's proxy (legally authorized representative) consents, have both the participant and the proxy sign the consent form.
7) Document the process using the Capacity to Assessment Checklist for IC (**CAC**).
8) Save the CAC and consent forms as part of the research record.

9.1.3. MRI screening

Share copy of pre-screening form with MRI technician.
Address any concerns raised by the MRI technician.
This may require further research and rescheduling

9.1.4. Visit Form Completion

For the MRI visit, make sure to complete all required forms:

- **MSE, Section B**- SOL MRI Screening and Enrollment form, refer to QxQs for details. CDART form.
- **PMS**- Pre-MRI Screening form (paper form only). Make sure you sign the form with your name and designation (most will be "other", coordinator).
- **CAC**- Capacity to Assessment Checklist for IC
- **IC-** Informed consent/Assent is completed, and signed by participant, proxy (if required), and study coordinator (witness). *Provide a copy of the signed Informed Consent to participant and/or Proxy.*

10. MRI Data Transfer

10.1. Overview

The exact details of data transfer will be determined by the particulars of the MRI facility at each field center. In particular, data transfer will be substantially simplified if the facility can use HCHS/SOL Participant_ID as participant identifiers. This section outlines the process of data transfer under multiple conditions.

After the subject has been scanned, the images are to be reviewed for the presence of significant pathology that may require a health alert. The image data, along with the report will then be transferred to the UCD IDeA Laboratory in DICOM format, the only HIPAA complaint imaging format. This may be done electronically through a DICOM server or by mail on a magnetic storage device.

10.2. Clinical Evaluation of Images

All MR image sets are to be read by a licensed clinician with qualifications sufficient to identify brain pathology. This is generally a neuro-radiologist, but could be a general radiologist or even a neurologist with radiographic training. This report needs to accompany the image data for review by the UCD IDeA Laboratory.

10.3. *Data Transfer*

10.3.1. Image De-identification

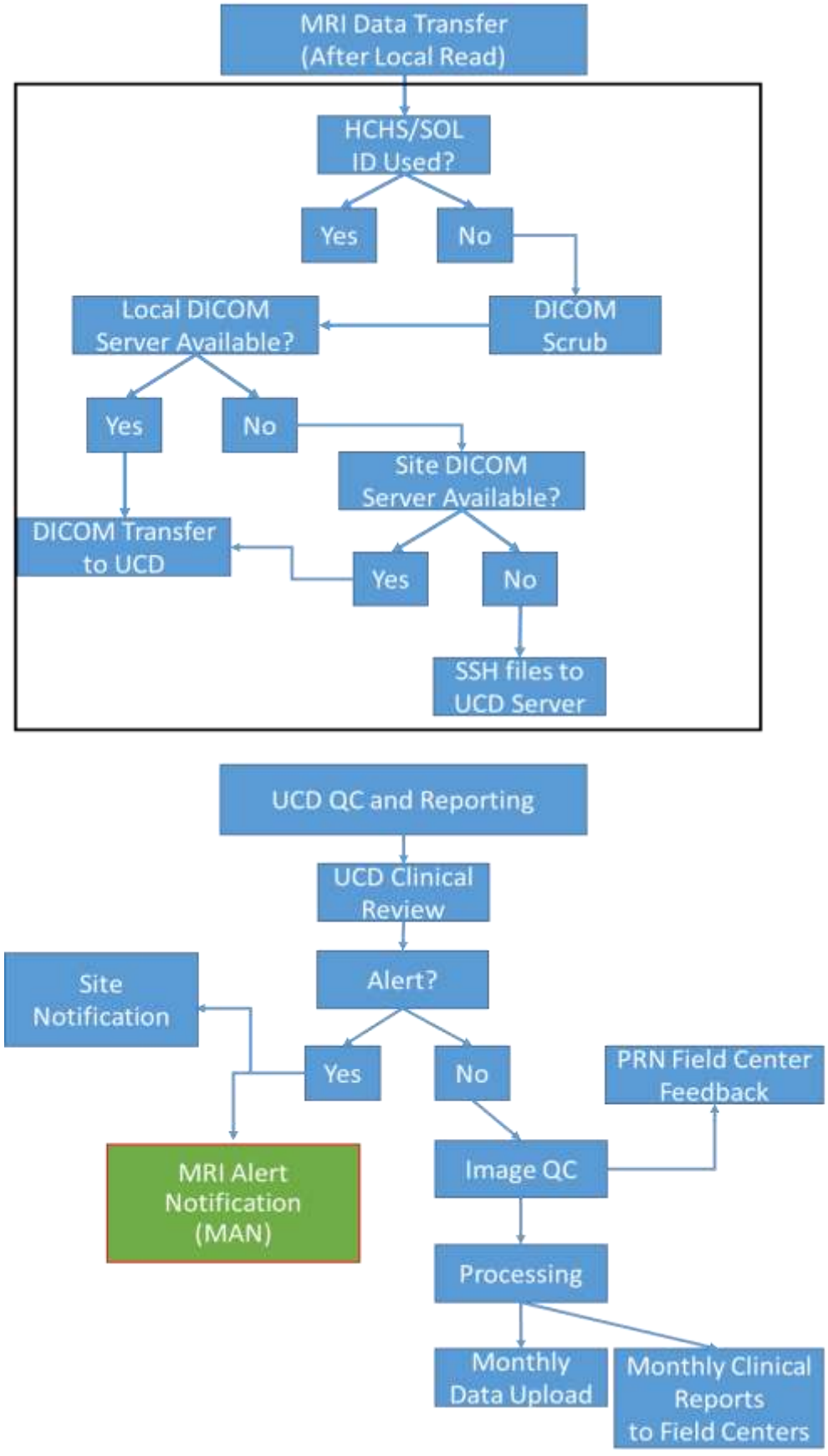
If the imaging site is able to perform clinical evaluation of the MRI using the HCHS/SOL ID, then no further de-identification is needed. If it not possible to use anonymous IDs, then de-identification will be necessary. This will require the use of additional software that will be made available to field centers as needed.

10.3.2. *Image Transfer*

Data transfer can be individualized for each field center.

1) DICOM Server: If your site has a DICOM server, we will only need the IP address. The transfer will be automatic.
2) Other electronic forms of transfer:
    a. SSH- this is a secure form of transfer generally acceptable to most sites with reasonable bandwidth. If your site wishes to use this approach, we will establish a secure transfer protocol with your site. MR research sites can often do this from an attached computer system. Alternatively, you may be able to transfer data directly from the MRI console to a local storage device that can then be used for subsequent transfer to the UCD IDeA Laboratory.
    b. Portable magnetic storage- it is also possible to “store-up” a number of DICOM image sets for monthly transfer to the UCD IDeA laboratory. This would be done by shipping of an electronic storage device between the field center and the UCD IDeA laboratory.

Flowchart 4: *Image Transfer and Safety Alert Flow Chart*



11. Safety Alerts

Participant safety is of paramount importance for this study. Like any epidemiological study, we are likely to find a few potentially serious abnormalities during routine research scanning. The need, therefore, for clinical review of all the images is essential. The ability of the reviewer to detect subtle brain abnormalities in the absence of clinical data is one limitation of this approach. A second limitation is the bias of various readers to report various degrees of common pathology. For example, white matter abnormalities (WMH), common to older subjects are often reported as microvascular pathology, when, in fact, there is clear evidence that the cause of WMH is quite complex and generally not clinically significant in most individuals. To control for clinical reader variability, each MRI report will be reviewed by an expert in clinical MRI at UC Davis. This second read will be used to identify individuals for whom a clinical alert is indicated. MRI reports identified by both the local read and confirmed by our central read will lead to a clinical safety alert. (see Flowchart 4, above).

11.1. Alert Process

Once an alert is identified, the PI (Dr. DeCarli) will contact the field center to share in the alert information. In addition, a formal safety letter using utilizing a structured reporting format (see attachment), will be sent to the field center to share with the participant. We also recommend that the field center review the participant's medical information prior to contacting the participant to place the finding in perspective with the participant's general health. For example, reporting a stroke may not be helpful to a participant for whom a clinical stroke already has been reported. Finally, Dr. DeCarli will work with the field centers to help identify local physicians who may assist the participants with further evaluation.

12. Reporting MRI Results to Participants

SOL-INCA-MRI will provide study results to the study participants that have value in the context of research. These reports are not intended for medical diagnosis or treatment. The participant reporting will be coordinated between UCDavis and the study field centers.

There will be 4 types of letters (see appendix for further information):

1) No definite abnormality (grossly normal findings)
1.5) Unclear medical significance
2) Potential medical concern that does not require immediate attention
3) Medical Alert, where immediate or urgent medical attention is highly recommended.

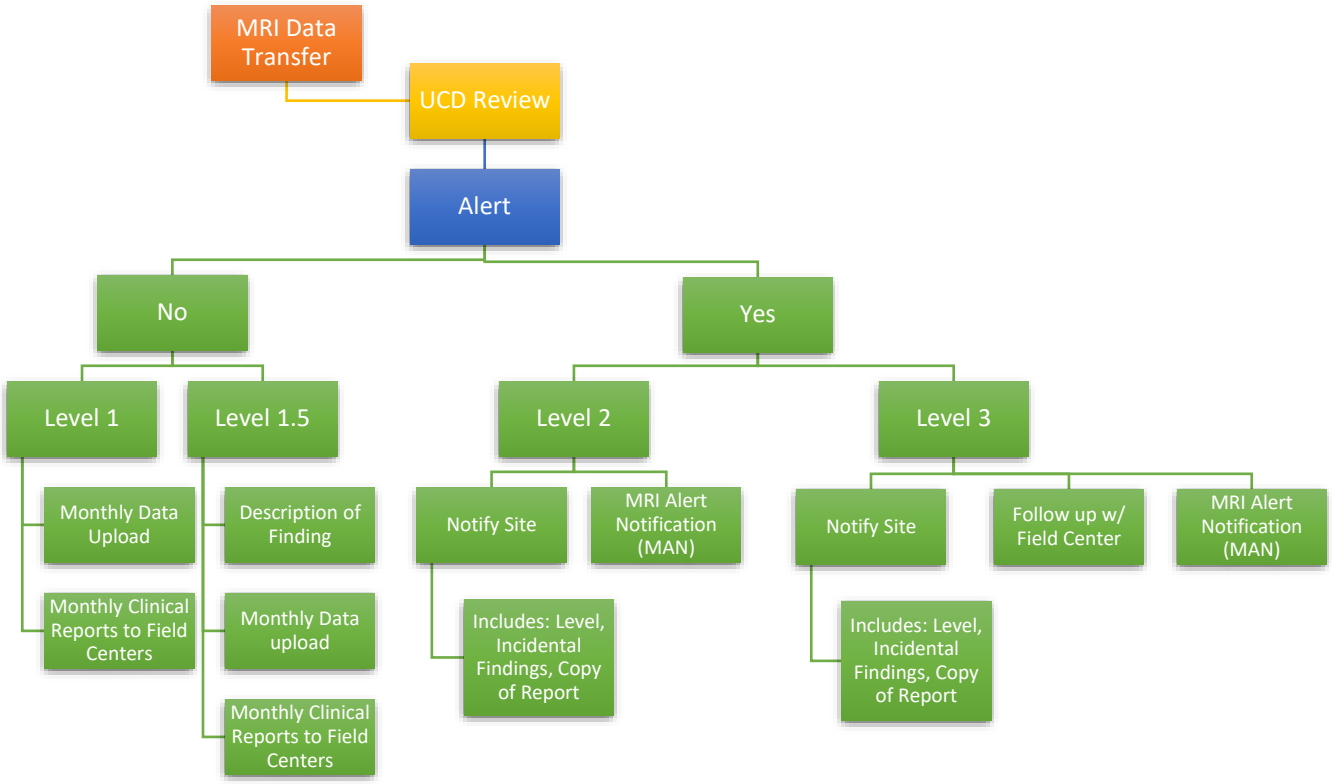
12.1. Reporting Process

Each field center is expected to the research MRI of each participant clinically evaluated by a qualified physician. These reports will be attached to the DICOM image file.

UC Davis will review each report to identify the letter type to go to each participant in response to their MRI visit on a monthly basis with the exception of medical alerts which will require notification within 1-2 business days.

Field Centers will send the appropriate letter to the participant.

Flowchart 5: *UCD MRI Findings Notification Process*



12.2. Exception for Medical Alerts:

It is expected that physicians at each center reviewing each MRI will contact the Center Coordinator immediately upon identification of any potentially serious abnormality identified on MRI. The Coordinator will then contact UC Davis regarding the finding. After consultation with UC Davis, the Coordinator will contact the Field Center PI as well as the participant to explain that an abnormality was detected. If the participant has an identified primary care provider, UC Davis will work with the Field Center to get a copy of the MRI and the clinical interpretation to the primary care provider. If there is no identified physician for follow-up UC Davis will work with the Field Center to identify an appropriate physician for follow-up.

A medical alert letter will also be sent to the participant from the Field Center and the Coordinating Center will be notified that a medical alert has occurred. The Coordinating center will also receive a notification of “unexpected findings” for those letters sent as a potential medical concern.

13. Adverse Events Reporting

In the event of an adverse event or an emergency, the SOL-INCA-MRI coordinator will follow procedures described in the HCHS/SOL Study MOP 2 (section 19), available in the study website (https://sites.cscc.unc.edu/hchs/protocols-and-manuals). There are 3 forms available in the SOL-INCA_MRI CDART group for the field centers to record these events.

13.1. Adverse events form list:

- MMA-SOL INCA MRI Minor Adverse Event Form
- SAE-SOL INCA MRI Serious Adverse Event Form
- UPM-SOL INCA MRI Unanticipated Problems

Appendix A: Forms and study Documents

SOL-MRI Phone Script- English

Hello, may I please speak to Mr./Mrs. _____?

Hi Mr./Mrs. _____. My name is _____ and I am calling from HCHS/SOL to tell you about a new study called SOL-INCA-MRI. May I take a few minutes to tell you about this new study?

→ **No**: May we call you another time?

- No: No problem. Thank you for your time. Please feel free to call us at [insert phone #] if you have any questions or would like to talk to someone from HCHS/SOL.
- Yes: When would be a good time to call you back? Thank you. We look forward to talking to you then. [Call is ended]

→ **Yes**: Thank you.

SOL-INCA-MRI is a study about differences in brain structure as part of the aging process or with declines in memory or thinking. The study includes a brain scan called a Magnetic Resonance Imaging (MRI) scan. Do you know about MRI studies? An MRI is a very safe, widely used medical test that will allow us to take pictures of your brain. We hope to discover how the brain differs with age and memory decline among Latinos. This has not been studied before.

If you agree, I would like to ask you some questions to see if the MRI scan is safe for you. [Proceed to screen for MRI exceptions on MRI safety form].

→ If participant answers no to all questions, proceed to schedule the appointment

→ If participant answers yes to any of the questions, explain to the participant that the project coordinator and a study investigator will need to review to make sure it is safe for the participant to complete the MRI and that we will be calling them back. [Call is ended]

If you decide to participate in SOL-INCA-MRI, you will be asked to go to [insert field site location] to consent to participate in the study and complete the MRI scan. Someone from HCHS/SOL will be with you at the medical center for your MRI scan.

For the MRI scan, you will lie down on a narrow bed which will then be placed in a tunnel that is 6 feet long by 30 inches wide and open at each end. You will need to lie there quietly for about one hour, during which time there will be a loud banging noise but you will be provided with ear plugs. You may feel warm during this procedure. The procedure is painless and there is no x-ray radiation exposure.

After you participate in this study, HCHS/SOL researchers will use the information you have provided to HCHS/SOL to learn about memory loss and thinking ability as part of the aging process. You will receive a report and will be contacted about the results only if clinically relevant problems are found. If you choose to participate, you will receive $50 to compensate you for your time and effort.

You may have costs related to travelling to and from the imaging center. We will provide you with transportation to the medical center if you need it. If you provide your own transportation we will reimburse you $50.

Your participation in SOL-INCA-MRI is voluntary. If you choose not to participate, your relationship with the HCHS/SOL study will not change. You will still be a HCHS/SOL participant and part of all HCHS/SOL activities.

Do you have any questions about the study?

Would you like to participate in SOL-MRI?

→ **No**: No problem. Could you please tell me the reason you are not interested in participating in SOL-MRI? Thank you for your time.

→ **Yes**: Thank you. When would you like to come for your study visit?

- After scheduling the appointment: We look forward to seeing you then. Please feel free to call us at [insert phone #] if you have any questions about your visit.

If you have any concerns about the participants ability to comprehend and consent to the study, please follow procedures outlined in HCHS/SOL MOP2 Section 4.5 “Proxy” to screen for proxy need.

SOL-MRI Phone Script- Spanish

HCHS\SOL INCA MRI Phone Script - Spanish

Guión telefónico de SOL-MRI

Hola, ¿puedo hablar con el Sr./la Sra. _____?

Hola Sr./Sra. _____. Mi nombre es _____ y llamo de HCHS/SOL para hablarle de un nuevo estudio llamado SOL-INCA-MRI. ¿Tiene unos minutos para que le explique de qué trata este nuevo estudio?

→ **No**: ¿Podría llamarle en otro momento?

- No: Está bien. Gracias por su tiempo. No dude en llamarnos al [insert phone #] si tiene preguntas o si le gustaría hablar con alguien de HCHS/SOL.
- Sí: ¿Cuándo sería un buen momento para llamarle otra vez? Gracias. Estaremos encantados de volver a hablar con usted. [Call is ended]

→ **Sí**: Gracias.

SOL-INCA-MRI es un estudio sobre las diferencias en la estructura cerebral que se producen como parte del proceso de envejecimiento o con la disminución de la memoria o de la actividad del pensar. El estudio incluye una exploración cerebral llamada una resonancia magnética (RM). ¿Conoce los estudios de RM? Una RM es una prueba médica muy segura que se utiliza con mucha frecuencia para tomar imágenes del cerebro. Esperamos descubrir cómo difiere el cerebro entre las personas con la edad y la disminución de la memoria en la población latina. Esto no se ha estudiado hasta ahora.

Si usted acepta, me gustaría hacerle algunas preguntas para ver si una RM es segura para usted. [Proceed to screen for MRI exceptions on MRI safety form].

→ Si el participante responde "no" a todas las preguntas, proceda a programar la cita.

→ Si el participante responde "sí" a alguna de las preguntas, explíquele que el coordinador del proyecto y un investigador del estudio necesitarán revisarlas para asegurar que la RM es segura para el participante y que le llamaremos otra vez. [Call is ended]

Si decide participar en el estudio SOL-INCA-MRI, le pediremos que vaya a [insert field site location] para dar su consentimiento para participar en el estudio y realizar la RM. Alguien de HCHS/SOL se reunirá con usted en el centro médico para su RM.

Para la RM, usted estará echado sobre una cama estrecha que se colocará en un túnel de unos 2 metros de largo y 76 cm de ancho, abierto en los dos extremos. Tendrá que permanecer echado ahí tranquilamente durante aproximadamente una hora, a lo largo de la cual escuchará un ruido fuerte, como de martilleo, pero se le darán tapones para los oídos. Es posible que sienta calor

durante este procedimiento. El procedimiento es indoloro y no hay exposición a los rayos X.

Después de participar en este estudio, los investigadores de HCHS/SOL utilizarán la información que ha proporcionado a HCHS/SOL para aprender nuevas cosas sobre la pérdida de la memoria y sobre la capacidad de pensar como parte del proceso de envejecimiento. Recibirá un informe y nos comunicaremos con usted para informarle de los resultados solo si se descubren problemas clínicamente relevantes. Si elige participar, recibirá $50 como compensación por su tiempo y esfuerzo.

Es posible que tenga costos relacionados con el desplazamiento al centro de estudios de imágenes. Le proporcionaremos transporte al centro médico si lo necesita. Si usted viene por sus propios medios, le reembolsaremos $50.

Su participación en SOL-INCA-MRI es voluntaria. Si elige no participar, su relación con el estudio HCHS/SOL no cambiará. Seguirá participando en el estudio HCHS/SOL y en todas las actividades del HCHS/SOL.

¿Tiene alguna pregunta sobre el estudio?

¿Le gustaría participar en SOL-MRI?

→ **No**: Está bien. ¿Le importaría decirme la razón por la que no está interesado en participar en SOL-MRI? Gracias por su tiempo.

→ **Sí**: Gracias. ¿Cuándo le gustaría venir para su visita del estudio?

- Después de programar la cita: Esperamos con impaciencia su visita. No dude en llamarnos al [insert phone #] si tiene preguntas sobre su visita.

PMS- Pre-MRI Screening Form (paper only)

HCHS/SOL INCA MRI Pre-MRI Screening Form

PMS ver. 11/29/2017

ADMINISTRATIVE INFORMATION

Date: ☐☐/☐☐/☐☐☐☐ (mm/dd/yyy)

DOB: ☐☐/☐☐/☐☐☐☐ (mm/dd/yyy) Staff ID: ☐☐☐

Height: _____ Weight: _____

Place PARTICIPANT information label here
Containing full name, HCHS ParticipantID
Site PI

***Instructions**: Participants with implants must be approved by the MRI safety officer before a MRI scan may be performed without exception.*

1. Have you ever had surgery or similar invasive procedure in which medical devices may have been implanted? No ☐ Yes ☐
   If yes, please list:

Type of surgery	Date (mm/dd/yyyy)
_____	☐☐/☐☐/☐☐☐☐
_____	☐☐/☐☐/☐☐☐☐

2. Have you had any previous MRI imaging studies? No ☐ Yes ☐
   If yes, please list:

Body Part	Date (mm/dd/yyyy)	Facility Location
_____	☐☐/☐☐/☐☐☐☐	_____
_____	☐☐/☐☐/☐☐☐☐	_____
_____	☐☐/☐☐/☐☐☐☐	_____

3. Have you ever worked with metal (grinding, fabricating, etc.) or ever had an injury to the eye involving a metallic object (e.g., metallic slivers, shavings, shrapnel, foreign body)? No ☐ Yes ☐
   If yes, please describe: _____

For female participants only:

4. Are you pregnant, or is there a possibility that you are pregnant? (if unsure, please notify MRI operator or Principal Investigator) No ☐ Yes ☐
5. Are you breastfeeding? No ☐ Yes ☐
6. Date of last menstrual period: ☐☐/☐☐/☐☐☐☐ (mm/dd/yyyy)
7. Are you taking any type of fertility medication or having fertility treatments? No ☐ Yes ☐
8. Are you taking oral contraceptives or receiving hormone treatment? No ☐ Yes ☐

9. Are you currently taking or have you recently taken any medication? No ☐ Yes ☐
   If yes, please list: _____
10. Do you have anemia or any diseases that affect your blood, or a history of renal disease? No ☐ Yes ☐
    If yes, please list: _____
11. Do you have a history of seizure disorder or epilepsy? No ☐ Yes ☐
12. Do you have any drug allergies? No ☐ Yes ☐
    If yes, please list: _____
13. Have you ever had asthma, allergic reaction, respiratory disease, or any type of reaction to a contrast medium or dye used for an MRI or CT examination? No ☐ Yes ☐
    If yes, please describe: _____

PMS-MRI Screening form-2017-11-29.docx Page | 1 of 2

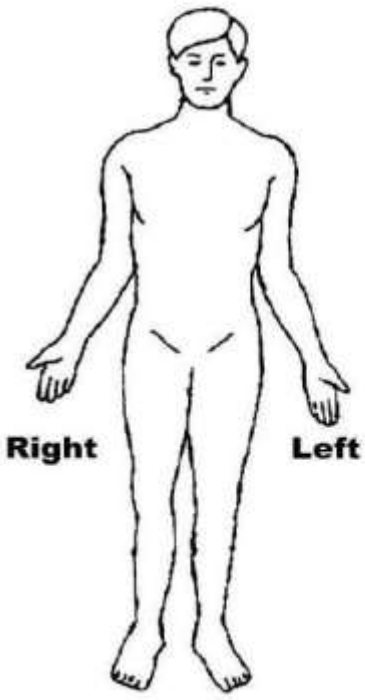
HCHS/SOL INCA Pre-MRI Screening Form

PARTICIPANTS WITH IMPLANTS MUST BE APPROVED BY THE MRI SAFETY OFFICER BEFORE A MRI SCAN MAY BE PERFORMED WITHOUT EXCEPTION.

Some of the following items may be hazardous to your safety and some can interfere with the MRI examination. Please check the correct answer for each of the following. Do you have any of the following:

Yes	No	Implant Location
☐	☐	Dental Hardware (e.g. metal crowns, braces, retainers)
☐	☐	Cardiac pacemaker
☐	☐	Implanted cardiac defibrillator
☐	☐	Aneurysm clip(s)
☐	☐	Carotid artery vascular clamp
☐	☐	Neurostimulator
☐	☐	Insulin or infusion pump
☐	☐	Implanted drug infusion device
☐	☐	Bone growth/fusion stimulator
☐	☐	Cochlear, otologic, or implant
☐	☐	Any type of prosthesis (eye, penile, etc.)
☐	☐	Heart valve prosthesis
☐	☐	Artificial limb or joint
☐	☐	Electrodes (on body, head, or brain)
☐	☐	Intravascular stents, filters, or coils
☐	☐	Shunt (spinal or intraventricular)
☐	☐	Vascular access port and/or catheter
☐	☐	Swan-Ganz catheter
☐	☐	Any implant held in place by a magnet
☐	☐	Transdermal Patch Delivery System (e.g. Nicotine.) (Remove before MRI)
☐	☐	IUD or diaphragm
☐	☐	Tattooed makeup (eyeliner, lips, etc.)
☐	☐	Body piercing(s) (Remove before MRI)
☐	☐	Any metal fragments (including bullets, shrapnel)
☐	☐	Internal pacing wires
☐	☐	Aortic clip
☐	☐	Metal or wire mesh implants
☐	☐	Wire sutures or surgical staples
☐	☐	Harrington rods (spine)
☐	☐	Metal rods in bones
☐	☐	Joint replacement: _____
☐	☐	Bone/joint in, screw, nail, wire, plate
☐	☐	Hearing aid (Remove before MRI)
☐	☐	Dentures (Remove before MRI)
☐	☐	Breathing disorder
☐	☐	Movement disorder
☐	☐	Claustrophobia
☐	☐	Anxiety
☐	☐	Other: _____

Please mark on the figure below, the location of any implant or metal inside of or on your body.



Before your MRI, please **remove all metallic objects** including keys, hairpins, barrettes, jewelry, watch, safety pins, paperclips, money clip, credit cards, coins, pens, belt, metal buttons, pocketknife, & clothing with metal in the material.

NOTE: YOU ARE REQUIRED TO WEAR EARPLUGS OR EARPHONES DURING THE MRI EXAMINATION.

_____ Date: ☐☐/☐☐/☐☐☐☐
Signature/Printed name of Person Completing Form Month Day Year

Form completed by: ☐ Participant ☐ Relative: _____
Name & relationship to participant

☐ Physician or other: _____
Name & relationship to participant

IRI- Implant Required Information form for MRI Safety Clearance (paper only)

HCHS/SOL INCA MRI
Implant Required Information Form
IRI ver. 1/19/2018

ADMINISTRATIVE INFORMATION

Date: ☐☐/☐☐/☐☐☐☐ (mm/dd/yyyy) Staff ID: ☐☐☐

Place PARTICIPANT information label here
Containing full name, HCHS ParticipantID
Site PI

***Instructions**: Participants with implants must be approved by the MRI safety officer before a MRI scan may be performed without exception. Provide required information on implants in this form*

Participant Information Required for MRI Safety Clearance

	Implant 1	Implant 2	Implant 3
1. Type of Implant:			
2. Location of Implant:			
3. Date of implantation:	☐☐/☐☐/☐☐☐☐	☐☐/☐☐/☐☐☐☐	☐☐/☐☐/☐☐☐☐
4. Manufacturer:			

_____/_____ Date: ☐☐/☐☐/☐☐☐☐
Signature/Printed name of Person Completing Form — Month Day Year

Implant Exception List

Implant Exception List

ADVISED:

While it is ultimately up to the Imaging center where the MRI will be taken to be the final approving authority whether a participant and their implant is safe to be scanned, this is a list of implants that have generally been approved so that the participant can be scanned. Also, the type of implant used (make, model), manufacturer, and when it was placed are the subjective details and may vary from implant to implant. Always be sure to verify the implant's contraindications by conducting thorough research of the implant in question with the strength of the MRI machine that will be used.

1. Lens implant such as those for cataracts
2. Tissue markers
3. Knee replacements
4. Shoulder surgery/repair such as for a torn rotator cuff
5. Screws in the feet, such as for fractured/repaired bones
6. Hernia repair using a mesh
7. Hip replacement
8. Dental implants such as crowns and abutments, however these can cause artifact in the image quality of the MRI and distort the brain image. Any metal dental work will make the MRI quality very distorted.
9. Tympanostomy tube
10. Breast implants

MSE – Sol-INCA-MRI Screening and Enrollment Form (CDART)

HCHS\SOL INCA MRI Screening and Enrollment Form
MSE

ID NUMBER: ☐☐☐☐☐☐☐☐ FORM CODE: MSE VERSION: A 1/24/2018 Contact Occasion ☐0 ☐2 SEQ # ☐0 ☐1

Instructions: ***Complete*** *this form for all contacted participants. Complete section A at time of phone contact, and section B at time of MRI visit. Refer to QxQ for additional information.*

A. PHONE CONTACT

1. Contact Date (mm/dd/yyyy): ☐☐/☐☐/☐☐☐☐ 2. Staff ID: ☐☐☐
3. Phone Call Screening information? ☐
   0= Unable to contact for screening or enrollment [**End form, call back]**
   1= Yes, contacted participant and screened
   2= Callback, participant was contacted but screen not completed [**End form, call back]**

A1. Call Pre-MRI –Screening

4. Pre-Screen completed? ☐ 0= No 1= Yes **[Go To 5]**
   4a. If No, reason ☐ 1= Need proxy [*Schedule Call back*, **End]**
   ☐ 2= Medical information incomplete [*Schedule Call back*, **End]**
5. **Absolute** contradictions found in prescreening? ☐ 0= No 1= Yes **[Set Q7=1, End]**
6. **Possible** contradictions found in prescreening? ☐ 0= No 1= Yes [*Follow protocol, confirm eligibility*]

A2. Call Pre Screen Result

7. Enrollment Status in Ancillary Study ☐ 1= Ineligible **[End]**
   2= Eligible but refused to participate [**End]**
   3= Eligible and agreed to participate
8. MRI schedule Date ☐☐/☐☐/☐☐☐☐ (mm/dd/yyyy)

B. MRI Visit

B1. Informed Consent Tracking

9. Consented by: ☐ 1= Proxy 2= Participant 10. Consenting Staff ID: ☐☐☐
11. Consent date: ☐☐/☐☐/☐☐☐☐ (mm/dd/yyyy)
12. Consent/assent Status ☐ 0= Refused to participate [**End]** 1= Agreed to participate

B2. MRI Technician Review

13. Did MRI Technician review contradictions? ☐ 0= No **[Go To 15]** 1= Yes
14. MRI eligibility approved by Technician? ☐ 0= No 1= Yes

B3. MRI Status

15. MRI exam was... ☐ 0= Not performed 1= Performed [**Go To 16**]
    15a. If not performed, Specify: _____ [**END**]
16. MRI exam Date ☐☐/☐☐/☐☐☐☐ (mm/dd/yyyy)

CAC- Capacity Assessment Form (paper only)

HCHS/SOL INCA MRI Capacity Assessment Checklist

CAC ver. 11/28/2017

ADMINISTRATIVE INFORMATION

Date of Consent: ☐☐/☐☐/☐☐☐☐ (mm/dd/yyyy)

Time: ☐☐:☐☐ am / pm Staff ID: ☐☐☐

Place PARTICIPANT information label here
Containing full name, HCHS ParticipantID

Instructions: *This paper form is to be administered to the participant in person after reading the IC, at the time of MRI visit. If participant is not able to consent, the alternate respondent (proxy) must complete Surrogate Maker form to complete Informed Consent for the participant.*

A. Consent Dialoque Name of *alternate respondent (proxy)*: _____

1. Was protocol presented to/discussed with participant? No ☐ 1=Yes ☐ Other: _____
2. Was protocol presented to/discussed with participant's alternate respondent (proxy)?
   No ☐ Yes ☐ Other: _____

B. CONSENT ABILITIES

3. Did participant *make a choice* to participate in SOL INCA MRI study? No ☐ Yes ☐ Marginal ☐
   Choice: Participate ☐ Not Participate ☐ Defer Decision ☐ Decision Unclear ☐ Other ☐
   Briefly explain _____
4. Did participant show *understanding* of the research protocol and its elements, including risks/benefits of participation?
   No ☐ Yes ☐ Marginal ☐ Briefly explain _____
5. Did participant *show reasoning/provide rational reasons* for participation/non-participation in the research protocol? No ☐ Yes ☐ Marginal ☐ Briefly explain _____
6. Did participant show an *appreciation of the personal risks/benefits* of participation/non-participation in the research protocol? No ☐ Yes ☐ Marginal ☐ Briefly explain _____

C. CAPACITY /INFORMED CONSENT/ASSENT

7. Was participant competent to consent to participation/non-participation in research protocol?
   No ☐ Yes ☐ Other ☐ Briefly explain: _____
8. Was informed consent for research participation obtained from the participant?
   No ☐ Yes ☐ Other ☐ Briefly explain: _____
9. If participant unable to consent, was informed consent for research participation obtained from *alternate respondent (proxy)*? No ☐ Yes ☐ Other ☐ Briefly explain: _____
10. If participant unable to consent and *alternate respondent (proxy)* approved participation, did participant show ***assent*** to participation? No ☐ Yes ☐ N/A ☐ Unclear ☐ Other ☐ _____
    Briefly explain: _____

Completed by: _____ [Signature] ***Date:*** ☐☐/☐☐/☐☐☐☐ (mm/dd/yyyy)

Appendix B: Research Capacity Policy

Policy and Procedures for Assessing Capacity
To Consent for Research

I. Policy

A. When to assess capacity for research consent

All persons having reached the age of majority are presumed to have capacity to give informed consent to research. In the absence of any indication to the contrary, such capacity can be assumed without further evaluation or documentation.

Indications of potentially diminished capacity are:

1. A diagnosis of dementia or cognitive impairment
2. Presenting for an evaluation of dementia
3. A report, in medical records or from a family member or person well acquainted with the subject, that the subject has symptoms of cognitive impairment or dementia
4. An abnormal degree of confusion, forgetfulness, or difficulties in communication that is observed in the course of interacting with the subject
5. Psychotic symptoms, bizarre or abnormal behavior exhibited by the subject

When there is an indication that capacity for consent may be diminished the subject's capacity to consent should be evaluated using the standards and procedures described below and the results should be recorded on the Capacity Assessment Checklist (CAC).

B. Standards for capacity

Even when there is an indication of diminished capacity, the presumption of capacity remains. As indicated on the CAC, there are four different standards that might be used to assess capacity[6]. They are listed a rough order of ascendancy. *It is the policy of the UC Davis Alzheimer's Disease Center to accept a subject as competent to consent to research only when the person is judged capable with regard to all 4 standards[1].*

Standard 1. Did the participant "make a choice"?
"This standard focuses on the presence or absence of a decision, and not on the quality of the decision"[6].

This is simply a question as to whether the subject can evidence a choice. If the subject offers a consistent choice about participating in the study this standard is met. If the subject's choice is ambiguous, either because it is inconsistent or unclearly demonstrated, then the standard is failed.

Standard 2. Did the participant show "understanding"?
"This standard requires memory for words, phrases, ideas, and sequences of information, and also comprehension of the fundamental meaning of information about treatment."[6]

A subject need not demonstrate complete or comprehensive understanding of the study in order to meet this standard. However, verbatim recitation of fact without evidence of comprehension is not sufficient either. Consider whether or not the potential subject grasps sufficient information to form the basis for a reasoned decision. If the subject comprehends and remembers (even with assistance) **a)** that participation is voluntary, **b)** the major procedures, **c)** main risks, and **d)** benefits, then this standard is met. Failure on any element (**a-d**) means this standard is failed.

Standard 3. Did the participant show "reasoning/rational reasons"?
"This standard tests the capacity to use logical processes to compare the benefits and risks of various treatment options and weigh this information to reach a decision. "[6]

The core of this standard is the ability to logically compare risks and benefits in order to reach a rational decision regarding participation. To meet this standard the subject needs to demonstrate the ability to consider both risk and benefit in relation to each other and use the information in a logical manner to come to a decision.

Standard 4. Did the participant show an "appreciation" of the personal risks/benefits of the study?
"This standard emphasizes the patients' awareness of the consequences of a treatment decision: its emotional impact, rational requirements and future consequences"[6].

Appreciation seems to imply something more than an intellectual understanding, and incorporates an affective judgment of the impact of study participation in the context of the particular individual in his or her particular situation. Meeting standard 3 would seem to generally suffice for meeting this standard as long as the subject has a realistic understanding of his or her circumstances.

C. Assent:
Subjects who are not capable of consent to research still must assent to research in order to take part. Assent implies willingness or, minimally, lack of objection to taking part. It does not imply understanding. An interpretable statement from the subject regarding assent must be taken as valid regardless of the subject's level of confusion or dementia. Thus, a statement such as "whatever my daughter says is OK with me" is fine. The demonstration of assent need not be verbal. Passive lack of objection is acceptable in an alert participant. Indications of distress such as crying or attempts to escape the situation should be taken as refusals to assent to the study.

II. Procedures

A. Who should assess capacity?
The evaluation of capacity should be done by trained research personnel at time of MRI visit. Capacity must be assessed based on direct assessment with the subject; the report of others will not suffice

B. Methods
Capacity judgments should be made during the informed consent process when, in the research personnel's opinion, the participant has failed in one or more standards. When there is any doubt, capacity should be specifically assessed in the course of attempting to obtain informed consent.

The routine assessment of capacity should begin with the research staff reviewing the informed consent form with the subject in the normal manner used to obtain consent. The simplified study summary, approved by the IRB, should be used as an aide, to emphasize and remind subjects of major points. When the research staff has reviewed the study, he or she should ask the subject to explain the major elements of the study. Those elements are **a)** this is a research study (not routine treatment), **b)** participation is voluntary, **c)** study procedures, **d)** risks, and **e)** benefits. In addition, as described in the standards above, the subject needs to make a rational choice based on an appreciation of the facts. *The subject can use the simplified study summary to answer the questions.* Based on the subject's responses the research staff should then make a final judgment about capacity for consent.

The consent process and capacity assessment should be recorded using the Capacity Assessment Checklist (CAC). Although the CAC requires that the evaluator make a decision with regard to each standard, there is no need to methodically evaluate each standard in every case. The evaluator may focus on any or all of them, as seems appropriate given what is known about the potential subject. Thus, it may quickly be clear that a severely demented participant cannot meet standard 2. The evaluator may then move directly to the issue of assent. Or, it may be clear that a subject with mild AD (Alzheimer's Disease) meets standards 1-3, and it is only 4 that is at issue. The reasons for your decision on each item should be documented, however briefly, using the CAC.

C. Suggested questions:

The sequence of questions listed below are provided for illustrative purposes, and to show how particular questions may be used to assess capacity with regard to particular standards for capacity. They pick up at the point that review of the consent form has been completed. This is not a script; clinical judgment remains the best guide for what to ask.

1. "Now I'd like to ask you some questions about study. Are we offering you your usual medical care, or are we asking you to be in a research study?"
   [*Ahora me gustaría preguntarle una pregunta sobre el estudio. ¿Le estamos ofreciendo cuidado médico de rutina, o le estamos preguntado si quiere participar en un estudio de investigación?]*

2. "Must you take part in this study, or is it OK to say 'no'?"
   [¿Está usted obligado a participar o puede negarse a participar?]

3. "Tell me the main things that you would do in this study."
   [¿Me puede decir que es lo más importante que hará en este estudio?]

4. "Tell me the main risks of this study."
   [*Dígame cual es el principal riesgo de participar en este estudio]*

5. "Tell me the benefits of this study."
   [*Dígame cuales son los beneficios de participar en este estudio]*

6. "Will this study mainly help you or others?"
   [¿Este estudio, le ayudará principalmente a usted o a otras personas?*]*

7. "Considering the risks and benefits we have discussed; would you like to take part in this study?"
   [Tomando en consideración los riesgos y beneficios que hemos discutido para este estudio, ¿le gustaría participar en este estudio?*]*

8. "Why?"
   [*¿Por qué?]*

D. Relating questions to standards

The suggested questions are repeated below, annotated to as to illustrate their relationship to the standards for capacity. *[Questions 1-6 pertain to standard 2 (Understanding). The subject need not know every detail in order to meet this standard, but neither does a rote recitation or reading of fact without comprehension suffice. If the subject does not understand 1 or more of these key elements about the study, standard 2 is failed.]*

1. "Now I'd like to ask you some questions about study. Are we offering you your usual medical care, or are we asking you to be in a research study?"

2. "Must you take part in this study, or is it OK to say 'no'?"

3. "Tell me the main things that you would do in this study"

4. "Tell me the main risks of this study"

5. "Tell me the benefits of this study."

6. "Will this study mainly help you or others?"

7. "Considering the risks and benefits we have discussed, would you like to take part in this study?" *[failure to respond in a consistent, unambiguous manner indicates that standard 1 is failed]*

8. "Why?" *[This is the single most important question for assessing standards 3 (Rational Reasons) and 4 (Appreciation).*

With regard to standard 3, if the answer indicates a balancing of risk and benefit, even if vague, this standard can be met. For example, "I'd like to help and there's not much to lose" might be sufficient, especially if other questions had indicated you that the subject had a reasonable idea of what the risks were. An answer that refers only to benefit should be questioned by pointing out there are risks. For example, if someone said "It seems like a good idea" you might ask "but what about the risks of the study?". If they can in response say something sensible that acknowledges the study's risks, this standard would be met. If they appeared not to understand that any risks were attached to the study, this standard would not be met. The greater the risks, the more specific must be the subject's consideration of those risks. In a pharmaceutical trial subjects must acknowledge that the extent of risk is not entirely defined and that there is some potential for serious adverse events.

Standard 4 is usually met if standard 3 is met. The key difference is that the appreciation standard requires relating the facts to one's own situation; thus, participants with an impaired sense of reality might fail standard 4 while meeting standard 3. If a subject is delusional or anosagnostic then they may be unable to relate information that they correctly understand to their own personal situation. Thus, for example, an amnestic participant may deny memory loss and so believe that although a study would be good for someone with memory loss that it is not a good idea for him. Or, for example, a participant might recognize that a drug carried special risk for people with diabetes, but might fail to comprehend that she is diabetic. Under such circumstances these participants might be fail only standard 4.]

D. Documentation

Record your actions and decisions using the CAC. This goes to the participant's chart, where it becomes part of his or her research records.

E. Summary of Process

1. Review Informed consent form with participant. Use the simplified study summary. If he or she cannot participate, then they lack capacity and no further assessment is needed.
2. Question the subject about the study using the simplified study summary.
3. Based on that, decide whether or not the subject has capacity.
4. If the subject has capacity and agrees to the study, have them sign the consent form.
5. If the subject lacks capacity or has marginal capacity, ask for the participant's assent to participate. [Marginal capacity indicates that the participant understands the basic details of the procedure, but may not be able to relate them back to you. This primarily for people who have memory loss, but are otherwise intact.]
6. If the subject assents, and the subject's representative (proxy/designated respondent) consents, have both the subject and the representative sign the consent form.
7. Document the process using the CAC.
8. CAC and consent forms go to the chart.

III. References

1. Bioethics Interest Group *Expert Panel Report to the National Institutes of Health (NIH) Research Involving Individuals with Questionable Capacity to Consent: Ethical Issues and Practical Considerations for Institutional Review Boards (IRBs)* http://www.nih.gov/sigs/bioethics/reports/exec_sum.htm
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IV. Attachments

1. Template for simplified study summary
2. Capacity Assessment Checklist (CAC)
3. Study summary for "The Reliability of MRI Measurements Made with Two Different Scanners."